PRODUCT BROCHURE

SPECIALIZED CLINICAL NUTRITION
MEDIFOOD®

Index

Abbreviations and acronyms 07

Amino acid metabolism disorders

Phenylketonuria (PKU) 08

Afenil® Uno 10
Afenil® 2 12
Afenil® Gel 14
Afenil® Medi 15 16
Afenil® Squash 15 18
Afenil® Micro 3H 20
NeutrAfenil® Micro R 22
Afenil® Buddy 24
Afenil® Lime 26
Afenil® GMP Up bars coconut 28
Afenil® GMP Up bars cream mou 30
Afenil® GMP Up shake 32
L-tyrosina 34
Protein and amino acid requirements 36

Type 1 Tyrosinemia 38

TYR Medi 2 40
TYR Medigel 42
TYR Medi 15 44
TYR Medimicro 3H 46
Protein and amino acid requirements 48

Glutaric Aciduria type 1 (GA) 50

GA Medi 2 52
GA Medigel 54
GA Medi 15 56
GA Medimicro 3H 58
Protein and amino acid requirements 60

Leucinosis or Maple syrup urine disease (MSUD) 62

MSUD Medi 2 64
MSUD Medigel 66
MSUD Medi 15 68
MSUD Medimicro 3H 70
Protein and amino acid requirements 72

Classical Homocystinuria (HOM) 74

HOM Medi 2 78
HOM Medigel 80
HOM Medi 15 82
HOM Medimicro 3H 84
Protein and amino acid requirements 86

Urea Cycle Disorders (UCD) 88

UCD Medi 2 92
UCD Medigel 94
UCD Medi 15 96
UCD Medimicro 3H 98
Protein and amino acid requirements 100

Isovaleric acidemia (IVA) 102

IVA Medi 2 104
IVA Medigel 106
IVA Medi 15 108
IVA Medimicro 3H 110
Protein and amino acid requirements 112

Methylmalonic acidemia (MMA) and propionic acidemia (PA) 114

MMA/PA Medi 2 118
MMA/PA Medigel 120
MMA/PA Medi 15 122
MMA/PA Medimicro 3H 124
Protein and amino acid requirements 126

Protein-free products 128

Milco® 130
Sineamin® 132

Special pediatric products 135

NEC® 136
Medigel 138
Rubrojunior 140
MCT Oil 142
Chiloil 144
DHA Medi Oil 146

AF (Antisecretory Factor) 148

SPC Flakes 150
Salovum 152

Useful tables and conversion factors 154

Abbreviations and acronyms

PKU	Phenylketonuria
HPA	Hyperphenylalaninemia
PAH	Phenylalanine hydroxylase
DBS	Dried blood spot
BMI	Body mass index
WHO	World Health Organization
PHE	Phenylalanine
TYR	Tyrosine
DHA	Docosahexaenoic acid
MSUD	Leucinosis or Maple syrup urine disease
EFSA	European food safety authority
CoA	AcetilCoA
IVA	Isovaleric acidemia
GA1	Glutaric aciduria type 1
FAH	Fumarylacetoacetate hydrolase
TYR1	Tyrosinemia type 1
MMA	Methylmalonic aciduria/acidemia
PA	Propionic aciduria/acidemia
MCM	Methylmalonyl-CoA mutase
PCC	Propionyl-CoA carboxylase
GFR	Glomerular filtration rate
HOM	Classical Homocystinuria
UCD	Urea Cycle Disorders

Hyperphenylalaninemia (HPA) / phenylketonuria (PKU)

HPA/PKU is an inborn error of metabolism due to deficiency in the enzyme phenylalanine-hydroxylase that affects the metabolism of the amino acid phenylalanine.

If not diagnosed and treated early, the pathology causes progressive and irreversible cerebral damage with onset of psychomotor and mental retardation, albeit with different phenotypic manifestations depending on the type of enzymatic mutation (> 600 possible forms).

The key treatment to prevent the above-mentioned clinical condition is dietary management with low and controlled intake of phenylalanine, based on individual tolerance, through the intake of protein-free products and protein substitutes devoid of phenylalanine, for the purpose of ensuring adequate protein requirements. Protein substitutes are further integrated with micronutrients and essential amino acids.

This dietary therapy must be scrupulously observed throughout one's lifetime and without interruption to ensure that adequate psychomotor development is achieved.

Around 30% of patients with a certain genetic mutation respond to pharmacological treatment with tetrahydrobiopterin (BH4), the only medicinal product used for this pathology to date.

Disease severity is determined by the concentration of phenylalanine in the blood: if it is below 360 μmol/L, no therapeutic intervention is necessary. For higher values, the treatment must be lifelong. Target concentrations to achieve with treatment are as follows: below 350 μmol/L for patients up to 12 years of age, and below 60 μmol/L for patients above 12 years of age (1).

For women who are trying to conceive and during pregnancy (maternal PKU), phenylalanine blood levels must be below 360 μmol/L. High phenylalanine levels are teratogenic for the fetus (1).

» ENZYME	Phenylalanine hydroxylase (PAH) deficiency (12q22-q24.2)
» TRANSMISSION	Autosomal recessive
» INCIDENCE	1: 10,000 in Europe (2)
» OMIM	261200
» TREATMENT	Dietary therapy / pharmacological therapy (if applicable)

Phenylketonuria (PKU), the most frequent of inborn errors of metabolism, now has European guidelines, the first ever published (1). The guidelines indicate minimal management and follow-up requirements based on age, compliance to the treatment, and clinical status. Indeed, nutritional, clinical, and biochemical follow-up is necessary for all patients, irrespective of therapy. The message from the guidelines is that a patient with phenylketonuria levels within therapeutic ranges can have an absolutely normal and rewarding life.

Guidelines are freely accessible at:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5639803/pdf/13023_2017_Article_685.pdf

References:

1. *Van Wegberg, A. M. J. et al. The Complete European Guidelines on Phenylketonuria: Diagnosis and Treatment. Orphanet Journal of Rare Diseases 12 (2017): 162. PMC. Web. 6 Mar. 2018.*
2. *van Spronsen, F. J et al. Key European guidelines for the diagnosis and management of patients with phenylketonuria. he Lancet Diabetes & Endocrinology, 2017, Volume 5, Issue 9, 743 - 756.*

afenil® UNO

1 per 500 ml
6 per 200 ml

PKU

0-12 months

Ready to use phenylalanine-free drink with long-chain fatty acids, vitamins, and minerals, indicated for dietary management of hyperphenylalaninemia, including newborn phenylketonuria, from birth to the first year of age.

» INDICATIONS

Ready to use phenylalanine-free drink, with long-chain fatty acids, indicated for the dietary management of newborns suffering from hyperphenylalaninemia including phenylketonuria, from birth up to 12 months of age, or as supplement beyond one year of age.

» DOSAGE AND ADMINISTRATION

According to the physician's prescription, taking into account age, body weight, clinical condition and nutritional needs of the subject.

» INSTRUCTIONS FOR USE

Shake the bottle well. Pour the required amount of food product into the baby bottle, heat in a water bath or a microwave oven to the desired temperature (37°C), and administer. After use, close the bottle well. Refrigerate and use within the second day.
The product is ready for use and should not be further diluted, unless specifically indicated by a pediatrician.

» STORAGE CONDITIONS

Store the product in a dry place at a temperature between 5°C and 25°C, away from light and sources of direct heat. The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS

Afenil® Uno must only be taken under medical supervision by individuals with known hyperphenylalaninemia including phenylketonuria. Afenil® Uno can be used as the sole food source. The product can result in health risks if consumed by individuals who do not have the specific disorder for which it is indicated. Keep out of the reach of children. Do not use by parenteral administration.

NUTRITIONAL INFORMATION

food for special medical purposes

	per 100 ml
Energy kJ/kcal	287/68
Fats	3.20 g
of which saturated fatty acids	1.4 g
of which Linolic acid (18:2)	0.40 g
of which Linolenic acid (18:3)	0.04 g
of which arachidonic acid	0.03 g
of which docosahexaenoic acid (DHA)	0.02 g
Carbohydrates	7.9 g
of which sugars	4.2 g
Fiber	0 g
Protein equivalent	2.0 g
Salt	0.06 g
VITAMINS	
Biotin	1.7 μg
Folic acid	8 μg
Niacin	900 μg
Pantothenic acid (Vitamin B5)	400 μg
Riboflavin (Vitamin B2)	100 μg
Thiamine (Vitamin B1)	50 μg
Vitamin A	75 μg
Vitamin B6	40 μg
Vitamin B12	0.23 μg
Vitamin C	15 mg
Vitamin D	1.7 μg
Vitamin E	0.7 mg
Vitamin K	6 μg
MINERALS	
Choline	24 mg
Calcium	60 mg
Chloride	55 mg
Chromium	2 μg

	per 100 ml
Iron	0.8 mg
Phosphorus	45 mg
Iodine	14 μg
Magnesium	6 mg
Manganese	45 μg
Molybdenum	5 μg
Potassium	75 mg
Copper	50 μg
Selenium	3 μg
Sodium	24 mg
Zinc	0.9 mg
AMINO ACIDS	
L-Alanine	0.12 g
L-Arginine	0.15 g
Ac. L-Aspartate	0.24 g
L-Carnitine	2.1 mg
L-Cystine	0.06 g
L-Phenylalanine	– g
Glycine	0.24 g
L-Isoleucine	0.16 g
L-Histidine	0.09 g
L-Leucine	0.25 g
L-Lysine	0.17 g
L-Methionine	0.04 g
L-Proline	0.17 g
L-Serine	0.11 g
L-Taurine	4.27 mg
L-Tyrosine	0.24 g
L-Threonine	0.16 g
L-Tryptophan	0.05 g
L-Valine	0.18 g

afenil® 2

500 g | PKU

Phenylalanine-free amino acid mixture indicated for dietary management of hyperphenylalaninemia, including phenylketonuria.

» INDICATIONS
For dietary management of children from the first year of age and of adults, with confirmed hyperphenylalaninemia including phenylketonuria, and maternal phenylketonuria.

» DOSAGE AND ADMINISTRATION
Following the physician's prescription, taking into account age, body weight and clinical conditions of the patient.

» INSTRUCTIONS FOR USE
Take the prescribed quantity of Afenil® 2, divided in 3-4 daily doses, in addition to other foods permitted by the diet. Afenil® 2 can also be taken as a cold drink, dissolving at first the necessary powder in a small quantity of water (20 ml), then further diluting until obtaining the consistency and the desired volume (80 ml). For dilution, one can use water or other allowed drinks, also flavored. Once prepared, it is recommended that the drink is consumed within 1 hour, or else store in a refrigerator (2-4°C) and consume within 24 hours.

» STORAGE CONDITIONS
After use, close the tub properly and store in cool and dry place, away from light and sources of direct heat. The expiry date refers to the product correctly stored in its intact package.

» IMPORTANT WARNINGS
Afenil® 2 must be used under medical supervision, by individuals with confirmed hyperphenylalaninemia, including phenylketonuria. Afenil® 2 cannot be used as one's sole food source. The product can result in health risks if consumed by individuals who do not have the specific disorder for which it is indicated. Keep out of the reach of children.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g of powder	per 100 ml reconstituted at 5% (5 g in 100 ml of liquid)
Energy kJ/kcal	1416/333	71/17
Carbohydrates	0.0 g	0.0 g
of which sugars	0.0 g	0.0 g
Fats	0.0 g	0.0 g
of which saturated fatty acids	0.0 g	0.0 g
Protein equivalent	83.3 g	4.2 g
Salt	0.0 g	0.0 g
AMINO ACIDS		
L-Alanine	3.56 g	0.178 g
L-Arginine	5.75 g	0.288 g
Ac. L-Aspartate	9.11 g	0.456 g
L-Carnitine	102.30 mg	5.115 mg
L-Cystine	2.32 g	0.116 g
Glycine	9.07 g	0.454 g
L-Glutamine	7.05 g	0.353 g
L-Isoleucine	6.21 g	0.311 g
L-Histidine	3.55 g	0.178 g
L-Leucine	9.75 g	0.488 g
L-Lysine	6.45 g	0.323 g
L-Methionine	1.72 g	0.086 g
L-Phenylalanine	– g	– g
L-Proline	6.49 g	0.325 g
L-Serine	4.05 g	0.203 g
Taurine	180.00 mg	9.000 mg
L-Tyrosine	9.16 g	0.458 g
L-Threonine	6.30 g	0.315 g
L-Tryptophan	1.95 g	0.098 g
L-Valine	7.19 g	0.360 g

afenil® gel

720 g
30 per 24 g

PKU 6+ months

Phenylalanine-free amino acid mixture with vitamins, minerals, selenium, taurine, and carnitine, indicated for dietary management of hyperphenylalaninemia including phenylketonuria.

» INDICATIONS
For the dietary management of infants over six month of age and adults, with known hyperphenylalaninemia including phenylketonuria and maternal phenylketonuria.

» DOSAGE AND ADMINISTRATION
According to the physician's prescription, taking into account age, body weight and clinical condition of the subject.

» INSTRUCTIONS FOR USE
Afenil® Gel can be consumed either as a gel or as a beverage.
To make a gel: pour the content of an Afenil® Gel sachet in a glass; if desired, add flavoring as preferred; add around 30 ml of cold water; mix well for around 10 seconds; to obtain a creamy gel: let it rest for around 2 minutes.
To make a drink: pour the content of an Afenil® Gel sachet in a glass; if desired, flavored as preferred; add around 80 ml of cold water; mix well for around 10 seconds; drink immediately.
Reconstituted Afenil® Gel can be consumed with a spoon or mixed with other allowed foods. For best results, Afenil® Gel should be prepared and consumed immediately. When necessary, the reconstituted and unused product can be kept for up to 24 hours in a refrigerator and mixed well before use. Once opened, the powder in the pouch should be completely consumed. Any excess product can be stored in a refrigerator and used within 24 hours.

» STORAGE CONDITIONS
Store in a cool and dry place, away from light and sources of direct heat. The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS
Afenil® Gel must only be taken under medical supervision by individuals with known hyperphenylalaninemia including phenylketonuria. Afenil® Gel must not be used as one's only food source. Keep out of the reach of children.
The product can result in health risks if consumed by individuals who do not have the specific disorder for which it is indicated.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g	per 24 g (1 sachet)
Energy kJ/kcal	1362/326	327/78
Fats	0 g	0 g
of which saturated fatty acids	0 g	0 g
Carbohydrates	39.4 g	9.5 g
of which sugars	25.5 g	6.1 g
Protein equivalent	42 g	10 g
Salt	0.95 g	0.23 g

VITAMINS	per 100 g	per 24 g (1 sachet)
Biotin	25 µg	6.0 µg
Choline	279 mg	67 mg
Folic acid	208 µg	49.9 µg
Niacin	14 mg	3.4 mg
Pantothenic Acid	5.0 mg	1.2 mg
Riboflavin (Vitamin B2)	1200 µg	290 µg
Thiamine (Vitamin B1)	1000 µg	240 µg
Vitamin A	600 µg (RE)	144 µg (RE)
Vitamin B6	1100 µg	260 µg
Vitamin B12	2.0 µg	0.48 µg
Vitamin C	63 mg	15 mg
Vitamin D	14.6 µg	3.5 µg
Vitamin E	9.0 mg (αTE)	2.2 mg (αTE)
Vitamin K	41 µg	9.8 µg

MINERALS	per 100 g	per 24 g (1 sachet)
Calcium	1083 mg	260 mg
Chloride	583 mg	140 mg
Chromium	71 µg	17 µg
Iron	14 mg	3.4 mg
Phosphorus	825 mg	198 mg
Iodine	138 µg	33.1 µg
Magnesium	167 mg	40 mg
Manganese	1.7 mg	0.41 mg
Molybdenum	50 µg	12 µg
Potassium	938 mg	225 mg
Copper	800 µg	190 µg
Selenium	35 µg	8.4 µg
Sodium	379 mg	91 mg
Zinc	11 mg	2.6 mg

AMINO ACIDS	per 100 g	per 24 g (1 sachet)
L-Alanine	1.8 g	0.4 g
L-Arginine	2.9 g	0.7 g
Ac. L-Aspartate	4.6 g	1.1 g
L-Carnitine	46 mg	11 mg
L-Cystine	1.2 g	0.3 g
Glycine	4.6 g	1.1 g
L-Glutamine	3.6 g	0.9 g
L-Isoleucine	3.1 g	0.7 g
L-Histidine	1.8 g	0.4 g
L-Leucine	4.7 g	1.1 g
L-Phenylalanine	– g	– g
L-Lysine	3.3 g	0.8 g
L-Methionine	0.9 g	0.2 g
L-Proline	3.3 g	0.8 g
L-Serine	2.0 g	0.5 g
Taurine	92 mg	22 mg
L-Tyrosine	4.6 g	1.1 g
L-Threonine	3.2 g	0.8 g
L-Tryptophan	1.0 g	0.2 g
L-Valine	3.6 g	0.9 g

afenil® medi15

750 g
30 per 25 g

PKU 3+

NEUTRAL OR ORANGE OR BERRIES FLAVOR

Phenylalanine-free amino acid mixture with vitamins, carbohydrates, and minerals, indicated in the dietary management of hyperphenylalaninemia, including phenylketonuria.

» INDICATIONS

For dietary management of children over three years of age and adults, with known hyperphenylalaninemia including phenylketonuria and maternal phenylketonuria.

» DOSAGE AND ADMINISTRATION

According to the physician's prescription, taking into account age, body weight, and clinical conditions of the subject.

» INSTRUCTIONS FOR USE

Dissolve one pouch of Afenil® Medi 15 in approximately 80 ml of water or other allowed liquids. Afenil® Medi 15 can be flavored as desired. Once reconstituted, the product should be consumed immediately. When necessary, the reconstituted product can be kept for up to 24 hours in the refrigerator and mixed well before use.

» STORAGE CONDITIONS

Store the product in a cool and dry place, away from light and sources of direct heat. Afenil® Medi 15 are single-dose pouches. Any prepared and unused product can be stored in the refrigerator and used within 24 hours, mixing well before use. The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS

Afenil® Medi 15 must only be taken under medical supervision by individuals with known hyperphenylalaninemia including phenylketonuria. Afenil® Medi 15 must not be used as one's only food source. Keep out of the reach of children. The product can result in health risks if consumed by individuals who do not have the specific disorder for which it is indicated.

NUTRITIONAL INFORMATION
food for special medical purposes

*	per 100 g	per 25 g
Energy kJ/kcal	1274/304	318/76
Fats	0 g	0 g
of which saturated fatty acids	0 g	0 g
Carbohydrates	16.1 g	4 g
of which sugars	1.1 g	0.3 g
Protein equivalent	60 g	15 g
Salt	1.27 g	0.32 g

* Nutritional Values refer to the neutral flavor. Orange flavor, x 100 g: Energy value x100 g 1211/289 kJ/kcal, x25 g: 303/72 kJ/kcal; Carbohydrates. x100 g: 11.9 g, of which sugars 0.6 g, x25 g: 3 g, of which sugars 0.1 g
Berries flavor, x 100 g: Energy value x100 g 1216/291 kJ/kcal, x25 g: 304/73 kJ/kcal; Carbohydrates. x100 g: 12.2 g, of which sugars 0.3 g, x25 g: 3.1 g, of which sugars 0.1 g

VITAMINS	per 100 g	per 25 g
Biotin	188 μg	47 μg
Choline	600 mg	150 mg
Folic acid	400 μg	100 μg
Pantothenic Acid	8.0 mg	2.0 mg
Niacin	24.8 mg	6.2 mg
Riboflavin (Vitamin B2)	2.3 mg	0.57 mg
Thiamine (Vitamin B1)	2.0 mg	0.50 mg
Vitamin A	832 μg (RE)	208 μg (RE)
Vitamin B12	4.8 μg	1.2 μg
Vitamin B6	2.8 mg	0.7 mg
Vitamin C	108 mg	27 mg
Vitamin D	13.2 μg	3.3 μg
Vitamin E	15.6 mg (αTE)	3.9 mg (αTE)
Vitamin K	100 μg	25 μg

MINERALS	per 100 g	per 25 g
Calcium	1196 mg	299 mg
Chloride	1004.8 mg	251.2 mg
Chromium	88 μg	22 μg
Iron	21.6 mg	5.4 mg
Phosphorus	1276 mg	319 mg
Iodine	252 μg	63 μg
Magnesium	376 mg	94 mg
Manganese	3.08 mg	0.77 mg
Molybdenum	144 μg	36 μg
Potassium	940 mg	235 mg
Copper	2240 μg	560 μg
Selenium	88 μg	22 μg
Sodium	508 mg	127 mg
Zinc	21.6 mg	5.4 mg

AMINO ACIDS	per 100 g	per 25 g
L-Alanine	2.56 g	0.64 g
L-Arginine	4.16 g	1.04 g
Ac. L-Aspartate	6.56 g	1.64 g
L-Carnitine	64 mg	16.0 mg
L-Cystine	1.68 g	0.42 g
Glycine	6.52 g	1.63 g
L-Glutamine	5.12 g	1.28 g
L-Isoleucine	4.48 g	1.12 g
L-Histidine	2.56 g	0.64 g
L-Leucine	7.04 g	1.76 g
L-Lysine	4.64 g	1.16 g
L-Methionine	1.24 g	0.31 g
L-Proline	4.68 g	1.17 g
L-Phenylalanine	– g	– g
L-Serine	2.92 g	0.73 g
Taurine	132 mg	33.0 mg
L-Tyrosine	6.6 g	1.65 g
L-Threonine	4.56 g	1.14 g
L-Tryptophan	1.4 g	0.35 g
L-Valine	5.16 g	1.29 g

afenil® squash 15

30 per 130 ml | PKU | 3+

ORANGE OR BERRIES FLAVOR

Ready to use phenylalanine-free amino acid mixture, enriched with EPA and DHA with vitamins and minerals, indicated in the dietary management of hyperphenylalaninemia, including phenylketonuria.

» INDICATIONS
For the dietary management of children over three years of age and adults, with known hyperphenylalaninemia including phenylketonuria and maternal phenylketonuria.

» DOSAGE AND ADMINISTRATION
According to the physician's prescription, taking into account age, body weight and clinical condition of the subject.

» INSTRUCTIONS FOR USE
Shake well before use. Once the package has been opened, the drink should be consumed within 24 hours.

» STORAGE CONDITIONS
Store the product in a cool and dry place, away from light and sources of direct heat. The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS
Afenil® Squash 15 must only be taken under medical supervision by individuals with known hyperphenylalaninemia including phenylketonuria. Afenil® Squash 15 must not be used as one's only source of food. Keep out of the reach of children. The product can result in health risks if consumed by individuals who do not have the specific disorder for which it is indicated.

NUTRITIONAL INFORMATION
food for special medical purposes

*	per 100 ml	per 130 ml (1 sachet)
Energy kJ/kcal	369/87	480/114
Fats	0.34 g	0.44 g
of which saturated fatty acids	0.03 g	0.04 g
of which DHA	88.5 mg	115 mg
of which EPA	17.7 mg	23 mg
Carbohydrates	6.9 g	9 g
of which sugars	4.8 g	6.2 g
Protein equivalent	11.5 g	15 g
Salt	0.25 g	0.32 g

* Nutritional Values refer to the orange flavor. Berries flavor, per 100 ml: Energy 399/94 kJ/kcal; per 130 ml (1 sachet): 519/122 kJ/kcal; Carbohydrates per 100 ml: 9.5 g of which sugars 5.43 g; per 130 ml (1 sachet): 12.3 g of which sugars 7.03 g

VITAMINS	per 100 ml	per 130 ml (1 sachet)
Biotin	36.2 µg	47 µg
Choline	115 mg	150 mg
Folic acid	76.9 µg (RE)	100 µg (RE)
Niacin	4.8 mg (NE)	6.2 mg (NE)
Pantothenic acid (Vitamin B5)	1.5 mg	2 mg
Riboflavin (Vitamin B2)	0.4 mg	0.57 mg
Thiamine (Vitamin B1)	0.38 mg	0.5 mg
Vitamin A	160 µg	208 µg
Vitamin B6	0.5 mg	0.7 mg
Vitamin B12	0.9 µg	1.2 µg
Vitamin C	21 mg	27 mg
Vitamin D	5.8 µg	7.5 µg
Vitamin E	3 mg (αTE)	3.7 mg (αTE)
Vitamin K	19.2 µg	25 µg

MINERALS	per 100 ml	per 130 ml (1 sachet)
Calcium	230 mg	299 mg
Chloride	140 mg	182 mg
Chromium	16.9 µg	22 µg
Iron	4.15 mg	5.4 mg
Phosphorus	205.4 mg	267 mg
Iodine	48.5 µg	63 µg
Magnesium	72.3 mg	94 mg
Manganese	0.6 mg	0.8 mg
Molybdenum	27.2 µg	35.4 µg
Potassium	180.8 mg	235 mg
Copper	420 µg	550 µg
Selenium	16.9 µg	22 µg
Sodium	99 mg	129.7 mg
Zinc	4.15 mg	5.4 mg
AMINO ACIDS		
L-Alanine	0.53 g	0.69 g
L-Arginine	0.86 g	1.12 g
Ac. L-Aspartate	1.36 g	1.77 g
L-Carnitine	13 mg	16.9 mg
L-Cystine	0.35 g	0.46 g
Glycine	1.35 g	1.76 g
L-Isoleucine	0.93 g	1.21 g
L-Histidine	0.53 g	0.69 g
L-Phenylalanine	– g	– g
L-Leucine	1.46 g	1.90 g
L-Lysine	0.96 g	1.25 g
L-Methionine	0.26 g	0.34 g
L-Proline	0.97 g	1.26 g
L-Serine	0.60 g	0.78 g
Taurine	24.6 mg	32 mg
L-Tyrosine	1.37 g	1.78 g
L-Threonine	0.93 g	1.21 g
L-Tryptophan	0.29 g	0.38 g
L-Valine	1.07 g	1.39 g
Choline	115 g	150 g

afenil® micro 3H

4 per 110 g | PKU | 3+

Slow-release micro-tablets. Phenylalanine-free amino acid mixture with fats and carbohydrates, indicated for the dietary management of hyperphenylalaninemia including phenylketonuria.

SLOW-RELEASE TECHNOLOGY

» INDICATIONS

For the dietary management of children and adults with known hyperphenylalaninemia including phenylketonuria and in maternal phenylketonuria. The micro-tablets are suitable for children of all ages in relation to their ability to swallow, as determined by the prescribing physician.

» DOSAGE AND ADMINISTRATION

Following the physician's prescription, taking into account age, body weight, the clinical condition of the subject, and the fact that the tablets are slow-release. Afenil® Micro 3H releases the amino acids contained in the tablets over three hours following intake. The cap of the jar contains about 13 g of micro-tablets (equal to approximately 9 g of protein equivalent).

» INSTRUCTIONS FOR USE

Take the prescribed amount with water or other allowed liquids. The micro-tablets have no taste; to retain this feature, it is recommended that they are not chewed, pulverized, or dissolved.

» STORAGE CONDITIONS

After use, close the jar properly. Store in a cool and dry place, away from light and sources of direct heat. The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS

Afenil® Micro 3H must only be taken under medical supervision by individuals with known hyperphenylalaninemia including phenylketonuria. Afenil® Micro 3H must not be used as one's only source of food. Keep out of the reach of children. The product can result in health risks if consumed by individuals who do not have the specific disorder for which it is indicated.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g
Energy kJ/kcal	1678/396
Fats	3.6 g
of which saturated fatty acids	3.59 g
Carbohydrates	13 g
of which sugars	0 g
Fiber	3.7 g
Protein equivalent	70.7 g
Salt *	1 g

AMINO ACIDS

Ac. L-Aspartate	7.76 g
Glycine	7.68 g
L-Alanine	3.07 g
L-Arginine	4.90 g
L-Carnitine	0.08 g
L-Cystine	2.01 g
L-Glutamine	6.02 g
L-Isoleucine	5.31 g
L-Histidine	3.07 g
L-Leucine	8.27 g
L-Lysine	5.50 g
L-Phenylalanine	– g
L-Methionine	1.42 g
L-Proline	5.54 g
L-Serine	3.42 g
Taurine	0.12 g
L-Tyrosine	7.78 g
L-Threonine	5.31 g
L-Tryptophan	1.65 g
L-Valine	6.13 g

* The salt content is due exclusively to the sodium in the product which equals 0.404 g/100 g

neutrafenil® micro R

4 per 110 g | PKU | 3+

Slow-release micro-tablets.
Phenylalanine-free LNAA (Large Neutral Amino Acids) mixture with fats, carbohydrates, arginine, and lysine, indicated for the dietary management of hyperphenylalaninemia including phenylketonuria.

SLOW-RELEASE TECHNOLOGY

» INDICATIONS

For the dietary management of children and adults with known hyperphenylalaninemia including phenylketonuria. The micro-tablets are suitable for children of all ages depending on their ability to swallow, as determined by the attending physician.

» DOSAGE AND ADMINISTRATION

Following the doctor's prescription, taking into account age, body weight, the clinical condition of the subject, and the fact that the tablets are delayed-release.
NeutrAfenil® Micro R releases the amino acids contained in the micro-tablets over a three hour period after it is taken. The cap of a jar contains about 9 g protein equivalents (equal to approximately 13 g of micro-tablets).

» INSTRUCTIONS FOR USE

Take the prescribed amount with water or other allowed liquids. The micro-tablets have no taste; do not chew, pulverize, or try to put them into solution.

» STORAGE CONDITIONS

After use, close the jar well. Store in a cool and dry place, away from light and sources of direct heat. The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS

The product must only be taken under medical supervision by individuals with known hyperphenylalaninemia including phenylketonuria. The product must not be used as one's only food source. Keep out of the reach of children. The product can result in health risks if consumed by individuals who do not have the specific disorder for which it is indicated.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g
Energy kJ/kcal	1686/399
Fats	5.3 g
of which saturated fatty acids	5.3 g
Carbohydrates	12 g
of which sugars	0 g
Fiber	5.8 g
Protein equivalent	70.79 g
Salt	1.6 g

AMINO ACIDS

L-Arginine	1.92 g
L-Aspartate	4.95 g
L-Phenylalanine	– g
L-Isoleucine	10 g
L-Histidine	3.36 g
L-Leucine	12 g
L-Lysine	5.44 g
L-Methionine	2.72 g
L-Tyrosine	24 g
L-Threonine	2.56 g
L-Tryptophan	8 g
L-Valine	10 g

afenil® Buddy

660 g
30 x 22 g

PKU 3+

CREME CARAMEL FLAVOR

Phenilalanine-free amino acid mixture, with sweeteners, indicated for the dietary management of hyperphenylalaninemia, including phenylketonuria.

» INDICATIONS

For the dietary management of children over three years of age and adults, with known hyperphenylalaninemia including phenylketonuria and maternal phenylketonuria.

» DOSAGE AND ADMINISTRATION

According to the doctor's prescription, taking into account age, body weight, and clinical condition of the subject.

» INSTRUCTIONS FOR USE

Afenil® Buddy is used to make a cream to be taken with a spoon. To prepare, pour the contents of one sachet into a glass and add at least 80 ml of protein-free drink such as Milco®, water or other allowed drinks, depending individual tastes. Sweeten if necessary. Mix well and allow the reconstituted mixture to sit for a couple of minutes.A warm liquid can be used to improve solubility of the product. The reconstituted product can be consumed immediately, stored in a refrigerator as a pudding for 24 hours or in the freezer, and eaten as an ice cream. After consuming, drink water or other allowed drinks.

» STORAGE CONDITIONS

Store in a cool and dry place, away from light and sources of direct heat. The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS

Afenil® Buddy must only be taken under medical supervision by individuals with known phenylalaninemia including phenylketonuria. Afenil® Buddy must not be used as one's only source of food. Keep out of the reach of children. The product can result in health risks if consumed by individuals who do not have the specific disorder for which it is indicated.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g of powder	x 22 g (1 sachet)
Energy kJ/kcal	1409/334	310/73
Fats	< 0.5 g	< 0.5 g
of which saturated fatty acids	< 0.1 g	< 0.1 g
Carbohydrates	28 g	6 g
of which sugars	2.9 g	0.6 g
Dietary fiber	21 g	5 g
Protein equivalent	45 g	10 g
Salt	0.48 g	0.1 g
Sodium equivalent	0.19 g	0.04 g

AMINO ACIDS

L-Alanine	1.81 g	0.40 g
L-Arginine	2.89 g	0.64 g
Ac. L-Aspartate	4.58 g	1.01 g
L-Carnitine	45 mg	9.9 mg
L-Cystine	1.19 g	0.26 g
Glycine	4.52 g	0.99 g
L-Glutamine	3.55 g	0.78 g
L-Isoleucine	3.13 g	0.69 g
L-Histidine	1.81 g	0.4 g
L-Leucine	4.87 g	1.07 g
L-Lysine	3.24 g	0.71 g
L-Phenylalanine	– g	– g
L-Methionine	0.83 g	0.18 g
L-Proline	3.27 g	0.72 g
L-Serine	2.01 g	0.44 g
Taurine	70 mg	15.4 mg
L-Tyrosine	4.58 g	1.01 g
L-Threonine	3.13 g	0.69 g
L-Tryptophan	0.97 g	0.21 g
L-Valine	3.61 g	0.79 g

afenil® lime

420 g
30 x 14 g

PKU 3+

LEMON-MINT FLAVOR

Phenilalanine-free amino acid mixture indicated for the dietary management of phenylketonuria for children from 3 years of age and in adults.

›› INDICATIONS
For the dietary management of adults and children over the age of three, with confirmed hyperphenylalaninemia including phenylketonuria and maternal phenylketonuria.

›› DOSAGE AND ADMINISTRATION
Following the physician's prescription, taking into account age, body weight and clinical conditions of the patient.

›› INSTRUCTIONS FOR USE
Dissolve one sachet of Afenil® Lime in approximately 80 ml of water or other allowed liquids. Once reconstituted, the product should be consumed immediately. When necessary, the reconstituted product can be kept for up to 24 hours in the refrigerator and mixed well before use.

›› STORAGE CONDITIONS
Store in a cool and dry place, away from light and sources of direct heat. The expiry date refers to the product in an unopened, correctly-stored package.

›› IMPORTANT WARNINGS
Afenil® Lime must only be taken under medical supervision by individuals with confirmed hyperphenylalaninemia, including phenylketonuria. Afenil® Lime cannot be used as one's sole food source. The product can result in health risks if consumed by individuals who do not have the specific disorder for which it is indicated. Keep out of the reach of children.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g of powder	per 14 g (1 sachet)
Energy kJ/kcal	1381/325	193/45
Fats	0.4 g	0.1 g
of which saturated fatty acids	0 g	0 g
Carbohydrates	0.4 g	0 g
of which sugars	0 g	0 g
Proteine equivalenti	74 g	10 g
Salt	0 g	0 g

AMINO ACIDS		
L-Alanine	3.13 g	0.44 g
L-Arginine	5.01 g	0.70 g
Ac. L-Aspartate	8.99 g	1.26 g
L-Carnitine	89.8 mg	12.6 mg
L-Cystine	2.04 g	0.29 g
Glycine	7.97 g	1.12 g
L-Glutamine	6.2 g	0.87 g
L-Isoleucine	5.46 g	0.76 g
L-Histidine	3.13 g	0.44 g
L-Leucine	8.57 g	1.20 g
L-Lysine	5.67 g	0.79 g
L-Methionine	1.51 g	0.21 g
L-Proline	5.71 g	0.80 g
L-Serine	3.56 g	0.50 g
Taurine	158 mg	22 mg
L-Tyrosine	8.04 g	1.13 g
L-Threonine	5.53 g	0.77 g
L-Tryptophan	1.72 g	0.24 g
L-Valine	6.32 g	0.88 g

afenil® GMP Up bars coconut

1800 g
30 x 60 g

PKU 3+

Low-phenylalanine protein substitute with Glycomacropeptide (GMP) isolated from casein with a selected blend of essential and no-essential amino acids, carbohydrates, vitamins and minerals, with sweetener.

» INDICATIONS For the dietary management of adults and children over three years of age, with confirmed hyperphenylalaninemia including phenylketonuria.

» DOSAGE AND ADMINISTRATION Following the physician's prescription, taking into account age, body weight, and clinical conditions of the subject.

» INSTRUCTIONS FOR USE Ready-to-eat bars.

» STORAGE CONDITIONS Store well closed in a cool and dry place, at a temperature below 25 °C, away from light, humidity and sources of direct heat. The date of minimum durability refers to the product in an unopened, correctly-stored package..

» IMPORTANT WARNINGS Afenil® GMP UP must only be taken under medical supervision by individuals with confirmed hyperphenylalaninemia, including phenylketonuria. Afenil® GMP UP cannot be used as one's sole food source. The product can result in health risks if consumed by individuals who do not have the specific disorder for which it is indicated. Protein substitutes based on GMP are a natural source of phenylalanine. Keep out of the reach of children.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g	per 60 g (1 bar)
Energy kJ/kcal	1473/349	884/210
Fats	7.2 g	4.3 g
of which saturated fatty acids	5.7 g	3.4 g
Carbohydrates	50 g	30.2 g
of which sugars	20 g	12 g
Protein equivalent	16.7 g	10 g
Fiber	8.4 g	5 g
Salt	0.35 g	0.21 g

VITAMINS	per 100 g	per 60 g (1 bar)
Biotin	52 µg	31 µg
Folic acid	111 µg	67 µg
Pantothenic acid	2.2 mg	1.3 mg
Niacin	7 mg (NE)	4.1 mg (NE)
Riboflavin (Vitamin B2)	0.6 mg	0.38 mg
Thiamine (Vitamin B1)	0.6 mg	0.3 mg
Vitamin A	231 µg (RE)	139 µg (RE)
Vitamin B12	1 µg	0.8 µg
Vitamin B6	0.8 mg	0.5 mg
Vitamin C	30 mg	18 mg
Vitamin D	4 µg	2.2 µg
Vitamin E	4 mg (αTE)	2.6 mg (αTE)
Vitamin K	28 µg	17 µg

MINERALS	per 100 g	per 60 g (1 bar)
Calcium	332 mg	199 mg
Chloride	279 mg	167 mg
Chromium	24 µg	15 µg
Iron	6 mg	3.6 mg
Phosphorus	354 mg	213 mg
Iodine	70 µg	42 µg
Magnesium	104 mg	63 mg
Manganese	0.9 mg	0.51 mg
Molybdenum	40 µg	24 µg
Potassium	261 mg	157 mg
Copper	622 µg	373 µg
Selenium	24 µg	15 µg
Sodium	141 mg	85 mg
Zinc	6 mg	4 mg

AMINO ACIDS	per 100 g	per 60 g (1 bar)
L-Alanine	0.75 g	0.45 g
L-Arginine	0.9 g	0.54 g
L-Aspartic Acid/ L-Asparagine	1.1 g	0.66 g
L-Cystine	10.52 mg	6.31 mg
L-Phenylalanine	21.03 mg	12.62 mg
Glycine	0.13 g	0.08 g
L-Glutamine/ L-Glutamic acid	2.5 g	1.5 g
L-Isoleucine	1.27 g	0.76 g
L-Histidine	0.68 g	0.41 g
L-Leucine	2.15 g	1.29 g
L-Lysine	1.3 g	0.78 g
L-Methionine	0.23 g	0.14 g
L-Proline	1.47 g	0.88 g
L-Serine	0.95 g	0.57 g
L-Tyrosine	2.38 g	1.43 g
L-Threonine	2.12 g	1.27 g
L-Tryptophan	0.37 g	0.22 g
L-Valine	1.35 g	0.81 g
Choline	167 mg	100 mg

afenil® GMP Up

bars cream-mou

1500 g
30 x 50 g

PKU 3+

Low-phenylalanine protein substitute with Glycomacropeptide (GMP) isolated from casein with a selected blend of essential and no-essential amino acids, carbohydrates, vitamins and minerals, with sweetener.

» INDICATIONS For the dietary management of adults and children over three years of age, with confirmed hyperphenylalaninemia including phenylketonuria.

» DOSAGE AND ADMINISTRATION Following the physician's prescription, taking into account age, body weight, and clinical conditions of the subject.

» INSTRUCTIONS FOR USE Ready-to-eat bars.

» STORAGE CONDITIONS Store well closed in a cool and dry place, at a temperature below 25 °C, away from light, humidity and sources of direct heat. The date of minimum durability refers to the product in an unopened, correctly-stored package.

» IMPORTANT WARNINGS Afenil® GMP UP must only be taken under medical supervision by individuals with confirmed hyperphenylalaninemia, including phenylketonuria. Afenil® GMP UP cannot be used as one's sole food source. The product can result in health risks if consumed by individuals who do not have the specific disorder for which it is indicated. Protein substitutes based on GMP are a natural source of phenylalanine. Keep out of the reach of children.

NUTRITIONAL INFORMATION

food for special medical purposes

	per 100 g	x 50 g (1 bar)
Energy kJ/kcal	1322/313	661/156
Fats	7.2 g	0.9 g
of which satured fatty acids	5.7 g	0.4 g
Carbohydrates	50 g	24.7 g
of which sugars	20 g	6.2 g
Protein equivalent	16.7 g	10 g
Fiber	8.4 g	5 g
Salt	0.35 g	0.21 g

VITAMINS	per 100 g	x 50 g (1 bar)
Biotin	63 µg	31 µg
Folic acid	133 µg	67 µg
Pantothenic acid	2.7 mg	1.3 mg
Niacin	8 mg (NE)	4.1 mg (NE)
Riboflavin (Vitamin B2)	0.76 mg	0.38 mg
Thiamine (Vitamin B1)	0.67 mg	0.3 mg
Vitamin A	277 µg (RE)	139 µg (RE)
Vitamin B12	2 µg	0.8 µg
Vitamin B6	0.9 mg	0.5 mg
Vitamin C	36 mg	18 mg
Vitamin D	4 µg	2.2 µg
Vitamin E	5 mg (αTE)	2.6 mg (αTE)
Vitamin K	33 µg	17 µg

MINERALS	per 100 g	x 50 g (1 bar)
Calcium	399 mg	199 mg
Chloride	335 mg	167 mg
Chromium	29 µg	15 µg
Iron	7 mg	3.6 mg
Phosphorus	425 mg	213 mg
Iodine	84 µg	42 µg
Magnesium	125 mg	63 mg
Manganese	1 mg	0.51 mg
Molybdenum	48 µg	24 µg
Potassium	313 mg	157 mg
Copper	747 µg	373 µg
Selenium	29 µg	15 µg
Sodium	169 mg	85 mg
Zinc	7 mg	4 mg

AMINO ACIDS	per 100 g	x 50 g (1 bar)
L-Alanine	0.9 g	0.45 g
L-Arginine	1.08 g	0.54 g
L-Aspartic Acid/ L-Asparagine	1.32 g	0.66 g
L-Cystine	12.62 mg	6.31 mg
L-Phenylalanine	25.24 mg	12.62 mg
Glycine	0.16 g	0.08 g
L-Glutamine/ L-Glutamic acid	3 g	1.5 g
L-Isoleucine	1.52 g	0.76 g
L-Histidine	0.82 g	0.41 g
L-Leucine	2.58 g	1.29 g
L-Lysine	1.56 g	0.78 g
L-Methionine	0.28 g	0.14 g
L-Proline	1.76 g	0.88 g
L-Serine	1.14 g	0.57 g
L-Tyrosine	2.86 g	1.43 g
L-Threonine	2.54 g	1.27 g
L-Tryptophan	0.44 g	0.22 g
L-Valine	1.62 g	0.81 g
Choline	200 mg	100 mg

afenil® GMP Up shake

750 g
30 x 25 g

PKU 3+

MILK OR ORANGE FLAVOR

Low-phenylalanine protein substitute with Glycomacropeptide (GMP) isolated from casein with a selected blend of essential and no-essential amino acids, carbohydrates, vitamins and minerals, with sweetener.

» INDICATIONS

For the dietary management of adults and children over three years of age with confirmed hyperphenylalaninemia, including phenylketonuria.

» DOSAGE AND ADMINISTRATION

Following the physician's prescription, taking into account age, body weight, and clinical conditions of the subject.

» INSTRUCTIONS FOR USE

Dissolve one sachet of Afenil® GMP UP Shake in at least 80 ml of water or other allowed liquids. Mix well. For an optimal result, the use of a shaker is recommended. Once reconstituted, the product should be consumed immediately. When necessary, the reconstituted product can be kept for up to 6 hours in the refrigerator and mixed well before use.

» STORAGE CONDITIONS

Store in a cool and dry place, away from light and sources of direct heat. The date of minimum durability refers to the product in an unopened package.

» IMPORTANT WARNINGS

Afenil® GMP UP Shake must only be taken under medical supervision by individuals with confirmed hyperphenylalaninemia, including phenylketonuria. Afenil® GMP UP Shake cannot be used as one's sole food source. The product can result in health risks if consumed by individuals who do not have the specific disorder for which it is indicated. All mixtures based on GMP are a natural source of phenylalanine. Use with caution in children aged 3-6 years. Keep out of the reach of children.

NUTRITIONAL INFORMATION
food for special medical purposes

*	per 100 g	per 25 g (1 sachet)
Energy kJ/kcal	1342/318	335/80
Fats	0.2 g	0.1 g
of which saturated fatty acids	0.1 g	0 g
Carbohydrates	39.1 g	9.8 g
of which sugars	2.4 g	0.6 g
Protein equivalent	40 g	10 g
Salt	0.85 g	0.21 g

* Nutritional Values refer to the milk flavor. Orange flavor, x 25 g: Energy 334/79 kj/kcal, Fats 0.1 g of which saturated fatty acids 0 g, Carbohydrates 9.7 g of which sugars 0.6 g, Protein equivalent 10 g, Salt 0.21 g. Orange flavor, x 100 g: Energy 1336/316 kj/kcal, Fats 0.2 g of which saturated fatty acids 0.1 g, Carbohydrates 38.8 g of which sugars 2.4 g, Protein equivalent 40 g, Salt 0.85 g.

VITAMINS	per 100 g	per 25 g (1 sachet)
Biotin	125 µg	31 µg
Folic acid	267 µg	67 µg
Pantothenic acid	5 mg	1.33 mg
Niacin	16.5 mg (NE)	4.13 mg (NE)
Riboflavin (Vitamin B2)	1.5 mg	0.38 mg
Thiamine (Vitamin B1)	1.3 mg	0.33 mg
Vitamin A	555 µg (RE)	139 µg (RE)
Vitamin B12	3.2 µg	0.8 µg
Vitamin B6	1.9 mg	0.47 mg
Vitamin C	72 mg	18 mg
Vitamin D	8.8 µg	2.2 µg
Vitamin E	10.4 mg (αTE)	2.6 mg (αTE)
Vitamin K	67 µg	17 µg

MINERALS	per 100 g	per 25 g (1 sachet)
Calcium	797 mg	199 mg
Chloride	670 mg	167.5 mg
Chromium	59 µg	15 µg
Iron	14.4 mg	3.6 mg
Phosphorus	851 mg	213 mg
Iodine	168 µg	42 µg
Magnesium	251 mg	63 mg
Manganese	2.05 mg	0.51 mg
Molybdenum	96 µg	24 µg
Potassium	627 mg	157 mg
Copper	1493 µg	373 µg
Selenium	59 µg	15 µg
Sodium	339 mg	85 mg
Zinc	14.4 mg	3.6 mg

AMINO ACIDS	per 100 g	per 25 g (1 sachet)
L-Alanine	1.82 g	0.45 g
L-Arginine	2.17 g	0.54 g
L-Aspartic Acid/ L-Asparagine	2.65 g	0.66 g
L-Cystine	25.23 mg	6.31 mg
L-Phenylalanine	50.46 mg	12.62 mg
Glycine	0.33 g	0.08 g
L-Glutamine/ L-Glutamic acid	5.98 g	1.5 g
L-Isoleucine	3.05 g	0.76 g
L-Histidine	1.63 g	0.41 g
L-Leucine	5.17 g	1.29 g
L-Lysine	3.11 g	0.78 g
L-Methionine	0.56 g	0.14 g
L-Proline	3.51 g	0.88 g
L-Serine	2.27 g	0.57 g
L-Tyrosine	5.73 g	1.43 g
L-Threonine	5.07 g	1.27 g
L-Tryptophan	0.86 g	0.22 g
L-Valine	3.25 g	0.81 g
Choline	400 mg	100 mg

L-tyrosina

30 capsules

PKU

Food supplement.

» INDICATIONS

As a food supplement for individuals with a deficiency or increased requirement for the amino acid tyrosine.

» INSTRUCTIONS FOR USE

It is recommended that 1-2 capsules are taken twice a day with water after a meal.

» STORAGE CONDITIONS

Store the product in a fresh and dry place, at room temperature; avoid exposure to localized sources of heat, sun, and contact with water. The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS

Keep out of reach of children under three years of age.
Do not exceed the recommended daily dose. Food supplements should not be intended as substitutes for a varied and balanced diet and a healthy lifestyle.

» NUTRITIONAL INFORMATION
food supplement

	per capsule	per 100 g
L-Tyrosine	500 mg	79 g

Protein and amino acid requirements

Protein intake in patient undergoing dietary management must be increased in order to correct for the lesser biological value of the proteins taken and optimize metabolic control. Minimal intake of the essential amino acid phenylalanine must be guaranteed to ensure protein synthesis; tyrosine must be considered a semi-essential amino acid and thus carefully assessed.

INTAKE OF PROTEINS (AMINO ACIDS) FROM RECOMMENDED PROTEIN SUBSTITUTE FOR PKU INDIVIDUALS

[(Ideal weight X proteins WHO) – natural proteins] X 1.4

body weight in Kg, proteins in g

The Complete European Guidelines on Phenylketonuria: Diagnosis and Treatment. Orphanet Journal of Rare Diseases 12 (2017): 162. PMC. Web. 6 Mar. 2018.

RECOMMENDED PHENYLALANINE AND TYROSINE INTAKE IN PKU INDIVIDUALS

	PHE (mg/day)	TYR (mg/day)
0 – 3 months	130-430	1100-1300
3 – 6 months	135-400	1400-2100
6 – 9 months	145-370	2500-3000
9 – 12 months	135-330	2500-3000
1 – 4 years	200-320	2800-3500
4 – 7 years	200-400	3200-4000
7 – 11 years	220-500	4000-5000
Adults	220-1000	5200-7000
Pregnancy		
First trimester	265-770	6000-7600
Second trimester	400-1650	6000-7600
Third trimester	700-2275	6000-7600

Nutrition management of patients with Inherited Metabolic Disorder, Phyllis B. Acosta

NOTES

Tyrosinemia type 1

Hereditary tyrosinemia type 1 (HT-1) is a hereditary recessive autosomal disease caused by a congenital defect of an enzyme involved in the catabolism of tyrosine, namely fumarylacetoacetate hydrolase (FAH). The incidence is estimated to range between 1:100,000 and 1:120,000 live births. Even though the pathology is extremely rare, its incidence is higher in some areas of North Europe and North America (1).

Type 1 tyrosinemia is characterized mainly by hepatorenal symptoms, although clinical manifestations of the pathology can vary considerably depending on the clinical form of the disease:

Acute form: the most common, manifesting before 6 months of age with severe and often fulminat hepatic involvement: in untreated children death by liver failure usually occurs within 2-8 months. Other symptoms of the disease, in its acute form, are growth retardation, vomit, diarrhea, and fever.

Sub-acute form: manifests between 6 months and one year of age, with slower clinical progression compared to the acute form and with similar symptoms, even if less severe than the latter. The sub-acute form is characterized by chronic progressive hepatopathy, tubular renal dysfunction (Fanconi syndrome), hypophosphatemia, growth retardation, rickets, hepatomegaly and easy formation of ecchymosis.

Chronic form: slow progression of the disease, which manifests after 12 months of age. This form is mostly characterized by rickets and tubulopathy.

The therapy is based upon two pillars that radical improve prognosis and natural evolution of patients: diet with low and controlled intake of tyrosine, phenylalanine, and methionine, and pharmacological therapy with nitisinone (NTBC). This pharmacological approach can lead to an increase in tyrosine blood levels, which must be kept under control with an adequate dietary regime, and to be continued throughout the patient's lifetime.

Once the patient has started therapy, he/she must be regularly undergo clinical, blood chemistry, and instrumental investigation. The interval between controls will vary depending on the severity of initial symptoms, time of diagnosis, and response to therapy. Given that dietary therapy can expose the patient to nutritional deficiency risks, it is fundamental to assess the nutritional state. Finally, long-term monitoring must include assessment of normal bone mineralszation, as well as adequate neuro-psychomotor development.

» ENZYME	Fumarylacetoacetate hydrolase (FAH, 15q23-q25) deficiency
» TRANSMISSION	Autosomal recessive
» INCIDENCE	1: 100,000-120,000 (1)
» OMIM	276700
» TREATMENT	Dietary therapy / pharmacological therapy with Nitisinone

Recommendations for management of patients suffering from type 1 tyrosinemia were recently published (1), and provide detailed recommendations on management of patients along with extensive information on clinical studies. **The recommendations can be freely accessed at:**

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3558375/pdf/1750-1172-8-8.pdf

References:

1. De Laet, C. et al. Recommendations for the Management of Tyrosinaemia Type 1." Orphanet Journal of Rare Diseases 8 (2013): 8. PMC. Web. 6 Mar. 2018.

TYR medi2

200 g

TYR

Amino acid mixture free of phenylalanine and tyrosine, recommended for dietary management of Tyrosinemia type 1.

» INDICATIONS
For dietary management of children from the first year of age to adults, with known type 1 Tyrosinemia.

» DOSAGE AND ADMINISTRATION
Following the physician's prescription, taking into account age, body weight and clinical conditions of the patient.
Recommended 5% w/v dilution (5 g of reconstituted product per 100 ml of liquid).

» INSTRUCTIONS FOR USE
Take the prescribed quantity of TYR Medi 2, divided in 3-4 daily doses, dissolved in water or other allowed cold liquids, even flavored or added to food.

» STORAGE CONDITIONS
After use, close the container properly and store in a cool and dry place, away from light and sources of direct heat. The expiry date refers to the product correctly stored in its intact package.

» IMPORTANT WARNINGS
TYR Medi 2 must be used under medical supervision, by individuals with known type 1 Tyrosinemia. TYR Medi 2 cannot be used as the only source of food.
The product can result in health risks if taken by individuals that do not have the specific disorder for which it is indicated. Keep out of the reach of children.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g of powder	per 100 ml reconstituted at 5% (5 g in 100 ml of liquid)
Energy kJ/kcal	1416/333	71/17
Fats	0.0 g	0.0 g
of which saturated fatty acids	0.0 g	0.0 g
Carbohydrates	0.0 g	0.0 g
of which sugars	0.0 g	0.0 g
Protein equivalent	83.3 g	4.2 g
Salt	0.0 g	0.0 g

AMINO ACIDS

L-Alanine	6.24 g	312.0 mg
L-Arginine	7.86 g	393.0 mg
Ac. L-Aspartate	11.10 g	555.0 mg
L-Carnitine	92.00 mg	4.6 mg
L-Cystine	2.86 g	143.0 mg
L-Phenylalanine	– g	– mg
Glycine	6.24 g	312.0 mg
L-Glutamine	7.58 g	379.0 mg
L-Isoleucine	6.96 g	348.0 mg
L-Histidine	4.18 g	209.0 mg
L-Leucine	10.50 g	525.0 mg
L-Lysine	7.94 g	397.0 mg
L-Methionine	1.78 g	89.0 mg
L-Proline	6.42 g	321.0 mg
L-Serine	4.90 g	245.0 mg
Taurine	184.00 mg	9.2 mg
L-Tyrosine	– g	– mg
L-Threonine	5.34 g	267.0 mg
L-Tryptophan	2.22 g	111.0 mg
L-Valine	7.58 g	379.0 mg

TYR medigel

720 g
30 per 24 g

TYR 6+ months

NEUTRAL FLAVOR

Amino acid mixture free of phenylalanine and tyrosine with vitamins, minerals, selenium, taurine, and carnitine, indicated for the dietary management of type 1 Tyrosinemia.

» INDICATIONS For the dietary management of children from six months of age and of adults with known type 1 tyrosinemia.

» DOSAGE AND ADMINISTRATION According to the physician's prescription, taking into account age, body weight, and clinical condition of the subject.

» INSTRUCTIONS FOR USE TYR Medigel can be consumed as either a gel or a beverage.
To prepare a gel: pour the contents of one TYR Medigel sachet into a glass; if desired, flavor to taste; add approximately 30 ml of cold water; mix well for about 10 seconds; to obtain a creamy gel: let it rest for around 2 minutes.
To make a drink: pour the contents of a TYR Medigel in a glass; if desired, add flavor as preferred; add around 80 ml of cold water; mix well for around 10 seconds; drink immediately.
Reconstituted TYR Medigel can be taken as is, with a spoon, or mixed with other allowed foods. For best results, when possible, TYR Medigel should be prepared and consumed immediately. When necessary, the reconstituted and unused product can be kept for up to 24 hours in a refrigerator and mixed well before use. Once opened, the powder in the pouch should be completely consumed. Any excess product can be stored in a refrigerator and used within 24 hours.

» STORAGE CONDITIONS Store in a cool and dry place, away from light and sources of direct heat. The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS TYR Medigel must only be taken under medical supervision by individuals with known type I Tyrosinemia. TYR Medigel must not be used as one's only source of food. The product can result in health risks if consumed by individuals who do not have the specific disorder for which it is indicated. Keep out of the reach of children.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g	per 24 g (1 sachet)
Energy kJ/kcal	1595/375	383/90
Fats	0 g	0 g
of which saturated fatty acids	0 g	0 g
Carbohydrates	45 g	11 g
of which sugars	25 g	6 g
Protein equivalent	41.7 g	10 g
Salt	1.1 g	0.3 g

VITAMINS	per 100 g	per 24 g (1 sachet)
Biotin	25 µg	6.0 µg
Choline	279 mg	67 mg
Folic acid	208 µg	49.9 µg
Niacin	14 mg	3.4 mg
Pantothenic acid	5.0 mg	1.2 mg
Riboflavin (Vitamin B2)	1.2 mg	0.29 mg
Thiamine (Vitamin B1)	1.0 mg	0.24 mg
Vitamin A	600 µg (RE)	144 µg (RE)
Vitamin B6	1.1 mg	0.26 mg
Vitamin B12	2.0 µg	0.48 µg
Vitamin C	63 mg	15 mg
Vitamin D	14.6 µg	3.5 µg
Vitamin E	9.0 mg (αTE)	2.2 mg (αTE)
Vitamin K	41 µg	9.8 µg

MINERALS	per 100 g	per 24 g (1 sachet)
Calcium	1083 mg	260 mg
Chloride	583 mg	140 mg
Chromium	71 µg	17 µg
Iron	14 mg	3.4 mg
Phosphorus	825 mg	198 mg
Iodine	138 µg	33.1 µg
Magnesium	167 mg	40 mg
Manganese	1.7 mg	0.41 mg
Molybdenum	50 µg	12 µg
Potassium	938 mg	225 mg
Copper	0.80 mg	0.19 mg
Selenium	35 µg	8.4 µg
Sodium	379 mg	91 mg
Zinc	11 mg	2.6 mg

AMINO ACIDS	per 100 g	per 24 g (1 sachet)
Ac. L-Aspartate	5.5 g	1332.00 mg
L-Alanine	3.12 g	748.80 mg
L-Arginine	3.93 g	943.20 mg
L-Carnitine	0.046 g	11.04 mg
L-Cystine	1.43 g	343.20 mg
L-Phenylalanine	– g	– mg
Glycine	3.12 g	748.80 mg
L-Glutamine	3.79 g	909.60 mg
L-Isoleucine	3.48 g	835.20 mg
L-Histidine	2.09 g	501.60 mg
L-Leucine	5.25 g	1260.00 mg
L-Lysine	3.97 g	952.80 mg
L-Methionine	0.89 g	213.60 mg
L-Proline	3.21 g	770.40 mg
L-Serine	2.45 g	588.00 mg
L-Tyrosine	– g	– mg
L-Threonine	2.67 g	640.80 mg
L-Tryptophan	1.11 g	266.40 mg
L-Valine	3.79 g	909.60 mg
Taurine	0.092 g	22.08 mg

TYR medi15

750 g
30 per 25 g

TYR 3+

Amino acid mixture free
of Phenylalanine and Tyrosine
with vitamins and minerals, indicated
for the dietary management of type 1
Tyrosinemia.

» INDICATIONS

For the dietary management of children from three years of age upwards and adults with known type 1 tyrosinemia.

» DOSAGE AND ADMINISTRATION

According to the physician's prescription, taking into account age, body weight, and clinical condition of the subject.

» INSTRUCTIONS FOR USE

Dissolve one sachet of TYR Medi 15 in approximately 80 ml of water or other allowed liquids. TYR Medi 15 can be flavored to taste. Once reconstituted, the product should be consumed immediately. When necessary, the reconstituted product can be kept for up to 24 hours in the refrigerator and mixed well before use.

» STORAGE CONDITIONS

Store the product in a cool and dry place, away from light and sources of direct heat.
TYR Medi 15 are single-dose sachets. Any prepared and unused product can be stored in the refrigerator and used within 24 hours. The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS

TYR Medi 15 must only be taken under medical supervision by individuals with known type I tyrosinemia. TYR Medi 15 must not be used as one's only source of food.
The product can result in health risks if taken by individuals who do not have the specific disorder for which it is indicated. Keep out of the reach of children.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g of powder	per 25 g (1 sachet)
Energy kJ/kcal	1550/365	388/91
Fats	0 g	0 g
of which saturated fatty acids	0 g	0 g
Carbohydrates	20 g	5 g
of which sugars	2.7 g	0.7 g
Protein equivalent	60 g	15 g
Salt	1.2 g	0.3 g

VITAMINS	per 100 g of powder	per 25 g (1 sachet)
Biotin	188 μg	47 μg
Choline	600 mg	150 mg
Folic acid	400 μg	100 μg
Pantothenic acid	8.0 mg	2.0 mg
Niacin	24.8 mg	6.2 mg
Riboflavin (Vitamin B2)	2.3 mg	0.57 mg
Thiamine (Vitamin B1)	2.0 mg	0.50 mg
Vitamin A	832 μg (RE)	208 μg (RE)
Vitamin B12	4.8 μg	1.2 μg
Vitamin B6	2.8 mg	0.7 mg
Vitamin C	108 mg	27 mg
Vitamin D	13.2 μg	3.3 μg
Vitamin E	15.6 mg (αTE)	3.9 mg (αTE)
Vitamin K	100 μg	25 μg

MINERALS	per 100 g of powder	per 25 g (1 sachet)
Calcium	1196 mg	299 mg
Chloride	728 mg	182 mg
Chromium	88 μg	22 μg
Iron	21.6 mg	5.4 mg
Phosphorus	1068 mg	267 mg
Iodine	252 μg	63 μg
Magnesium	376 mg	94 mg
Manganese	3.2 mg	0.80 mg
Molybdenum	144 μg	36 μg
Potassium	940 mg	235 mg
Copper	2.2 mg	0.55 mg
Selenium	88 μg	22 μg
Sodium	508 mg	127 mg
Zinc	21.6 mg	5.4 mg

AMINO ACIDS	per 100 g of powder	per 25 g (1 sachet)
Ac. L-Aspartate	7.99 g	1998.0 mg
L-Leucine	7.56 g	1890.0 mg
L-Lysine	5.71 g	1429.2 mg
L-Arginine	5.65 g	1414.8 mg
L-Glutamine	5.45 g	1364.4 mg
L-Valine	5.45 g	1364.4 mg
L-Isoleucine	5.01 g	1252.8 mg
L-Proline	4.62 g	1155.6 mg
L-Alanine	4.49 g	1123.2 mg
Glycine	4.49 g	1123.2 mg
L-Threonine	3.84 g	961.2 mg
L-Serine	3.52 g	882.0 mg
L-Histidine	3.01 g	752.4 mg
L-Cystine	2.05 g	514.8 mg
L-Tryptophan	1.59 g	399.6 mg
L-Methionine	1.28 g	320.4 mg
Taurine	0.13 g	33.1 mg
L-Carnitine	0.06 g	16.6 mg

TYR medimicro3H

440 g
4 per 110 g

TYR 3+

Slow-release micro-tablets.
Amino acid mixture free of tyrosine and phenylalanine, indicated for the dietary management of type 1 Tyrosinemia.

SLOW-RELEASE TECHNOLOGY

» INDICATIONS
For the dietary management of subjects starting from three years of age with ascertained type 1 tyrosinemia. Micro-tablets are suitable for children from three years of age upwards, depending on their ability to swallow, as determined by the attending physician.

» DOSAGE AND ADMINISTRATION
According to the physician's prescription, taking into account age, body weight, the clinical condition of the subject, and the fact that the tablets are delayed-release. After being taken, TYR Medimicro 3H releases the amino acids in the tablets over a three hour period. The cap of the jar contains about 13 g of micro-tablets (equal to approximately 8 g of protein equivalent).

» INSTRUCTIONS FOR USE
Take the prescribed amount with water or other allowed liquids. The micro-tablets have no taste; to retain this feature, it is recommended that they are not chewed, pulverized, or dissolved.

» STORAGE CONDITIONS
After use, close the jar properly and store it in a cool and dry place below 25°C, away from light and sources of direct heat. The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS
TYR Medimicro 3H must only be taken under medical supervision by individuals with known type I tyrosinemia. TYR Medimicro 3H must not be used as one's only source of food. The product can result in health risks if consumed by individuals who do not have the specific disorder for which it is indicated. Keep out of the reach of children.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g of micro-tablets
Energy kJ/kcal	1628/389
Fats	2.6 g
of which saturated fatty acids	2.6 g
Carbohydrates	12 g
of which sugars	0 g
Protein equivalent	65 g
Fiber	10 g
Salt	1 g

AMINO ACIDS

L-Aspartic acid	8.6 g
L-Alanine	5 g
L-Arginine	6.1 g
L-Cystine	2.2 g
Glycine	5 g
L-Glutamine	6 g
L-Isoleucine	5.4 g
L-Histidine	3.2 g
L-Leucine	8.2 g
L-Lysine	6.2 g
L-Methionine	1.4 g
L-Proline	5 g
L-Serine	3.8 g
L-Threonine	4.1 g
L-Tryptophan	1.7 g
L-Valine	6 g
L-Phenylalanine	– g
L-Tyrosine	– g
Taurine	143 mg
L-Carnitine	71 mg

Protein and amino acid requirements

The main objective of dietary therapy in type 1 tyrosinemia is to provide adequate nutrition that allows for normal growth and development, rigorosly controlling blood tyrosine levels. As a guide the aim should be to keep Tyrosine concentrations between 200 – 400 μmol/l up to the age of about 12 years, as described in the recommendations for the management of patients affected by type 1 tyrosinemia (Laet, C et al. Recommendations for the Management of Tyrosinemia Type 1. Orphanet Journal of Rare Diseases 8 (2013): 8. PMC. Web. 6 Mar. 2018).

NATURAL PROTEIN TOLERANCE EXPECTED IN HT-1

Age years	Proteins (g/day)	Proteins (g/kg/die)
<2	2–6	0,4-0,5
2-9	5-10	0,2-0,5
10-14	9-20	0,3-0,4
>15	11-25	0,2-0,4

Around 70-90% of total proteins must be contained in the amino acid mixture.

Note: tolerance to natural proteins must be defined individually. Intake of tyrosine / natural protein is altered depending on the plasma concentration of tyrosine (influenced by residual enzymatic activity and growth speed).

van Spronsen F.J., et al. Dietary Considerations in Tyrosinemia Type I. Adv Exp Med Biol. 2017;959:197-204.

NOTES

Glutaric Aciduria type 1 (GA)

Type 1 glutaric aciduria (GA-1) is a hereditary metabolic disease caused by glutaryl Co-A dehydrogenase deficiency involving metabolism of L-lysine, L-hydroxylysine, and L-tryptophan, leading to progressive neurological deterioration.

The enzymatic defect results in elevated concentrations of glutaric acid (GA), 3-hydroxyglutaric acid (3-OH-GA), glutaconic acid, and glutarylcarnitine.

Worldwide prevalence is of 1 of 100,000 newborns. It is more common in Amish communities of the Old Order, Irish nomads, Oji-Cree natives of Canada, and Lumbee Americans (Orphanet).

The majority of untreated subjects experience acute encephalopathies during the first 6 years of life, which are triggered by infectious diseases and febrile reactions to vaccinations and surgery. These crises provoke striatal lesions and dystonic movement disorders. In some patients, neurological disease can also develop without clinically apparent crises, at any age.

The possibility for neonatal screening of this pathology, which in Europe is available only in some countries, is of primary importance, since early diagnosis allows metabolic therapy to start immediately.

Treatment consists of a low lysine content diet with carnitine, associated with emergency treatment in the presence of concurrent diseases (catabolic activation). Treatment is effective and improves neurological outcomes in individuals who are promptly diagnosed; however, treatment after symptoms arise is less effective.

Dietary management must be adapted depending on the individual's age, through the intake of protein-free products and lysine-free amino acid mixtures with low tryptophan content, in order to meet the patient's protein requirements. This dietary therapy must be scrupulously observed for one's entire lifetime without interruption.

» ENZYME	Glutaryl Co-A dehydrogenase (1.3.99.7) deficiency
» TRANSMISSION	Autosomal recessive
» INCIDENCE	1: 110,000 (1)
» OMIM	231670
» TREATMENT	Dietary therapy

New recommendations for diagnosis and management of patients suffering from GA-1 were recently published (second revision) (1). The main objective of the second revision was to re-evaluate previous recommendations (2) and update with the latest data and important clinical aspects (1).

The recommendations can be accessed at:

https://link.springer.com/article/10.1007%2Fs10545-016-9999-9

References:

1. Boy, N. et al. Proposed recommendations for diagnosing and managing individuals with glutaric aciduria type I: second revision. J Inherit Metab Dis. 2017 Jan;40(1):75-101.
2. Kölker et al., J Inherit Metab Dis 30: 5-22, 2007b; J Inherit Metab Dis 34: 677-694, 2011.

GA medi2

200 g

GA

Amino acid mixture,
free of lysine-derived and with a low content of tryptophan for dietary management of glutaric aciduria type 1.

» INDICATIONS

For dietary management of children from the first year of age to adults, with known type 1 glutaric aciduria.

» DOSAGE AND ADMINISTRATION

Following the physician's prescription, taking into account age, body weight, and clinical conditions of the patient.
Recommended 5% w/v dilution (5 g of reconstituted product per 100 ml of liquid).

» INSTRUCTIONS FOR USE

Take the prescribed quantity of GA Medi 2, divided in 3-4 daily doses, dissolved in water or other allowed cold liquids, even flavored or added to food.

» STORAGE CONDITIONS

After use, close the container properly and store in a cool and dry place, away from light and sources of direct heat. The expiry date refers to the product correctly stored in its intact package.

» IMPORTANT WARNINGS

GA Medi 2 must be used under medical supervision, by individuals with known type 1 glutaric aciduria. GA Medi 2 cannot be used as the only source of food.
The product can result in health risks if taken by individuals that do not have the specific disorder for which it is indicated. Keep out of the reach of children.

NUTRITIONAL INFORMATION

food for special medical purposes

	per 100 g of powder	per 100 ml reconstituted at 5% (5 g in 100 ml of liquid)
Energy kJ/kcal	1416/333	71/17
Fats	0.0 g	0.0 g
of which saturated fatty acids	0.0 g	0.0 g
Carbohydrates	0.0 g	0.0 g
of which sugars	0.0 g	0.0 g
Protein equivalent	83.3 g	4.2 g
Salt	0.0 g	0.0 g

AMINO ACIDS

	per 100 g of powder	per 100 ml reconstituted at 5%
L-Alanine	8.14 g	407.0 mg
L-Arginine	6.60 g	330.0 mg
Ac. L-Aspartate	5.28 g	264.0 mg
L-Carnitine	192.00 mg	9.6 mg
L-Cystine	3.06 g	153.0 mg
L-Phenylalanine	6.10 g	305.0 mg
Glycine	5.28 g	264.0 mg
L-Glutamine	6.02 g	301.0 mg
L-Isoleucine	7.32 g	366.0 mg
L-Histidine	3.71 g	185.5 mg
L-Leucine	11.72 g	586.0 mg
L-Lysine	– g	– mg
L-Methionine	2.24 g	112.0 mg
L-Proline	7.12 g	356.0 mg
L-Serine	5.60 g	280.0 mg
Taurine	184.00 mg	9.2 mg
L-Tyrosine	7.10 g	355.0 mg
L-Threonine	6.10 g	305.0 mg
L-Tryptophan	0.10 g	4.7 mg
L-Valine	8.14 g	407.0 mg

GA medigel

720 g
30 per 24 g

NEUTRAL FLAVOR

Amino acid mixture free from lysine and with low tryptophan content with vitamins, minerals, selenium, taurine, and carnitine, indicated for the dietary management of type 1 Glutaric Aciduria.

» INDICATIONS

For the dietary management of children from six months of age and adults with known type 1 glutaric aciduria.

» DOSAGE AND ADMINISTRATION

According to the physician's prescription, taking into account age, body weight, and clinical conditions of the subject.

» INSTRUCTIONS FOR USE

GA Medigel can be consumed either as a gel or as a beverage.
To make a gel: pour the contents of one sachet of GA Medigel into a glass; if desired, add flavor to taste; add approximately 30 ml of cold water; mix well for about 10 seconds; to obtain a creamy gel, let the product stand for about 2 minutes.
To make a drink: pour the contents of one GA Medigel sachet into a glass; if desired, add flavor to taste; add approximately 80 ml of cold water; mix well for about 10 seconds; drink immediately.
GA Medigel can be consumed as is with a spoon or mixed with other allowed foods. For best results, when possible, GA Medigel should be prepared and consumed immediately. When necessary, the reconstituted and unused product can be kept for up to 24 hours in a refrigerator and mixed well before use. Once opened, the powder in the pouch should be completely consumed. Any excess product can be stored in a refrigerator and used within 24 hours.

» STORAGE CONDITIONS

Store in a cool and dry place, away from light and sources of direct heat. The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS

GA Medigel must be taken under medical supervision by individuals with known type I Glutaric Aciduria. GA Medigel must not be used as one's only source of food.
The product can result in health risks if taken by individuals who do not have the specific disorder for which it is indicated. Keep out of the reach of children.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g	per 24 g (1 sachet)
Energy kJ/kcal	1595/375	383/90
Fats	0 g	0 g
of which saturated fatty acids	0 g	0 g
Carbohydrates	45 g	11 g
of which sugars	25 g	6 g
Protein equivalent	41.7 g	10 g
Salt	1.1 g	0.3 g

VITAMINS	per 100 g	per 24 g (1 sachet)
Biotin	25 µg	6.0 µg
Choline	279 mg	67 mg
Folic acid	208 µg	49.9 µg
Niacin	14 mg	3.4 mg
Pantothenic acid	5.0 mg	1.2 mg
Riboflavin (Vitamin B2)	1.2 mg	0.29 mg
Thiamine (Vitamin B1)	1.0 mg	0.24 mg
Vitamin A	600 µg (RE)	144 µg (RE)
Vitamin B6	1.1 mg	0.26 mg
Vitamin B12	2.0 µg	0.48 µg
Vitamin C	63 mg	15 mg
Vitamin D	14.6 µg	3.5 µg
Vitamin E	9.0 mg (αTE)	2.2 mg (αTE)
Vitamin K	41 µg	9.8 µg

MINERALS	per 100 g	per 24 g (1 sachet)
Calcium	1083 mg	260 mg
Chloride	583 mg	140 mg
Chromium	71 µg	17 µg
Iron	14 mg	3.4 mg
Phosphorus	825 mg	198 mg
Iodine	138 µg	33.1 µg
Magnesium	167 mg	40 mg
Manganese	1.7 mg	0.41 mg
Molybdenum	50 µg	12 µg
Potassium	938 mg	225 mg
Copper	0.80 mg	0.19 mg
Selenium	35 µg	8.4 µg
Sodium	379 mg	91 mg
Zinc	11 mg	2.6 mg

AMINO ACIDS	per 100 g	per 24 g (1 sachet)
Ac. L-Aspartate	2.64 g	633.6 mg
L-Alanine	4.07 g	976.8 mg
L-Arginine	3.3 g	792 mg
L-Carnitine	0.096 g	23.04 mg
L-Cystine	1.53 g	367.2 mg
L-Phenylalanine	3.05 g	732 mg
Glycine	2.64 g	633.6 mg
L-Glutamine	3.01 g	722.4 mg
L-Isoleucine	3.66 g	878.4 mg
L-Histidine	1.855 g	445.2 mg
L-Leucine	5.86 g	1406.4 mg
L-Lysine	– g	– mg
L-Methionine	1.12 g	268.8 mg
L-Proline	3.56 g	854.4 mg
L-Serine	2.8 g	672 mg
L-Tyrosine	3.55 g	852 mg
L-Threonine	3.05 g	732 mg
L-Tryptophan	0.047 g	11.28 mg
L-Valine	4.07 g	976.8 mg
Taurine	0.092 g	22.08 mg

GA medi15

750 g
30 per 25 g

GA 3+

Lysine-free amino acid mixture with low tryptophan content with vitamins and minerals, indicated for dietary management of type 1 glutaric aciduria.

›› INDICATIONS
For dietary management of children from three years of age upwards and adults with known type 1 glutaric aciduria.

›› DOSAGE AND ADMINISTRATION
According to the physician's prescription, taking into account age, body weight and clinical condition of the subject.

›› INSTRUCTIONS FOR USE
Dissolve one sachet of GA Medi 15 in approximately 80 ml of water or other allowed liquids. GA Medi 15 can be flavored to taste. Once reconstituted, the product should be consumed immediately. When necessary, the reconstituted product can be kept for up to 24 hours in the refrigerator and mixed well before use.

›› STORAGE CONDITIONS
Store the product in a cool and dry place, away from light and sources of direct heat. GA Medi 15 are single-dose sachets.
Any prepared and unused product can be stored in the refrigerator and used within 24 hours. The expiry date refers to the product in an unopened, correctly stored package.

›› IMPORTANT WARNINGS
GA Medi 15 must be taken under medical supervision by individuals with known type 1 glutaric aciduria. GA Medi 15 must not be used as one's only source of food.
The product can result in health risks if taken by individuals who do not have the specific disorder for which it is indicated. Keep out of the reach of children.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g of powder	per 25 g (1 sachet)
Energy kJ/kcal	1550/365	388/91
Fats	0 g	0 g
of which saturated fatty acids	0 g	0 g
Carbohydrates	20 g	5 g
of which sugars	2.7 g	0.7 g
Protein equivalent	60 g	15 g
Salt	1.2 g	0.3 g

VITAMINS		
Biotin	188 µg	47 µg
Choline	600 mg	150 mg
Folic acid	400 µg	100 µg
Pantothenic acid	8.0 mg	2.0 mg
Niacin	24.8 mg	6.2 mg
Riboflavin (Vitamin B2)	2.3 mg	0.57 mg
Thiamine (Vitamin B1)	2.0 mg	0.50 mg
Vitamin A	832 µg (RE)	208 µg (RE)
Vitamin B12	4.8 µg	1.2 µg
Vitamin B6	2.8 mg	0.7 mg
Vitamin C	108 mg	27 mg
Vitamin D	13.2 µg	3.3 µg
Vitamin E	15.6 mg (αTE)	3.9 mg (αTE)
Vitamin K	100 µg	25 µg

MINERALS	per 100 g of powder	per 25 g (1 sachet)
Calcium	1196 mg	299 mg
Chloride	728 mg	182 mg
Chromium	88 µg	22 µg
Iron	21.6 mg	5.4 mg
Phosphorus	1068 mg	267 mg
Iodine	252 µg	63 µg
Magnesium	376 mg	94 mg
Manganese	3.2 mg	0.80 mg
Molybdenum	144 µg	36 µg
Potassium	940 mg	235 mg
Copper	2.2 mg	0.55 mg
Selenium	88 µg	22 µg
Sodium	508 mg	127 mg
Zinc	21.6 mg	5.4 mg

AMINO ACIDS		
L-Alanine	5.86 g	1465.2 mg
L-Arginine	4.75 g	1188.0 mg
Ac. L-Aspartate	3.80 g	950.4 mg
L-Carnitine	140 mg	34.6 mg
L-Cystine	2.20 g	550.8 mg
L-Phenylalanine	4.39 g	1098.0 mg
Glycine	3.80 g	950.4 mg
L-Glutamine	4.33 g	1083.6 mg
L-Isoleucine	5.27 g	1317.6 mg
L-Histidine	2.67 g	667.8 mg
L-Leucine	8.44 g	2109.6 mg
L-Lysine	– g	– mg
L-Methionine	1.61 g	403.2 mg
L-Proline	5.13 g	1281.6 mg
L-Serine	4.03 g	1008.0 mg
Taurine	132 mg	33.1 mg
L-Tyrosine	5.11 g	1278.0 mg
L-Threonine	4.39 g	1098.0 mg
L-Tryptophan	0.07 g	16.9 mg
L-Valine	5.86 g	1465.2 mg

GA medimicro3H

440 g
4 per 110 g

GA 3+

Slow-release micro-tablets.
Lysine-free amino acid mixture with low tryptophan content indicated for the dietary management of type 1 glutaric aciduria.

SLOW-RELEASE TECHNOLOGY

» INDICATIONS

For dietary management of subjects starting from three years of age with ascertained type 1 glutaric aciduria. Micro-tablets are suitable for children from three years of age upwards, depending on their ability to swallow, as determined by the attending physician.

» DOSAGE AND ADMINISTRATION

Following the physician's prescription, taking into account age, body weight, clinical condition of the subject, and the fact that the tablets are delayed-release. After being taken, GA Medimicro 3H releases the amino acids in the tablets over a three hour period. The cap of the jar contains about 13 g of micro-tablets (equal to approximately 8 g of protein equivalent).

» INSTRUCTIONS FOR USE

Take the prescribed amount with water or other allowed liquids. The micro-tablets have no taste; to retain this feature, it is recommended that they are not chewed, pulverized, or dissolved.

» STORAGE CONDITIONS

After use, close the jar properly and store it in a cool and dry place, below 25°C, away from light and sources of direct heat. The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS

GA Medimicro 3H must only be taken under medical supervision by individuals with known type I glutaric aciduria. GA Medimicro 3H must not be used as one's only source of food.
The product can result in health risks if taken by individuals who do not have the specific disorder for which it is indicated. Keep out of the reach of children.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g of micro-tablets
Energy kJ/kcal	1628/389
Fats	2.6 g
of which saturated fatty acids	2.6 g
Carbohydrates	12 g
of which sugars	0 g
Protein equivalent	65 g
Salt	0.02 g
of which sodium	7.9 mg
Fiber	10 g

AMINO ACIDS

L-Alanine	6.4 g
L-Arginine	5.0 g
Ac. L-Aspartate	4.0 g
L-Carnitine	152 mg
L-Cystine	2.4 g
L-Phenylalanine	4.8 g
Glycine	4.0 g
L-Glutamine	4.8 g
L-Isoleucine	5.8 g
L-Histidine	2.9 g
L-Leucine	9.3 g
L-Lysine	– g
L-Methionine	1.8 g
L-Proline	5.6 g
L-Serine	4.4 g
Taurine	145 mg
L-Tyrosine	5.5 g
L-Threonine	4.8 g
L-Tryptophan	0.1 g
L-Valine	6.4 g

Protein and amino acid requirements

Dietary management must be adapted depending on the individual's age, through the intake of protein-free products and lysine-free amino acid mixtures with low tryptophan content, in order to meet the patient's protein requirements. This dietary therapy must be scrupulously observed for one's entire lifetime without interruption.

METABOLIC MAINTENANCE TREATMENT (PROTOCOL PROPOSED BY THE "GUIDELINE DEVELOPMENTAL GROUP"). IF NORMAL GROWTH AND DEVELOPMENT ARE NOT ACHIEVED, THESE RECOMMENDATIONS MUST BE MODIFIED BASED ON INDIVIDUAL REQUIREMENTS.

Treatment	Age				
	0-6 months	7-12 months	1-3 years	4-6 years	> 6 years
1. Low lysine content diet					
Lysine (from natural protein)[a] (mg/kg per day)	100	90	80-60	60-50	Avoid the excessive intake of natural protein; use natural proteins with low lysine content; use "safety levels" as reference
Amino acid mix (protein)[b] (g/kg per day)	1.3-0.8	1.0-0.8	0.8	0.8	
Energy (kcal/kg per day)	115-80	95-80	95-80	90-80	
2. Micronutrient[c] (%)	≥ 100	≥ 100	≥ 100	≥ 100	≥ 100
3. Carnitine (mg/kg per day)	100	100	100	100-50	30-50

a. The lysine/protein ratio varies considerably in natural foods and thus the intake of natural proteins by children with a low-lysine diet depends upon the source of natural proteins. The intake of natural proteins is relatively high if patients use mainly natural protein sources with a low content of lysine.

b. Lysine-free amino acid mixtures with low tryptophan content should be supplemented with minerals and micronutrients as required in order to maintain normal levels. Adequate intake of essential amino acids is provided by natural proteins and by lysine-free amino acid supplements with low tryptophan content. The quantity of amino-acid based supplements is adjusted to reach at least the "safety levels" (Dewey et al. 1996).

c. In compliance with international dietary recommendations.

Kölker, S. et al. "Diagnosis and Management of Glutaric Aciduria Type I – Revised Recommendations." Journal of Inherited Metabolic Disease 34.3 (2011): 677–694. PMC. Web. 8 March 2018.

NOTES

Leucinosis
or Maple Syrup Urine Disease (MSUD)

Maple Syrup Urine Disease (MSUD), most commonly termed “leucinosis”, is a rare defect affecting the metabolism of branched-chain amino acids (BCAA). In particular, MSUD is due to the mutation of genes coding for E1a, E1b, and E2 subunits of the branched-chain alpha-keto acid dehydrogenase (BCKAD) complex, involved in the second step of enzymatic degradation of amino acids leucine, isoleucine, and valine.

The prevalence is estimated at around 1/150,000 newborns, based on published and unpublished data obtained from neonatal screening (Orphanet).

MSUD is typically characterized by difficulty feeding, lethargy, vomit, and wax, noticed immediately after birth (and later urine), that smells of maple syrup, followed, in the absence of treatment, by progressive encephalopathy and central respiratory failure. The four overlapping phenotypic subtypes are classic, intermediate, intermittent and thiamine-sensitive MSUD. Classic MSUD is the most serious form of MSUD and probably the most frequent (around 50-75% of cases).

In newborns, classic MSUD constitutes a medical emergency. Treatment of the acute phase requires considerable strengthening of protein anabolism through administration of glucose and insulin, and intravenous administration of lipids, monitoring of amino acids in plasma, and supplementation with isoleucine and valine. Hemodialysis is often necessary. Stabilized newborns need hypercaloric powdered milk without BCAA, restricted dietary intake of leucine, and careful outpatient monitoring.

Patients must follow a rigoros diet for their entire life, with low and controlled BCAA intake, depending on individual tolerance, through intake of protein-free products and amino acid mixtures devoid of BCAA, in order to meet the patient’s protein requirements (1).

» **ENZYME**	Branched-chain alpha-keto acid dehydrogenase (BCKAD) deficiency
» **TRANSMISSION**	Autosomal recessive
» **INCIDENCE**	1: 185,000 (1)
» **OMIM**	24860
» **TREATMENT**	Dietary therapy

Guidelines for nutritional management of MSUD (1) have been recently developed.

They can be freely accessed at:

www.mgmjournal.com/article/S1096-7192(14)00160-7/pdf

References:

1. Frazier, D. M. et al. Nutrition management guideline for maple syrup urine disease: An evidence- and consensus-based approach. Mol Genet Metab. 2014 Jul;112(3):210-7

MSUD medi 2

200 g | MSUD

Amino acid mixture free of leucine, valine, and isoleucine, indicated for dietary management of leucinosis.

» INDICATIONS
For dietary management of children from the first year of age to adults, with known Leucinosis.

» DOSAGE AND ADMINISTRATION
Following the doctor's prescription, taking into account age, body weight and clinical conditions of the patient.
Recommended 5% w/v dilution (5 g of reconstituted product per 100 ml of liquid).

» INSTRUCTIONS FOR USE
Take the prescribed quantity of MSUD Medi 2, divided in 3-4 daily doses, dissolved in water or other allowed cold liquids, even flavored or added to food.

» STORAGE CONDITIONS
After use, close the container properly and store in a cool and dry place, away from light and sources of direct heat. The expiry date refers to the product correctly stored in its intact package.

» IMPORTANT WARNINGS
MSUD Medi 2 must be used under medical supervision, by individuals with known leucinosis. MSUD Medi 2 cannot be used as the only source of food.
The product can result in health risks if taken by individuals that do not have the specific disorder for which it is indicated. Keep out of the reach of children.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g of powder	per 100 ml reconstituted at 5% (5 g in 100 ml of liquid)
Energy kJ/kcal	1416/333	71/17
Fats	0.0 g	0.0 g
of which saturated fatty acids	0.0 g	0.0 g
Carbohydrates	0.0 g	0.0 g
of which sugars	0.0 g	0.0 g
Protein equivalent	83.3 g	4.2 g
Salt	0.0 g	0.0 g

AMINO ACIDS

L-Alanine	10.22 g	511.0 mg
L-Arginine	9.70 g	485.0 mg
Ac. L-Aspartate	11.26 g	563.0 mg
L-Carnitine	92.00 mg	4.6 mg
L-Cystine	2.90 g	145.0 mg
L-Phenylalanine	5.46 g	273.0 mg
Glycine	8.12 g	406.0 mg
L-Glutamine	10.80 g	540.0 mg
L-Isoleucine	– g	– mg
L-Histidine	3.48 g	174.0 mg
L-Leucine	– g	– mg
L-Lysine	7.30 g	365.0 mg
L-Methionine	2.10 g	105.0 mg
L-Proline	8.58 g	429.0 mg
L-Serine	5.80 g	290.0 mg
Taurine	184.00 mg	9.2 mg
L-Tyrosine	5.80 g	290.0 mg
L-Threonine	5.22 g	261.0 mg
L-Tryptophan	2.90 g	145.0 mg
L-Valine	– g	– mg

MSUD medigel

720 g
30 per 24 g

NEUTRAL FLAVOR

Amino acid mixture free of valine, leucine and isoleucine with vitamins, minerals, selenium, taurine, and carnitine, indicated for the dietary management of leucinosis.

» INDICATIONS
For the dietary management of children from six months of age and of adults with known leucinosis.

» DOSAGE AND ADMINISTRATION
According to the physician's prescription, taking into account age, body weight, and clinical conditions of the subject.

» INSTRUCTIONS FOR USE
MSUD Medigel can be consumed as either a gel or a beverage.
To make a gel: pour the contents of one MSUD Medigel sachet into a glass; if desired, add flavor to taste; add approximately 30 ml of cold water; mix well for about 10 seconds; to obtain a creamy gel, let it stand for about 2 minutes.
To make a drink: pour the content of a MSUD Medigel sachet in a glass; if desired, add flavor as preferred; add around 80 ml of cold water; mix well for around 10 seconds; drink immediately.
MSUD Medigel can be consumed as is with a spoon or mixed with other allowed foods. For best results, where possible, MSUD Medigel should be prepared and consumed immediately. When necessary, the reconstituted and unused product can be kept for up to 24 hours in a refrigerator and mixed well before use. Once opened, the powder in the pouch should be completely consumed. Any excess product can be stored in a refrigerator and used within 24 hours.

» STORAGE CONDITIONS
Store in a cool and dry place, away from light and sources of direct heat. The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS
MSUD Medigel must only be taken under medical supervision by individuals with known leucinosis. MSUD Medigel cannot be used as the sole source of nutrition. The product can result in health risks if consumed by individuals who do not have the specific disorder for which it is indicated. Keep out of the reach of children.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g	per 24 g (1 sachet)
Energy kJ/kcal	1595/375	383/90
Fats	0 g	0 g
of which saturated fatty acids	0 g	0 g
Carbohydrates	45 g	11 g
of which sugars	25 g	6 g
Protein equivalent	41.7 g	10 g
Salt	1.1 g	0.3 g

VITAMINS	per 100 g	per 24 g (1 sachet)
Biotin	25 µg	6.0 µg
Choline	279 mg	67 mg
Folic acid	208 µg	49.9 µg
Niacin	14 mg	3.4 mg
Pantothenic acid	5.0 mg	1.2 mg
Riboflavin (Vitamin B2)	1.2 mg	0.29 mg
Thiamine (Vitamin B1)	1.0 mg	0.24 mg
Vitamin A	600 µg (RE)	144 µg (RE)
Vitamin B6	1.1 mg	0.26 mg
Vitamin B12	2.0 µg	0.48 µg
Vitamin C	63 mg	15 mg
Vitamin D	14.6 µg	3.5 µg
Vitamin E	9.0 mg (αTE)	2.2 mg (αTE)
Vitamin K	41 µg	9.8 µg

MINERALS	per 100 g	per 24 g (1 sachet)
Calcium	1083 mg	260 mg
Chloride	583 mg	140 mg
Chromium	71 µg	17 µg
Iron	14 mg	3.4 mg
Phosphorus	825 mg	198 mg
Iodine	138 µg	33.1 µg
Magnesium	167 mg	40 mg
Manganese	1.7 mg	0.41 mg
Molybdenum	50 µg	12 µg
Potassium	938 mg	225 mg
Copper	0.80 mg	0.19 mg
Selenium	35 µg	8.4 µg
Sodium	379 mg	91 mg
Zinc	11 mg	2.6 mg

AMINO ACIDS	per 100 g	per 24 g (1 sachet)
Ac. L-Aspartate	5.63 g	1351.20 mg
L-Alanine	5.11 g	1226.40 mg
L-Arginine	4.85 g	1164.00 mg
L-Carnitine	0.046 g	11.04 mg
L-Cystine	1.45 g	348.00 mg
L-Phenylalanine	2.73 g	655.20 mg
Glycine	4.06 g	974.40 mg
L-Glutamine	5.4 g	1296.00 mg
L-Isoleucine	– g	– mg
L-Histidine	1.74 g	417.60 mg
L-Leucine	– g	– mg
L-Lysine	3.65 g	876.00 mg
L-Methionine	1.05 g	252.00 mg
L-Proline	4.29 g	1029.60 mg
L-Serine	2.9 g	696.00 mg
L-Tyrosine	2.9 g	696.00 mg
L-Threonine	2.61 g	626.40 mg
L-Tryptophan	1.45 g	348.00 mg
L-Valine	– g	– mg
Taurine	0.092 g	22.08 mg

MSUD medi15

750 g
30 per 25 g

MSUD 3+

Amino acid mixture free of isoleucine, leucine, and valine with vitamins and minerals, indicated for the dietary management of leucinosis.

» INDICATIONS
For the dietary management of children from three years of age upwards and of adults with known leucinosis.

» DOSAGE AND ADMINISTRATION
According to the physician's prescription, taking into account age, body weight, and clinical condition of the subject.

» INSTRUCTIONS FOR USE
Dissolve one sachet of MSUD Medi 15 in approximately 80 ml of water or other allowed liquids.
MSUD Medi 15 can be flavored to taste. Once reconstituted, the product should be consumed immediately. When necessary, the reconstituted product can be kept for up to 24 hours in the refrigerator and mixed well before use.

» STORAGE CONDITIONS
Store the product in a cool and dry place, away from light and sources of direct heat. MSUD Medi 15 are single-dose sachets. Any prepared and unused product can be stored in the refrigerator and used within 24 hours. The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS
MSUD Medi 15 must only be taken under medical supervision by individuals with known leucinosis. MSUD Medi 15 cannot be used as one's only source of food.
The product can result in health risks if taken by individuals who do not have the specific disorder for which it is indicated. Keep out of the reach of children.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g of powder	per 25 g (1 sachet)
Energy kJ/kcal	1550/365	388/91
Fats	0 g	0 g
of which saturated fatty acids	0 g	0 g
Carbohydrates	20 g	5 g
of which sugars	2.7 g	0.7 g
Protein equivalent	60 g	15 g
Salt	1.2 g	0.3 g

VITAMINS		
Biotin	188 μg	47 μg
Choline	600 mg	150 mg
Folic acid	400 μg	100 μg
Pantothenic acid	8.0 mg	2.0 mg
Niacin	24.8 mg	6.2 mg
Riboflavin (Vitamin B2)	2.3 mg	0.57 mg
Thiamine (Vitamin B1)	2.0 mg	0.50 mg
Vitamin A	832 μg (RE)	208 μg (RE)
Vitamin B12	4.8 μg	1.2 μg
Vitamin B6	2.8 mg	0.7 mg
Vitamin C	108 mg	27 mg
Vitamin D	13.2 μg	3.3 μg
Vitamin E	15.6 mg (αTE)	3.9 mg (αTE)
Vitamin K	100 μg	25 μg

MINERALS	per 100 g of powder	per 25 g (1 sachet)
Calcium	1196 mg	299 mg
Chloride	728 mg	182 mg
Chromium	88 μg	22 μg
Iron	21.6 mg	5.4 mg
Phosphorus	1068 mg	267 mg
Iodine	252 μg	63 μg
Magnesium	376 mg	94 mg
Manganese	3.2 mg	0.80 mg
Molybdenum	144 μg	36 μg
Potassium	940 mg	235 mg
Copper	2.2 mg	0.55 mg
Selenium	88 μg	22 μg
Sodium	508 mg	127 mg
Zinc	21.6 mg	5.4 mg

AMINO ACIDS		
L-Alanine	7.36 g	1839.6 mg
L-Arginine	6.98 g	1746.0 mg
Ac. L-Aspartate	8.11 g	2026.8 mg
L-Carnitine	66 mg	16.6 mg
L-Cystine	2.09 g	522.0 mg
L-Phenylalanine	3.93 g	982.8 mg
Glycine	5.85 g	1461.6 mg
L-Glutamine	7.78 g	1944.0 mg
L-Isoleucine	– g	– mg
L-Histidine	2.51 g	626.4 mg
L-Leucine	– g	– mg
L-Lysine	5.26 g	1314.0 mg
L-Methionine	1.51 g	378.0 mg
L-Proline	6.18 g	1544.4 mg
L-Serine	4.18 g	1044.0 mg
Taurine	132 mg	33.1 mg
L-Tyrosine	4.18 g	1044.0 mg
L-Threonine	3.76 g	939.6 mg
L-Tryptophan	2.09 g	522.0 mg
L-Valine	– g	– mg

MSUD medimicro3H

440 g
4 per 110 g

MSUD 3+

Slow-release micro-tablets.
Amino acid mixture free of isoleucine, leucine, and valine, indicated for the dietary management of leucinosis.

SLOW-RELEASE TECHNOLOGY

» INDICATIONS

For the dietary management of subjects starting from three years of age with ascertained leucinosis. Micro-tablets are suitable for children from three years of age upwards, depending on their ability to swallow, as determined by the attending physician.

» DOSAGE AND ADMINISTRATION

According to the physician's prescription, taking into account age, body weight, clinical condition of the subject, and the fact that the tablets are slow-release. After being taken, MSUD Medimicro 3H releases the amino acids in the tablets over a three hour period. The cap of the jar contains about 13 g of micro-tablets (equal to approximately 8 g of protein equivalents).

» INSTRUCTIONS FOR USE

Take the prescribed amount with water or other allowed liquids. The micro-tablets have no taste; to retain this feature, it is recommended that they are not chewed, pulverized, or dissolved.

» STORAGE CONDITIONS

After use, close the container properly and store it in a cool and dry place, below 25°C, away from light and sources of direct heat. The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS

MSUD Medimicro 3H must only be taken under medical supervision by individuals with known leucinosis. MSUD Medimicro 3H must not be used as one's only source of food.
The product can result in health risks if taken by individuals who do not have the specific disorder for which it is indicated. Keep out of the reach of children.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g of micro-tablets
Energy kJ/kcal	1628/389
Fats	2.6 g
of which saturated fatty acids	2.6 g
Carbohydrates	12 g
of which sugars	0 g
Protein equivalent	65 g
Fiber	10 g
Salt	1 g

AMINO ACIDS

L-Aspartic acid	9 g
L-Alanine	8 g
L-Arginine	7.5 g
L-Cystine	2.3 g
L-Phenylalanine	4.2 g
Glycine	6.5 g
L-Glutamine	8.5 g
L-Histidine	2.7 g
L-Lysine	5.7 g
L-Methionine	1.6 g
L-Proline	6.7 g
L-Serine	4.5 g
L-Tyrosine	4.5 g
L-Threonine	4 g
L-Tryptophan	2.3 g
L-Leucine	– g
L-Isoleucine	– g
L-Valine	– g
Taurine	143 mg
L-Carnitine	71 mg

Protein and amino acid requirements

RECOMMENDED DAILY INTAKE OF BCAA NUTRIENTS, PROTEINS ENERGY AND LIQUIDS FOR INDIVIDUALS WITH MSUD WHEY THEY ARE IN GOOD HEALTH.

	Nutrient					
	LEU (mg/kg)	ILE (mg/kg)	VAL (mg/kg)	Protein (g/kg)	Energy (kcal/kg)	Liquid (ml/kg)
0 – 6 months	40-100	30-90	40-95	2,5-3,5	95-145	125-160
7 – 12 months	40-75	30-70	30-80	2,5-3,0	80-135	125-145
1 – 3 years	40-70	20-70	30-70	1,5-2,5	80-130	115-135
4 – 8 years	35-65	20-30	30-50	1,3-2,0	50-120	90-115
9 – 13 years	30-60	20-30	25-40	1,2-1,8	40-90	70-90
14 – 18 years	15-50	10-30	15-30	1,2-1,8	35-70	40-60
19 years	15-50	10-30	15-30	1,1-1,7	35-45	40-50

Frazier, D.M. et al. Nutrition management guideline for maple syrup urine disease: An evidence- and consensus- Mol Genet Metab. 2014 luglio;112(3):210-7

NOTES

Classical Homocystinuria (HOM)

Classical homocystinuria or cystathionine beta-synthase (CBS) deficiency is a multi-systemic disease, involving the eyes, skeleton, nervous system, and vascular apparatus.

CBS deficiency occurs worldwide, but its prevalence varies considerably depending on the ethnic group and investigation method. The actual population frequency is unknown, with estimates ranging between 1: 1800 and 1: 900,000, based on the incidence of birth of patients detected by neonatal screening and/or estimates from clinically confirmed patients (1).

CBS deficiency compromises the conversion of homocysteine to cystathione and leads to its accumulation. Patients with classical homocystinuria show a wide spectrum of severity. Some patients show severe multi-systemic disease that develops during childhood, while others are asymptomatic in adulthood. Patients show normal growth; in the absence of therapy, the disease is progressive. Eye anomalies include ectopic crystalline lens (85% of cases), associated with significant myopia. Skeletal alterations include genu valgum and high arches, dolichostenomelia, pectus excavatum or pectus carinatum, kyphosis or scoliosis, and osteoporosis. Thromboembolic complications, which affect small and large arteries and veins constitute the main cause of morbidity and mortality. Mental retardation rarely manifests before the first-second year of life. In 51% of cases, a clinically significant psychiatric illness was found. Liver, skin, and hair can be affected.

For patients diagnosed early, the treatment aims at preventing all complications of CBS deficiency, while maintaining normal growth and nutrition and allowing a good quality of life. For patient with a late diagnosis, the objective is to prevent further complications, in particular thromboembolism (1).

Three types of treatment are currently available. For patients who respond to pyridoxine, treatment involves the use of pyridoxine at pharmacological doses, in combination with supplementation with folic acid and vitamin B12. In patients who do not respond to pyridoxine, the recommended treatment involves a methionine-poor and cystine-rich diet, in combination with supplementation with pyridoxine, folic acid, and vitamin B12. Anhydrous betaine is a methyl donor, lowering homocysteine levels in patients; for this reason, it can be considered to complement one's diet.

Dietary management must be taken into consideration for all patients with CBS deficiency, unless homocysteine target levels are reached entirely by supplementation of pyridoxine. Diet can be used as either the sole treatment or additional therapy together with pyridoxine and/or betaine (1). The majority of patients who do not respond to pyridoxine require a low natural protein content diet, with methionine-free L-AA mixes. Lifelong treatment is required (1).

›› ENZYME	Cystathionine beta synthase (CBS) deficiency
›› TRANSMISSION	Autosomal recessive
›› INCIDENCE	Da 1: 1,800 a 1: 900,000 (1)
›› OMIM	236200
›› TREATMENT	For patients who respond to pyridoxine, treatment involves the use of pyridoxine at pharmacological doses, in combination with supplementation with folic acid and vitamin B12. In patients who do not respond to pyridoxine, the recommended treatment involves a methionine-poor and cystine-rich diet, in combination with supplementation with pyridoxine, folic acid, and vitamin B12.

Guidelines for the diagnosis and management of cystathionine beta-synthase deficiency (classic homocystinuria) have recently been developed. **They can be freely accessed at:**

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5203861/pdf/10545_2016_Article_9979.pdf

References:

1. Morris, A. M. et al. "Guidelines for the Diagnosis and Management of Cystathionine Beta-Synthase Deficiency." Journal of Inherited Metabolic Disease 40.1 (2017): 49–74. PMC. Web. 6 Mar. 2018.

NOTES

HOM medi 2

200 g | HOM

Amino acid mixture free of methionine, indicated for the dietary management of homocystinuria.

» INDICATIONS
For dietary management in children from the first year of age to adults, with known homocystinuria.

» DOSAGE AND ADMINISTRATION
Following the physician's prescription, taking into account age, body weight, and clinical conditions of the patient. Dilution recommended at 5% w/v (5 g of reconstituted product at 100 ml per 100 ml of liquid).

» INSTRUCTIONS FOR USE
Take the prescribed quantity of HOM Medi 2, divided in 3-4 daily doses, dissolved in water or other allowed cold liquids, even flavored or added to food.

» STORAGE CONDITIONS
After use, close the container properly and store in a cool and dry place, away from light and sources of direct heat. The expiry date refers to the product correctly stored in its intact package.

» IMPORTANT WARNINGS
HOM Medi 2 must be used under medical supervision, by individuals with known homocystinuria. HOM Medi 2 cannot be used as the only source of food.
The product can result in health risks if taken by individuals that do not have the specific disorder for which it is indicated. Keep out of the reach of children.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g of powder	per 100 ml reconstituted at 5% (5 g in 100 ml of liquid)
Energy kJ/kcal	1416/333	71/17
Fats	0.0 g	0.0 g
of which saturated fatty acids	0.0 g	0.0 g
Carbohydrates	0.0 g	0.0 g
of which sugars	0.0 g	0.0 g
Protein equivalent	83.3 g	4.2 g
Salt	0.0 g	0.0 g

AMINO ACIDS

L-Alanine	4.10 g	205.0 mg
L-Arginine	6.82 g	341.0 mg
Ac. L-Aspartate	9.12 g	456.0 mg
L-Carnitine	92.00 mg	4.6 mg
L-Cystine	2.74 g	137.0 mg
L-Phenylalanine	4.96 g	248.0 mg
Glycine	6.00 g	300.0 mg
L-Glutamine	7.90 g	395.0 mg
L-Isoleucine	6.42 g	321.0 mg
L-Histidine	4.28 g	214.0 mg
L-Leucine	10.50 g	525.0 mg
L-Lysine	7.18 g	359.0 mg
L-Methionine	– g	– mg
L-Proline	6.26 g	313.0 mg
L-Serine	4.80 g	240.0 mg
Taurine	184.00 mg	9.2 mg
L-Tyrosine	4.92 g	246.0 mg
L-Threonine	4.50 g	225.0 mg
L-Tryptophan	2.14 g	107.0 mg
L-Valine	7.06 g	353.0 mg

HOM medigel

720 g
30 per 24 g

HOM | 6+ months

NEUTRAL FLAVOR

Amino acid mixture free of methionine with vitamins, minerals, selenium, taurine, and carnitine, indicated for the dietary management of homocystinuria.

» INDICATIONS
For the dietary management of children from six months of age and of adults with known homocystinuria.

» DOSAGE AND ADMINISTRATION
According to the physician's prescription, taking into account age, body weight, and clinical condition of the subject.

» INSTRUCTIONS FOR USE
HOM Medigel can be consumed as either a gel or a beverage.
To make a gel: pour the contents of one pouch of HOM Medigel into a glass; if desired, add flavor to taste; add approximately 30 ml of cold water; mix well for about 10 seconds; to obtain a creamy gel, let stand for about 2 minutes.
To make a drink: pour the contents of one HOM Medigel sachet into a glass; if desired, add flavor to taste; add approximately 80 ml of cold water; mix well for about 10 seconds; drink immediately.
HOM Medigel can be consumed as is with a spoon or mixed with other allowed foods. For best results, when possible, HOM Medigel should be prepared and consumed immediately. When necessary, the reconstituted and unused product can be kept for up to 24 hours in a refrigerator and mixed well before use. Once opened, the powder in the pouch should be completely consumed. Any excess product can be stored in a refrigerator and used within 24 hours.

» STORAGE CONDITIONS
Store in a cool and dry place, away from light and sources of direct heat. The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS
HOM Medigel must only be taken under medical supervision by individuals with known homocystinuria HOM Medigel must not be used as one's only source of food. The product can result in health risks if consumed by individuals who do not have the specific disorder for which it is indicated. Keep out of the reach of children.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g	per 24 g (1 sachet)
Energy kJ/kcal	1595/375	383/90
Fats	0 g	0 g
of which saturated fatty acids	0 g	0 g
Carbohydrates	45 g	11 g
of which sugars	25 g	6 g
Protein equivalent	41.7 g	10 g
Salt	1.1 g	0.3 g

VITAMINS	per 100 g	per 24 g (1 sachet)
Biotin	25 µg	6.0 µg
Choline	279 mg	67 mg
Folic acid	208 µg	49.9 µg
Niacin	14 mg	3.4 mg
Pantothenic acid	5.0 mg	1.2 mg
Riboflavin (Vitamin B2)	1.2 mg	0.29 mg
Thiamine (Vitamin B1)	1.0 mg	0.24 mg
Vitamin A	600 µg (RE)	144 µg (RE)
Vitamin B6	1.1 mg	0.26 mg
Vitamin B12	2.0 µg	0.48 µg
Vitamin C	63 mg	15 mg
Vitamin D	14.6 µg	3.5 µg
Vitamin E	9.0 mg (αTE)	2.2 mg (αTE)
Vitamin K	41 µg	9.8 µg

MINERALS	per 100 g	per 24 g (1 sachet)
Calcium	1083 mg	260 mg
Chloride	583 mg	140 mg
Chromium	71 µg	17 µg
Iron	14 mg	3.4 mg
Phosphorus	825 mg	198 mg
Iodine	138 µg	33.1 µg
Magnesium	167 mg	40 mg
Manganese	1.7 mg	0.41 mg
Molybdenum	50 µg	12 µg
Potassium	938 mg	225 mg
Copper	0.80 mg	0.19 mg
Selenium	35 µg	8.4 µg
Sodium	379 mg	91 mg
Zinc	11 mg	2.6 mg

AMINO ACIDS		
Ac. L-Aspartate	4.56 g	1094.4 mg
L-Alanine	2.05 g	492 mg
L-Arginine	3.41 g	818.4 mg
L-Carnitine	0.046 g	11.04 mg
L-Cystine	1.37 g	328.8 mg
L-Phenylalanine	2.48 g	595.2 mg
Glycine	3 g	720 mg
L-Glutamine	3.95 g	948 mg
L-Isoleucine	3.21 g	770.4 mg
L-Histidine	2.14 g	513.6 mg
L-Leucine	5.25 g	1260 mg
L-Lysine	3.59 g	861.6 mg
L-Methionine	– g	– mg
L-Proline	3.13 g	751.2 mg
L-Serine	2.4 g	576 mg
L-Tyrosine	2.46 g	590.4 mg
L-Threonine	2.25 g	540 mg
L-Tryptophan	1.07 g	256.8 mg
L-Valine	3.53 g	847.2 mg
Taurine	0.092 g	22.08 mg

HOM medi15

750 g
30 per 25 g

HOM 3+

Amino acid mixture free of methionine with vitamins and minerals, indicated for the dietary management of homocystinuria.

» INDICATIONS
For the dietary management of children from three years of age upwards and of adults with known homocystinuria.

» DOSAGE AND ADMINISTRATION
According to the physician's prescription, taking into account age, body weight, and clinical condition of the subject.

» INSTRUCTIONS FOR USE
Dissolve one sachet of HOM Medi 15 in approximately 80 ml of water or other allowed liquids. HOM Medi 15 can be flavored to taste. Once reconstituted, the product should be consumed immediately. When necessary, the reconstituted product can be kept for up to 24 hours in the refrigerator and mixed well before use.

» STORAGE CONDITIONS
Store the product in a cool and dry place, away from light and sources of direct heat. HOM Medi 15 are single-dose sachets. Any prepared and unused product can be stored in the refrigerator and used within 24 hours. The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS
HOM Medi 15 must only be taken under medical supervision by individuals with known homocystinuria. HOM Medi 15 must not be used as one's only food source. The product can result in health risks if consumed by individuals who do not have the specific disorder for which it is indicated. Keep out of the reach of children.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g of powder	per 25 g (1 sachet)
Energy kJ/kcal	1550/365	388/91
Fats	0 g	0 g
of which saturated fatty acids	0 g	0 g
Carbohydrates	20 g	5 g
of which sugars	2.7 g	0.7 g
Protein equivalent	60 g	15 g
Salt	1.2 g	0.3 g

VITAMINS		
Biotin	188 µg	47 µg
Choline	600 mg	150 mg
Folic acid	400 µg	100 µg
Pantothenic acid	8.0 mg	2.0 mg
Niacin	24.8 mg	6.2 mg
Riboflavin (Vitamin B2)	2.3 mg	0.57 mg
Thiamine (Vitamin B1)	2.0 mg	0.50 mg
Vitamin A	832 µg (RE)	208 µg (RE)
Vitamin B12	4.8 µg	1.2 µg
Vitamin B6	2.8 mg	0.7 mg
Vitamin C	108 mg	27 mg
Vitamin D	13.2 µg	3.3 µg
Vitamin E	15.6 mg (αTE)	3.9 mg (αTE)
Vitamin K	100 µg	25 µg

MINERALS	per 100 g of powder	per 25 g (1 sachet)
Calcium	1196 mg	299 mg
Chloride	728 mg	182 mg
Chromium	88 µg	22 µg
Iron	21.6 mg	5.4 mg
Phosphorus	1068 mg	267 mg
Iodine	252 µg	63 µg
Magnesium	376 mg	94 mg
Manganese	3.2 mg	0.80 mg
Molybdenum	144 µg	36 µg
Potassium	940 mg	235 mg
Copper	2.2 mg	0.55 mg
Selenium	88 µg	22 µg
Sodium	508 mg	127 mg
Zinc	21.6 mg	5.4 mg

AMINO ACIDS		
L-Alanine	2.95 g	738.0 mg
L-Arginine	4.91 g	1227.6 mg
Ac. L-Aspartate	6.57 g	1641.6 mg
L-Carnitine	66 mg	16.6 mg
L-Cystine	1.97 g	493.2 mg
L-Phenylalanine	3.57 g	892.8 mg
Glycine	4.32 g	1080.0 mg
L-Glutamine	5.69 g	1422.0 mg
L-Isoleucine	4.62 g	1155.6 mg
L-Histidine	3.08 g	770.4 mg
L-Leucine	7.56 g	1890.0 mg
L-Lysine	5.17 g	1292.4 mg
L-Methionine	– g	– mg
L-Proline	4.51 g	1126.8 mg
L-Serine	3.46 g	864.0 mg
Taurine	132 mg	33.1 mg
L-Tyrosine	3.54 g	885.6 mg
L-Threonine	3.24 g	810.0 mg
L-Tryptophan	1.54 g	385.2 mg
L-Valine	5.08 g	1270.8 mg

HOM medimicro3H

440 g
4 per 110 g

HOM 3+

Slow-release micro-tablets.
Methionine-free amino acid mixture indicated for the dietary management of homocystinuria.

SLOW-RELEASE TECHNOLOGY

» INDICATIONS

For the dietary management of subjects starting from three years of age with ascertained homocystinuria. Micro-tablets are suitable for children from three years of age upwards, depending on their ability to swallow, as determined by the attending physician.

» DOSAGE AND ADMINISTRATION

According to the physician's prescription, taking into account age, body weight, the clinical condition of the subject, and the fact that the tablets are slow-release. After being taken, HOM Medimicro 3H releases the amino acids in the tablets over a three hour period. The cap of the container contains about 13 g of microtablets (equal to approximately 8 g of protein equivalent).

» INSTRUCTIONS FOR USE

Take the prescribed amount with water or other allowed liquids. The micro-tablets have no taste; to retain this feature, it is recommended that they are not chewed, pulverized, or dissolved.

» STORAGE CONDITIONS

After use, close the jar properly and store it in a cool and dry place, at a temperature below 25°C, away from light and sources of direct heat. The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS

HOM Medimicro 3H must only be taken under medical supervision by individuals with known Homocystinuria. HOM Medimicro 3H must not be used as one's only source of food. The product can result in health risks if consumed by individuals who do not have the specific disorder for which it is indicated. Keep out of the reach of children.

NUTRITIONAL INFORMATION

food for special medical purposes

	per 100 g of micro-tablets
Energy kJ/kcal	1628/389
Fats	2.6 g
of which saturated fatty acids	2.6 g
Carbohydrates	12 g
of which sugars	0 g
Protein equivalent	65 g
Fiber	10 g
Salt	1 g

AMINO ACIDS

L-Aspartic acid	7.1 g
L-Alanine	3.2 g
L-Arginine	5.4 g
L-Cystine	2.1 g
L-Phenylalanine	4 g
Glycine	4.7 g
L-Glutamine	6.1 g
L-Isoleucine	5 g
L-Histidine	3.3 g
L-Leucine	8.2 g
L-Lysine	5.6 g
L-Proline	5 g
L-Serine	3.7 g
L-Tyrosine	4 g
L-Threonine	3.5 g
L-Tryptophan	1.7 g
L-Valine	5.5 g
L-Methionine	– g
Taurine	143 mg
L-Carnitine	71 mg

Protein and amino acid requirements

There currently are no specific recommendations concerning the requirement for proteins and methionine-free amino acid mixtures. WHO/FAO/UNU recommendations (2007) can be used s a guide for total protein requirements (WHO et al 2007). However, research on PKU suggests that a greater intake of proteins is required compared to WHO recommendations to compensate for the suboptimal bioavailability of current L-AA preparations. It is recommended that L-AA supplement is administered in three or four doses a day to maximize nitrogen retention and achieve adequate growth (Morris, A. M. et al. “Guidelines for the Diagnosis and Management of Cystathionine Beta-Synthase Deficiency.” Journal of Inherited Metabolic Disease 40.1 (2017): 49-74. PMC. Web. 6 Mar. 2018).

NOTES

Urea Cycle Disorders (UCD)

Urea Cycle Disorders (UCDs) comprise a group of rare genetic disorders caused by a partial or total deficiency in mitochondrial enzymes or transporters involved in this metabolic pathway. Even though genetically distinct, UCDs share important features (metabolic imbalances with severe increase in blood ammonium levels) and are thus generally considered as a group. They are usually diagnosed at birth (neonatal onset), but can be identified later in life (late onset).

All defects underpinning the different disorders are transmitted through a recessive autosomal hereditary mechanism, with the exception of ornithine transcarbamylase (OTC) deficiency, whose inheritance is associated with the X chromosome. Among all disorders, OTC is the most commonly diagnosed deficiency (>50%) (1).

Unfortunately, there currently is no published information on with prevalence of the disease in the Italian population, and global prevalence data are not clear (1). The difficulty calculating prevalence lies in the fact that the available data does not allow identification of undiagnosed patients or those who die before enrolment (1). The available data suggests that the general frequency of urea cycle deficiencies and the distribution of each is similar in Europe and North America (1).

Overall, according to a recent study, based on neonatal screening data on more than 6 million births in the United States (US) and on data obtained by the two largest accredited registries on urea cycle (American and European), the total incidence for urea cycle disorders, including the late onset forms, is around 1: 35,000 (1).

The most important clinical manifestations, shared by all urea cycle disorders, can be attributed to hyperammonemia. Hyperammonemia is a toxic condition, and a delay in diagnosis and treatment can lead to severe and irreversible neurological damage, comprising neurocognitive alterations, convulsion, cerebral paralysis, and even death if left untreated; for this reason, early diagnosis and prompt therapeutic intervention must be considered a priority.

Long-term treatment (excluding the acute phase one, which is a genuine medical emergency) of patients with UCDs has the purpose of maintaining a metabolic compensation condition that ensures normal psycho-physical development and blocks repeated crises of hyperammonemia. In this context, diet undoubtedly plays an important role: to reduce nitrogen load on the urea cycle, a low-protein diet is necessary to ensure both a sufficient level of protein intake to allow normal growth, especially in pediatric patients, and adequate metabolism by various tissues and systems.

Even though some milder UCD forms can be treated exclusively through a restriction of proteins in food, combined with supplementation with specific amino acids (arginine, citrulline), in the majority of UCDs this approach is insufficient: it is necessary to intervene with the use of medicinal products that favor the removal of nitrogen through alternative routes to the urea cycle, which is a nitrogen scavenger (2).

» **ENZYME**	Variable, depends on the specific pathology
» **TRANSMISSION**	Autosomal recessive / X- Linked (OTC)
» **INCIDENCE**	1: 35,000 (1)
» **OMIM**	/
» **TREATMENT**	Dietary therapy / pharmacological therapy (if applicable)

UCDs are extremely serious pathologies, for which prompt diagnosis is essential. In order to promote awareness of these disorders, standardized treatment and the dissemination of best practice **European guidelines have been published, which were written by an international team of specialists** (2).

The document, published in the Orphanet Journal of Rare Diseases, has the objective of providing sufficient tools to manage acute and chronic episodes, guide diagnosis and monitoring, and assess the outcomes and psychosocial and ethical issues associated with UCDs (2).

Guidelines for the management and diagnosis of urea cycle disorders can be freely accessed at:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3488504/pdf/1750-1172-7-32.pdf

References:

1. *Summar, M. L. et al. "The Incidence of Urea Cycle Disorders." Molecular genetics and metabolism 110.0 (2013): 179–180. PMC. Web. 7 Mar. 2018.*

2. *Häberle, J. et al. "Suggested Guidelines for the Diagnosis and Management of Urea Cycle Disorders." Orphanet Journal of Rare Diseases 7 (2012): 32. PMC. Web. 7 Mar. 2018.*

NOTES

UCD medi 2

200 g | UCD | 1+

Essential amino acid mixture indicated for the dietary management of urea cycle disorders.

» INDICATIONS
For dietary management of children from the first year of age to adults, with a known urea cycle disorder.

» DOSAGE AND ADMINISTRATION
Following the doctor's prescription, taking into account age, body weight, and clinical conditions of the patient. Dilution recommended at 5% w/v (5 g of reconstituted product at 100 mlper 100 ml of liquid).

» INSTRUCTIONS FOR USE
Take the prescribed quantity of UCD Medi 2, divided in 3-4 daily doses, dissolved in water or other allowed cold liquids, even flavored or added to food.

» STORAGE CONDITIONS
After use, close the container properly and store in a cool and dry place, away from light and sources of direct heat. The expiry date refers to the product correctly stored in its intact package.

» IMPORTANT WARNINGS
UCD Medi 2 must be used under medical supervision, by individuals with known urea cycle disorder. UCD Medi 2 cannot be used as the only source of food.
The product can result in health risks if taken by individuals that do not have the specific disorder for which it is indicated. Keep out of the reach of children.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g of powder	per 100 ml reconstituted at 5% (5 g in 100 ml of liquid)
Energy kJ/kcal	1416/333	71/17
Fats	0.0 g	0.0 g
of which saturated fatty acids	0.0 g	0.0 g
Carbohydrates	0.0 g	0.0 g
of which sugars	0.0 g	0.0 g
Protein equivalent	83.3 g	4.2 g
Salt	0.0 g	0.0 g

AMINO ACIDS

L-Leucine	18.08 g	904.0 mg
L-Valine	14.20 g	710.0 mg
L-Lysine	12.90 g	645.0 mg
L-Threonine	10.40 g	520.0 mg
L-Isoleucine	10.10 g	505.0 mg
L-Tyrosine	9.40 g	470.0 mg
L-Phenylalanine	6.10 g	305.0 mg
L-Histidine	3.80 g	190.0 mg
L-Methionine	3.60 g	180.0 mg
L-Cystine	3.50 g	175.0 mg
L-Tryptophan	2.30 g	115.0 mg
L-Carnitine	0.30 g	15.0 mg

UCD medigel

720 g
30 per 24 g

UCD 6+ months

NEUTRAL FLAVOR

Essential amino acid mixture with vitamins and minerals, indicated for the dietary management of urea cycle disorders.

» INDICATIONS

For the dietary management of children from six months of age and of adults with known urea cycle disorder.

» DOSAGE AND ADMINISTRATION

According to the physician's prescription, taking into account age, body weight, and clinical condition of the subject.

» INSTRUCTIONS FOR USE

UCD Medigel can be consumed as either a gel or as a beverage.
To make a gel: pour the contents of one sachet of UCD Medigel into a glass; if desired, add flavor to taste; add approximately 30 ml of cold water; mix well for about 10 seconds; to obtain a creamy gel, let stand for about 2 minutes.
To make a drink: pour the content of an UCD Medigel sachet in a glass; if desired, add flavor as preferred; add around 80 ml of cold water; mix well for around 10 seconds; drink immediately.
UCD Medigel can be consumed as is with a spoon or mixed with other allowed foods. For best results, when possible, UCD Medigel should be prepared and consumed immediately. When necessary, the reconstituted and unused product can be kept for up to 24 hours in a refrigerator and mixed well before use. Once opened, the powder in the pouch should be completely consumed. Any excess product can be stored in a refrigerator and used within 24 hours.

» STORAGE CONDITIONS

Store in a cool and dry place, away from light and sources of direct heat. The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS

UCD Medigel must be taken under medical supervision by individuals with known urea cycle disorder. UCD Medigel must not be used as one's only source of food. The product can result in health risks if taken by individuals who do not have the specific disorder for which it is indicated. Keep out of the reach of children.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g	per 24 g (1 sachet)
Energy kJ/kcal	1595/375	383/90
Fats	0 g	0 g
of which saturated fatty acids	0 g	0 g
Carbohydrates	45 g	11 g
of which sugars	25 g	6 g
Protein equivalent	41.7 g	10 g
Salt	1.1 g	0.3 g

VITAMINS		
Biotin	25 µg	6.0 µg
Choline	279 mg	67 mg
Folic acid	208 µg	49.9 µg
Niacin	14 mg	3.4 mg
Pantothenic acid	5.0 mg	1.2 mg
Riboflavin (Vitamin B2)	1.2 mg	0.29 mg
Thiamine (Vitamin B1)	1.0 mg	0.24 mg
Vitamin A	600 µg (RE)	144 µg (RE)
Vitamin B6	1.1 mg	0.26 mg
Vitamin B12	2.0 µg	0.48 µg
Vitamin C	63 mg	15 mg
Vitamin D	14.6 µg	3.5 µg
Vitamin E	9.0 mg (αTE)	2.2 mg (αTE)
Vitamin K	41 µg	9.8 µg

MINERALS	per 100 g	per 24 g (1 sachet)
Calcium	1083 mg	260 mg
Chloride	583 mg	140 mg
Chromium	71 µg	17 µg
Iron	14 mg	3.4 mg
Phosphorus	825 mg	198 mg
Iodine	138 µg	33.1 µg
Magnesium	167 mg	40 mg
Manganese	1.7 mg	0.41 mg
Molybdenum	50 µg	12 µg
Potassium	938 mg	225 mg
Copper	0.80 mg	0.19 mg
Selenium	35 µg	8.4 µg
Sodium	379 mg	91 mg
Zinc	11 mg	2.6 mg

AMINO ACIDS		
L-Leucine	9.04 g	2169.56 mg
L-Lysine	6.45 g	1548.00 mg
L-Valine	7.10 g	1704.00 mg
L-Threonine	5.20 g	1248.00 mg
L -Isoleucine	5.05 g	1212.00 mg
L -Tyrosine	4.70 g	1128.00 mg
L-Phenylalanine	3.05 g	732.00 mg
L-Histidine	1.90 g	456.00 mg
L-Methionine	1.80 g	432.00 mg
L-Cystine	1.75 g	420.00 mg
L-Tryptophan	1.15 g	276.00 mg
L-Carnitine	0.15 g	36.00 mg

UCD medi15

750 g
30 per 25 g

UCD 3+

Essential amino acid mixture with vitamins and minerals indicated for the dietary management of urea cycle disorders.

» INDICATIONS
For the dietary management of children beyond 3 months of age and of adults with a known urea cycle disorder.

» DOSAGE AND ADMINISTRATION
According to the physician's prescription, taking into account age, body weight and clinical condition of the subject.

» INSTRUCTIONS FOR USE
Dissolve one sachet of UCD Medi 15 in approximately 80 ml of water or other allowed liquids. UCD Medi 15 can be flavored to taste. Once reconstituted, the product should be consumed immediately. Where necessary, the reconstituted product can be stored for 24 hours in the refrigerator and mixed well before use.

» STORAGE CONDITIONS
Store the product in a cool and dry place, away from light and sources of direct heat. UCD Medi 15 are single-dose sachets. Any prepared and unused product can be stored in the refrigerator and used within 24 hours.The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS
UCD Medi 15 must be taken under medical supervision by individuals with a known urea cycle disorder. UCD Medi 15 must not be used as one's only source of food. The product can result in health risks if taken by individuals who do not have the specific disorder for which it is indicated. Keep out of the reach of children.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g of powder	per 25 g (1 sachet)
Energy kJ/kcal	1550/365	388/91
Fats	0 g	0 g
of which saturated fatty acids	0 g	0 g
Carbohydrates	20 g	5 g
of which sugars	2.7 g	0.7 g
Protein equivalent	60 g	15 g
Salt	1.2 g	0.3 g

VITAMINS

	per 100 g of powder	per 25 g (1 sachet)
Biotin	188 µg	47 µg
Choline	600 mg	150 mg
Folic acid	400 µg	100 µg
Pantothenic acid	8.0 mg	2.0 mg
Niacin	24.8 mg	6.2 mg
Riboflavin (Vitamin B2)	2.3 mg	0.57 mg
Thiamine (Vitamin B1)	2.0 mg	0.50 mg
Vitamin A	832 µg (RE)	208 µg (RE)
Vitamin B12	4.8 µg	1.2 µg
Vitamin B6	2.8 mg	0.7 mg
Vitamin C	108 mg	27 mg
Vitamin D	13.2 µg	3.3 µg
Vitamin E	15.6 mg (αTE)	3.9 mg (αTE)
Vitamin K	100 µg	25 µg

MINERALS	per 100 g of powder	per 25 g (1 sachet)
Calcium	1196 mg	299 mg
Chloride	728 mg	182 mg
Chromium	88 µg	22 µg
Iron	21.6 mg	5.4 mg
Phosphorus	1068 mg	267 mg
Iodine	252 µg	63 µg
Magnesium	376 mg	94 mg
Manganese	3.2 mg	0.80 mg
Molybdenum	144 µg	36 µg
Potassium	940 mg	235 mg
Copper	2.2 mg	0.55 mg
Selenium	88 µg	22 µg
Sodium	508 mg	127 mg
Zinc	21.6 mg	5.4 mg

AMINO ACIDS

	per 100 g of powder	per 25 g (1 sachet)
L-Leucine	13.017 g	3254.3 mg
L-Valine	10.224 g	2556.0 mg
L-Lysine	9.288 g	2322.0 mg
L-Threonine	7.488 g	1872.0 mg
L-Isoleucine	7.272 g	1818.0 mg
L-Tyrosine	6.768 g	1692.0 mg
L-Phenylalanine	4.392 g	1098.0 mg
L-Histidine	2.736 g	684.0 mg
L-Methionine	2.592 g	648.0 mg
L-Cystine	2.52 g	630.0 mg
L-Tryptophan	1.656 g	414.0 mg
L-Carnitine	0.216 g	54.0 mg

UCD medimicro3H

440 g
4 per 110 g

UCD 3+

Slow-release micro-tablets.
Essential amino acid mixture indicated in the dietary management of urea cycle disorders.

SLOW-RELEASE TECHNOLOGY

›› INDICATIONS

For the dietary management of subjects starting from three years of age with ascertained urea cycle disorder. Micro-tablets are suitable for children from three years of age upwards, depending on their ability to swallow, as determined by the attending physician.

›› DOSAGE AND ADMINISTRATION

Following the physician's prescription, taking into account age, body weight, the clinical condition of the subject, and the fact that the tablets are slow-release.
After being taken, UCD Medimicro 3H releases the amino acids in the tablets over a three hour period. The cap of the jar contains about 13 g of micro-tablets (equal to approximately 8 g of protein equivalent).

›› INSTRUCTIONS FOR USE

Take the prescribed amount with water or other allowed liquids. The micro-tablets have no taste; to retain this feature, it is recommended that they are not chewed, pulverized, or dissolved.

›› STORAGE CONDITIONS

After use, close the container properly and store it in a cool and dry place, at a temperature below 25°C, away from light and sources of direct heat. The expiry date refers to the product in an unopened, correctly stored package.

›› IMPORTANT WARNINGS

UCD Medimicro 3H must be taken under medical supervision by individuals with a known urea cycle disorder. UCD Medimicro 3H must not be used as one's only source of food. The product can result in health risks if taken by individuals who do not have the specific disorder for which it is indicated. Keep out of the reach of children.

NUTRITIONAL INFORMATION

food for special medical purposes

	per 100 g of micro-tablets
Energy kJ/kcal	1628/389
Fats	2.6 g
of which saturated fatty acids	2.6 g
Carbohydrates	12 g
of which sugars	0 g
Protein equivalent	65 g
Fiber	10.0 g
Salt	0.02 g
of which sodium	7.9 mg

AMINO ACIDS

L-Cystine	3.03 g
L-Phenylalanine	5.15 g
L-Isoleucine	8.33 g
L-Histidine	3.26 g
L-Leucine	14.61 g
L-Lysine	10.45 g
L-Methionine	3.11 g
L-Tyrosine	7.80 g
L-Threonine	8.56 g
L-Tryptophan	2.13 g
L-Valine	11.58 g
L-Carnitine	250 mg

Protein and amino acid requirements

Long-term dietary management must minimize nitrogen load on the urea cycle. The quantity of natural proteins tolerated by each patient must be individually adjusted. WHO/FAO/UNU recommendations (2007) can be used to guide total protein requirements (WHO et al 2007). If intake is too low, supplementation with essential amino acids (EAA) can be indicated. Furthermore, an adequate energy supply must be guaranteed to prevent catabolism and consequent hyperammonemia. The 2007 FAO/WHO/UNU report can be used as guide for energy intake.

NOTES

Isovaleric acidemia (IVA)

Isovaleric acidemia (IVA) is an organic aciduria with recessive autosomal transmission, associated with isovaleryl CoA-dehydrogenase deficiency, associated with variable clinical profile, with onset at birth, with acute vomiting episodes, growth retardation, epileptic seizures, lethargy, acute pancreatitis, and mild-severe development retardation, or, with onset during childhood, with metabolic acidosis (provoked by prolonged fasting, greater intake of high-protein food or infections). In the absence of immediate treatment, it can be lethal. Intermittent chronic cases and asymptomatic individuals have also been described.

The main objective of IVA management is to reduce production and increase excretion of isovaleryl-CoA. This is obtained by (1):

1. limiting the intake of leucine through a low protein diet. If necessary, protein requirements are met by supplementing the diet with a leucine-free mixture of amino acids;
2. improvement of alternative metabolic pathways using carnithine and glycine (pharmacological treatment), conjugating isovaleryl-CoA to produce the non-toxic compounds isovalerylglycine and isovalerylcarnithine;
3. implementation of an emergency management protocol during episodes of metabolic stress (e.g. illness and fasting).

Accumulation of organic acids can lead to urea cycle inhibition with ensuing hyperammonemia. Hyperammonemia is a genuine medical emergency and treated in a specialist intensive care unit. The main objective of therapy is to rapidly reduce ammonium levels and prevent possible cerebral damage. Carglumic acid can be used in the treatment of IVA-linked hyperammonemia.

» **ENZYME**	Isovaleric acid CoA dehydrogenase deficiency.
» **TRANSMISSION**	Autosomal recessive
» **INCIDENCE**	Da 1: 62,500 a 1: 250,000 (EIMD)
» **OMIM**	243500
» **TREATMENT**	Dietary therapy / pharmacological therapy

A document has recently been published **describing the main dietary practises in the management of IVA**.

They can be freely accessed at:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5328917/pdf/main.pdf

References:

1. *Pinto, A. et al. "Dietary Practices in Isovaleric Acidemia: A European Survey." Molecular Genetics and Metabolism Reports 12 (2017): 16–22. PMC. Web. 7 Mar. 2018.*

IVA medi 2

200 g | IVA

Amino acid mixture free of leucine indicated for dietary management of isovaleric aciduria.

» INDICATIONS

For dietary management of children from the first year of age to adults with known isovaleric aciduria.

» DOSAGE AND ADMINISTRATION

According to the physician's prescription, taking into account age, body weight, and clinical condition of the subject. Dilution recommended at 5% w/v (5 g of reconstituted product at 100 ml per 100 ml of liquid).

» INSTRUCTIONS FOR USE

Take the prescribed quantity of IVA Medi 2, divided in 3-4 daily doses, dissolved in water or other allowed cold liquids, even flavored or added to food.

» STORAGE CONDITIONS

After use, close the container properly and store in a cool and dry place, away from light and sources of direct heat. The expiry date refers to the product correctly stored in its intact package.

» IMPORTANT WARNINGS

IVA Medi 2 must be used under medical supervision, by individuals with known isovaleric aciduria. IVA Medi 2 cannot be used as the only source of food.
The product can result in health risks if taken by individuals that do not have the specific disorder for which it is indicated. Keep out of the reach of children.

NUTRITIONAL INFORMATION

food for special medical purposes

	per 100 g of powder	per 100 ml reconstituted at 5% (5 g in 100 ml of liquid)
Energy kJ/kcal	1416/333	71/17
Fats	0.0 g	0.0 g
of which saturated fatty acids	0.0 g	0.0 g
Carbohydrates	0.0 g	0.0 g
of which sugars	0.0 g	0.0 g
Protein equivalent	83.3 g	4.2 g
Salt	0.0 g	0.0 g

AMINO ACIDS

	per 100 g of powder	per 100 ml reconstituted at 5%
L-Alanine	4.80 g	239.9 mg
L-Arginine	7.85 g	392.3 mg
Ac. L-Aspartate	6.61 g	330.7 mg
L-Carnitine	65 mg	3.2 mg
L-Cystine	2.85 g	142.7 mg
L-Phenylalanine	5.32 g	265.9 mg
Glycine	14.14 g	706.9 mg
L-Glutamine	8.75 g	437.7 mg
L-Isoleucine	2.72 g	136.2 mg
L-Histidine	4.54 g	227.0 mg
L-Leucine	– g	– mg
L-Lysine	6.87 g	343.7 mg
L-Methionine	1.95 g	97.3 mg
L-Proline	14.20 g	710.1 mg
L-Serine	4.41 g	220.5 mg
Taurine	195 mg	9.7 mg
L-Tyrosine	5.19 g	259.4 mg
L-Threonine	4.67 g	233.5 mg
L-Tryptophan	1.75 g	87.5 mg
L-Valine	3.11 g	155.6 mg

IVA medigel

720 g
30 per 24 g

IVA

6+ months

NEUTRAL FLAVOR

Amino acid mixture free of leucine with vitamins, minerals, selenium, taurine and carnitine, indicated for the dietary management of isovaleric aciduria.

» INDICATIONS For the dietary management of children from six months of age and of adults with a known urea cycle disorder.

» DOSAGE AND ADMINISTRATION According to the physician's prescription, taking into account age, body weight, and clinical condition of the subject.

» INSTRUCTIONS FOR USE IVA Medigel can be consumed as either a gel or as a beverage.
To make a gel: pour the contents of one sachet of IVA Medigel into a glass; if desired, add flavor to taste; add approximately 30 ml of cold water; mix well for about 10 seconds; to obtain a creamy gel, let stand for about 2 minutes.
To make a drink: pour the content of an IVA Medigel sachet in a glass; if desired, add flavor as preferred; add around 80 ml of cold water; mix well for around 10 seconds; drink immediately.
IVA Medigel can be consumed as is with a spoon or mixed with other allowed foods. For best results, when possible, IVA Medigel should be prepared and consumed immediately. When necessary, the reconstituted and unused product can be kept for up to 24 hours in a refrigerator and mixed well before use. Once opened, the powder in the pouch should be completely consumed. Any excess product can be stored in a refrigerator and used within 24 hours.

» STORAGE CONDITIONS Store in a cool and dry place, away from light and sources of direct heat. The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS IVA Medigel must be taken under medical supervision by individuals with known isovaleric aciduria. IVA Medigel must not be used as one's only source of food. The product can result in health risks if taken by individuals who do not have the specific disorder for which it is indicated. Keep out of the reach of children.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g	per 24 g (1 sachet)
Energy kJ/kcal	1595/375	383/90
Fats	0 g	0 g
of which saturated fatty acids	0 g	0 g
Carbohydrates	45 g	11 g
of which sugars	25 g	6 g
Protein equivalent	41.7 g	10 g
Salt	1.1 g	0.3 g

VITAMINS	per 100 g	per 24 g (1 sachet)
Biotin	25 µg	6.0 µg
Choline	279 mg	67 mg
Folic acid	208 µg	49.9 µg
Niacin	14 mg	3.4 mg
Pantothenic acid	5.0 mg	1.2 mg
Riboflavin (Vitamin B2)	1.2 mg	0.29 mg
Thiamine (Vitamin B1)	1.0 mg	0.24 mg
Vitamin A	600 µg (RE)	144 µg (RE)
Vitamin B6	1.1 mg	0.26 mg
Vitamin B12	2.0 µg	0.48 µg
Vitamin C	63 mg	15 mg
Vitamin D	14.6 µg	3.5 µg
Vitamin E	9.0 mg (αTE)	2.2 mg (αTE)
Vitamin K	41 µg	9.8 µg

MINERALS	per 100 g	per 24 g (1 sachet)
Calcium	1083 mg	260 mg
Chloride	583 mg	140 mg
Chromium	71 µg	17 µg
Iron	14 mg	3.4 mg
Phosphorus	825 mg	198 mg
Iodine	138 µg	33.1 µg
Magnesium	167 mg	40 mg
Manganese	1.7 mg	0.41 mg
Molybdenum	50 µg	12 µg
Potassium	938 mg	225 mg
Copper	0.80 mg	0.19 mg
Selenium	35 µg	8.4 µg
Sodium	379 mg	91 mg
Zinc	11 mg	2.6 mg

AMINO ACIDS	per 100 g	per 24 g (1 sachet)
Ac. L-Aspartate	3.307 g	793.8 mg
L-Alanine	2.399 g	575.9 mg
L-Arginine	3.923 g	941.6 mg
L-Carnitine	32 mg	7.8 mg
L-Cystine	1.427 g	342.4 mg
L-Phenylalanine	2.659 g	638.1 mg
Glycine	7.069 g	1696.5 mg
L-Glutamine	4.377 g	1050.6 mg
L-Isoleucine	1.362 g	326.8 mg
L-Histidine	2.27 g	544.7 mg
L-Leucine	– g	– mg
L-Lysine	3.437 g	824.9 mg
L-Methionine	0.973 g	233.5 mg
L-Proline	7.101 g	1704.3 mg
L-Serine	2.205 g	529.2 mg
L-Tyrosine	2.594 g	622.6 mg
L-Threonine	2.335 g	560.3 mg
L-Tryptophan	0.875 g	210.1 mg
L-Valine	1.556 g	373.5 mg
Taurine	97 mg	23.3 mg

IVA medi15

750 g
30 per 25 g

IVA 3+

Leucine-free amino acid mixture with vitamins and minerals, indicated for the dietary management of isovaleric aciduria.

» INDICATIONS For the dietary management of children from three years of age upwards and of adults with known isovaleric aciduria.

» DOSAGE AND ADMINISTRATION According to the physician's prescription, taking into account age, body weight, and clinical condition of the subject.

» INSTRUCTIONS FOR USE Dissolve an IVA Medi 15 sachet in around 80 ml of water or other allowed liquids. IVA Medi 15 can be flavored to taste. Once reconstituted, the product should be consumed immediately. When necessary, the reconstituted product can be kept for up to 24 hours in the refrigerator and mixed well before use.

» STORAGE CONDITIONS Store the product in a cool and dry place, away from light and direct heat sources. IVA Medi 15 sachets are single-use. Any prepared and unused product can be stored in the refrigerator and used within 24 hours. The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS IVA Medi 15 must be taken under medical supervision only by individuals with known isovaleric aciduria. IVA Medi 15 must not be used as one's only source of food. The product can result in health risks if taken by individuals who do not have the specific disorder for which it is indicated. Keep out of the reach of children.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g of powder	per 25 g (1 sachet)
Energy kJ/kcal	1550/365	388/91
Fats	0 g	0 g
of which saturated fatty acids	0 g	0 g
Carbohydrates	20 g	5 g
of which sugars	2.7 g	0.7 g
Protein equivalent	60 g	15 g
Salt	1.2 g	0.3 g

VITAMINS		
Biotin	188 μg	47 μg
Choline	600 mg	150 mg
Folic acid	400 μg	100 μg
Pantothenic acid	8.0 mg	2.0 mg
Niacin	24.8 mg	6.2 mg
Riboflavin (Vitamin B2)	2.3 mg	0.57 mg
Thiamine (Vitamin B1)	2.0 mg	0.50 mg
Vitamin A	832 μg (RE)	208 μg (RE)
Vitamin B12	4.8 μg	1.2 μg
Vitamin B6	2.8 mg	0.7 mg
Vitamin C	108 mg	27 mg
Vitamin D	13.2 μg	3.3 μg
Vitamin E	15.6 mg (αTE)	3.9 mg (αTE)
Vitamin K	100 μg	25 μg

MINERALS	per 100 g of powder	per 25 g (1 sachet)
Calcium	1196 mg	299 mg
Chloride	728 mg	182 mg
Chromium	88 μg	22 μg
Iron	21.6 mg	5.4 mg
Phosphorus	1068 mg	267 mg
Iodine	252 μg	63 μg
Magnesium	376 mg	94 mg
Manganese	3.2 mg	0.80 mg
Molybdenum	144 μg	36 μg
Potassium	940 mg	235 mg
Copper	2.2 mg	0.55 mg
Selenium	88 μg	22 μg
Sodium	508 mg	127 mg
Zinc	21.6 mg	5.4 mg

AMINO ACIDS		
L-Alanine	3.45 g	863.8 mg
L-Arginine	5.65 g	1412.5 mg
Ac. L-Aspartate	4.76 g	1190.7 mg
L-Carnitine	47 mg	11.7 mg
L-Cystine	2.05 g	513.6 mg
L-Phenylalanine	3.83 g	957.2 mg
Glycine	10.18 g	2544.7 mg
L-Glutamine	6.30 g	1575.9 mg
L-Isoleucine	1.96 g	490.3 mg
L-Histidine	3.27 g	817.1 mg
L-Leucine	– g	– mg
L-Lysine	4.95 g	1237.4 mg
L-Methionine	1.40 g	350.2 mg
L-Proline	10.23 g	2556.4 mg
L-Serine	3.17 g	793.8 mg
Taurine	140 mg	35.0 mg
L-Tyrosine	3.73 g	933.9 mg
L-Threonine	3.36 g	840.5 mg
L-Tryptophan	1.26 g	315.2 mg
L-Valine	2.24 g	560.3 mg

IVA medimicro3H

440 g
4 per 110 g

IVA 3+

Slow-release micro-tablets.
Leucine-free amino acid mixture indicated for the dietary management of isovaleric aciduria.

SLOW-RELEASE TECHNOLOGY

›› INDICATIONS

For the dietary management of subjects starting from three years of age with a certained isovaleric aciduria. Micro-tablets are suitable for children from three years of age upwards, depending on their ability to swallow, as determined by the attending physician.

›› DOSAGE AND ADMINISTRATION

According to the physician's prescription, taking into account age, body weight, the clinical condition of the subject, and the fact that the tablets are slow-release. After being taken, IVA Medimicro 3H releases the amino acids in the tablets over a three hour period. The cap of the jar contains about 13 g of micro-tablets (equal to approximately 8 g of protein equivalent).

›› INSTRUCTIONS FOR USE

Take the prescribed amount with water or other allowed liquids. The micro-tablets have no taste; to retain feature not to be lost, it is recommended that they are not chewed, pulverized, or dissolved.

›› STORAGE CONDITIONS

After use, close the container properly and store it in a cool and dry place, below 25°C, away from light and sources of direct heat. The expiry date refers to the product in an unopened, correctly stored package.

›› IMPORTANT WARNINGS

IVA Medimicro 3H must only be taken under medical supervision by individuals with isovaleric aciduria. IVA Medimicro 3H must not be used as one's only source of food. The product can result in health risks if taken by individuals who do not have the specific disorder for which it is indicated. Keep out of the reach of children.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g of micro-tablets
Energy kJ/kcal	1628/389
Fats	2.6 g
of which saturated fatty acids	2.6 g
Carbohydrates	12 g
of which sugars	0 g
Protein equivalent	65 g
Fiber	10 g
Salt	1 g

AMINO ACIDS

L-Aspartic acid	5 g
Alanine	3.8 g
Arginine	6 g
Cystine	2.3 g
Phenylalanine	4 g
Glycine	11.2 g
Glutamine	6.9 g
Isoleucine	2.2 g
Histidine	3.6 g
Lysine	5.4 g
Methionine	1.5 g
Proline	11.2 g
Serine	3.5 g
Tyrosine	4 g
Threonine	3.7 g
Tryptophan	1.4 g
Valine	2.5 g
Leucine	– g
Taurine	154 mg
Carnitine	51 mg

Protein and amino acid requirements

A recent survey demonstrated broad differences in dietary practices associated with the management of IVA across Europe. Following are data comparing dietary therapy of different European centers (using/not using leucine-free amino acid mixes; LFAA): total proteins (g/kg), natural proteins (g/kg), LFAA (g/kg) and % proteins provided by LFAA compared to the total protein prescription.

DESCRIPTIVE STATISTICS COMPARING CENTERS (USING/NOT USING LFAA) FOR THE DIETARY PRESCRIPTION OF: TOTAL PROTEINS (G/KG), NATURAL PROTEIN (G/KG), LFAA(G/KG) AND % OF PROTEINS PROVIDED BY LFAA COMPARED TO TOTAL PROTEIN PRESCRIPTION

	Centers using LFAA				
	0-6 months (n=2)	7-12 months (n=2)	1-10 years (n=40)	11-16 years (n=16)	>16 years (n=5)
Total protein (g/kg)					
Median	2.2	1.9	1.7	1.1	1.1
Min	1.7	1.8	0.9	1.0	1.0
Max	2.6	2.0	2.3	1.5	1.5
Natural protein (g/kg)					
Median	1.1	0.4	1.0	0.7	0.7
Min	1.0	0.4	0.4	0.4	0.4
Max	1.1	0.5	1.9	1.0	0.8
LFAA (g/kg)					
Median	1.1	1.5	0.7	0.5	0.6
Min	0.7	1.3	0.2	0.4	0.3
Max	1.5	1.7	1.2	0.6	0.8
% quantity of total protein compared to LFAA					
Median	50	77	44	42	48
Min	41	72	17	29	27
Max	58	82	75	60	64

	Centers that do not use LFAA				
	0-6 months (n=3)	7-12 months (n=0)	1-10 years (n=31)	11-16 years (n=15)	>16 years (n=19)
Total protein (g/kg)					
Median	1.6	Not reported	1.3	1.0	0.9
Min	1.4		1.0	0.2	0.5
Max	1.8		2.0	1.8	1.1
Natural protein (g/kg)					
Median	1.6	Not reported	1.3	1.0	0.9
Min	1.4		1.0	0.2	0.5
Max	1.8		2.0	1.8	1.1
LFAA (g/kg)					
Median	0	Not reported	0	0	0
Min	0		0	0	0
Max	0		0	0	0
% quantity of total protein compared to LFAA					
Median	0	Not reported	0	0	0
Min	0		0	0	0
Max	0		0	0	0

AA = Leucine-free L-amino acids

n = number of patients

Pinto, A. et al. "Dietary Practices in Isovaleric Acidemia: A European Survey." Molecular Genetics and Metabolism Reports 12 (2017): 16-22. PMC. Web. 7 marzo 2018.

Methylmalonic acidemia (MMA) and propionic acidemia (PA)

Methylmalonic and propionic acidemia (MMA/PA) are congenital disorders resulting in errors in the catabolism of propionate, caused by defects in enzymes methylmalonyl-CoA mutase (MUT) or propionyl-CoA carboxylase (PCC); the disorders are characterized by the accumulation of metabolites arising from catabolism of branched-chain amino acids such as a 3- hydroxyproprionic acid, methylcitric acid and/or methylmalonic acid in plasma, urine, and other body fluids.

MMA has an estimated incidence of ~ 1: 50,000 and PA of ~1: 100,000 - 150,000 (1).

Patients with complete enzymatic deficiency show acute deterioration in their general clinical conditions in the first days or weeks of life, along with metabolic acidosis and hyperammonemia, progressing to coma and death if untreated. Cases of late onset of MMA and PA can manifest at any age, i.e. in childhood or even later, with a more heterogeneous clinical profile. The mental outcome tends to be worse in and late complications include chronic kidney disease nearly exclusively in MMA and cardiomyopathy mainly in PA (1).

The overall outcome is poor notwithstanding the existence of apparently effective therapy with a low protein content and carnithine, except for MMA forms that are responsive to vitamin B12 (mainly cblA type MMA), which have a better outcome if diagnosed promptly and treated adequately (1).

Prognosis is strongly influenced by duration of coma and the ammonium peak in the blood, especially in newborns; patients must be identified and adequately treated as soon as possible (1).

Long-term treatment (chronic, not in the acute phase) has the objectives of achieving normal development and preventing metabolic imbalance episodes, while providing a good quality of life and avoiding side effects and complications (1).

Standard therapy includes:

- L-carnitine
- Antibiotics to reduce intestinal flora
- Low protein diet with reduction in the level of Ile, Val, Met, and Thr (based on individual protein requirements)
- Supplemented with vitamins and minerals

Key dietary management principles are similar for patients with MMA and PA. Diet aside, the most common medical therapies used in the long-term treatment of MMA/PA are L-carnitine, antibiotics to reduce intestinal flora, and vitamin B12, as previously reported (1).

» **ENZYME**	Methylmalonyl-CoA mutase (MCM) or propionyl-CoA carboxylase (PCC) deficiency.
» **TRANSMISSION**	Autosomal recessive
» **INCIDENCE**	1: 50,000 MMA | 1: 100,000 - 150,000 PA (1)
» **OMIM**	277380 277400 277410 614857 MMA | 606054 PA
» **TREATMENT**	Dietary therapy / pharmacological therapy

Guidelines for diagnosis and management of MMA and PA have recently been published. The objective of this document is to standardize diagnosis, therapy, and long-term management of MMA/PA.

Guidelines for diagnosis and management of MMA/PA are freely available at:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4180313/pdf/13023_2014_Article_130.pdf

References:

1. Baumgartner, M. R. et al. "Proposed Guidelines for the Diagnosis and Management of Methylmalonic and Propionic Acidemia." Orphanet Journal of Rare Diseases 9 (2014): 130. PMC. Web. 7 Mar. 2018.

NOTES

MMA/ PA medi 2

200 g

Amino acid mixture free of methionine, threonine, valine and with low isoleucine content indicated in the dietary management of methylmalonic/propionic acidemia.

» INDICATIONS
For dietary management in children from the first year of age to adults with known methylmalonic/propionic acidemia.

» DOSAGE AND ADMINISTRATION
Following the physician's prescription, taking into account age, body weight, and clinical conditions of the patient.
Recommended 5% w/v dilution (5 g of reconstituted product per 100 ml of liquid).

» INSTRUCTIONS FOR USE
Take the prescribed quantity of MMA/PA Medi 2, divided in 3-4 daily doses, dissolved in water or other allowed cold liquids, even flavored or added to food.

» STORAGE CONDITIONS
After use, close the container properly and store in a cool and dry place, away from light and sources of direct heat. The expiry date refers to the product correctly stored in its intact package.

» IMPORTANT WARNINGS
MMA/PA Medi 2 must be used under medical supervision, by individuals with known methylmalonic/propionic acidemia. MMA/PA Medi 2 must not be used as one's only source of food. This product can result in health risks if consumed by individuals who do not have the specific disorder for which it is indicated. Keep out of the reach of children.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g of powder	per 100 ml reconstituted at 5% (5 g in 100 ml of liquid)
Energy kJ/kcal	1416/333	71/17
Fats	0.0 g	0.0 g
of which saturated fatty acids	0.0 g	0.0 g
Carbohydrates	0.0 g	0.0 g
of which sugars	0.0 g	0.0 g
Protein equivalent	83.3 g	4.2 g
Salt	0.0 g	0.0 g
AMINO ACIDS		
L-Alanine	8.30 g	415.0 mg
L-Arginine	8.60 g	430.0 mg
Ac. L-Aspartate	13.80 g	690.0 mg
L-Carnitine	92.00 mg	4.6 mg
L-Cystine	3.54 g	177.0 mg
L-Phenylalanine	5.56 g	278.0 mg
Glycine	3.90 g	195.0 mg
L-Glutamine	10.12 g	506.0 mg
L-Isoleucine	0.30 g	15.0 mg
L-Histidine	5.56 g	278.0 mg
L-Leucine	13.16 g	658.0 mg
L-Lysine	9.16 g	458.0 mg
L-Methionine	– g	– mg
L-Proline	4.04 g	202.0 mg
L-Serine	5.86 g	293.0 mg
Taurine	184.00 mg	9.2 mg
L-Tyrosine	5.56 g	278.0 mg
L-Threonine	– g	– mg
L-Tryptophan	2.22 g	111.0 mg
L-Valine	– g	– mg

MMA/PA medigel

720 g
30 per 24 g

MMA /PA 6+ months

NEUTRAL FLAVOR

Amino acid mixture free of methionine, threonine, valine and with low isoleucine content with vitamins, minerals, selenium, taurine and carnitine, indicated for the dietary management of methylmalonyl acidemia/propionic acidemia.

» INDICATIONS For the dietary management of children from six months of age and of adults with known methymalonic acidemia/propionic acidemia.

» DOSAGE AND ADMINISTRATION According to the physician's prescription, taking into account age, body weight, and clinical condition of the subject.

» INSTRUCTIONS FOR USE MMA/PA Medigel can be taken both as gel and as beverage.
To make a gel: pour the contents of one MMA/PA Medigel sachet into a glass; if desired, add flavor to taste; add approximately 30 ml of cold water; mix well for about 10 seconds; to obtain a creamy gel, let stand for about 2 minutes.
To make a drink: pour the contents of one MMA/PA Medigel sachet into a glass; if desired, add flavor to taste; add approximately 80 ml of cold water; mix well for about 10 seconds; drink immediately.
Reconstituted MMA/PA Medigel can be consumed as is with a spoon or mixed with other allowed foods. For best results, where possible, MMA/PA Medigel should be prepared and consumed immediately. When necessary, the reconstituted and unused product can be kept for up to 24 hours in a refrigerator and mixed well before use. Once opened, the powder in the pouch should be completely consumed. Any excess product should be stored in a refrigerator and used within 24 hours.

» STORAGE CONDITIONS Store in a cool and dry place, away from light and sources of direct heat. The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS MMA/PA Medigel must be taken only under medical supervision by individuals with known methymalonic acidemia/propionic acidemia. MMA/PA Medigel must not be used as one's only source of food. The product can result in health risks if consumed by individuals who do not have the specific disorder for which it is indicated. Keep out of the reach of children.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g	per 24 g (1 sachet)
Energy kJ/kcal	1595/375	383/90
Fats	0 g	0 g
of which saturated fatty acids	0 g	0 g
Carbohydrates	45 g	11 g
of which sugars	25 g	6 g
Protein equivalent	41.7 g	10 g
Salt	1.1 g	0.3 g

VITAMINS	per 100 g	per 24 g (1 sachet)
Biotin	25 μg	6.0 μg
Choline	279 mg	67 mg
Folic acid	208 μg	49.9 μg
Niacin	14 mg	3.4 mg
Pantothenic acid	5.0 mg	1.2 mg
Riboflavin (Vitamin B2)	1.2 mg	0.29 mg
Thiamine (Vitamin B1)	1.0 mg	0.24 mg
Vitamin A	600 μg (RE)	144 μg (RE)
Vitamin B6	1.1 mg	0.26 mg
Vitamin B12	2.0 μg	0.48 μg
Vitamin C	63 mg	15 mg
Vitamin D	14.6 μg	3.5 μg
Vitamin E	9.0 mg (αTE)	2.2 mg (αTE)
Vitamin K	41 μg	9.8 μg

MINERALS	per 100 g	per 24 g (1 sachet)
Calcium	1083 mg	260 mg
Chloride	583 mg	140 mg
Chromium	71 μg	17 μg
Iron	14 mg	3.4 mg
Phosphorus	825 mg	198 mg
Iodine	138 μg	33.1 μg
Magnesium	167 mg	40 mg
Manganese	1.7 mg	0.41 mg
Molybdenum	50 μg	12 μg
Potassium	938 mg	225 mg
Copper	0.80 mg	0.19 mg
Selenium	35 μg	8.4 μg
Sodium	379 mg	91 mg
Zinc	11 mg	2.6 mg

AMINO ACIDS		
Ac. L-Aspartate	6.9 g	1656 mg
L-Alanine	4.15 g	996 mg
L-Arginine	4.3 g	1032 mg
L-Carnitine	0.046 g	11.04 mg
L-Cystine	1.77 g	424.8 mg
L-Phenylalanine	2.78 g	667.2 mg
Glycine	1.95 g	468 mg
L-Glutamine	5.06 g	1214.4 mg
L-Isoleucine	0.15 g	36 mg
L-Histidine	2.78 g	667.2 mg
L-Leucine	6.58 g	1579.2 mg
L-Lysine	4.58 g	1099.2 mg
L-Methionine	– g	– mg
L-Proline	2.02 g	484.4 mg
L-Serine	2.93 g	703.2 mg
L-Tyrosine	2.78 g	667.2 mg
L-Threonine	– g	– mg
L-Tryptophan	1.11 g	266.4 mg
L-Valine	– g	– mg
Taurine	0.092 g	22.08 mg

MMA/PA medi15

750 g
30 per 25 g

MMA / PA 3+

Amino acid mixture free of methionine, threonine, valine and with low isoleucine content with vitamins and minerals, indicated for the dietary management of methymalonic acidemia/propionic acidemia.

» INDICATIONS For the dietary management of children from three years of age upwards and of adults with known methymalonic acidemia/ propionic acidemia.

» DOSAGE AND ADMINISTRATION According to the physician's prescription, taking into account age, body weight, and clinical condition of the subject.

» INSTRUCTIONS FOR USE Dissolve one sachet of MMA/PA Medi 15 in approximately 80 ml of water or other allowed liquids.
MMA/PA Medi 15 can be flavored to taste. Once reconstituted, the product should be consumed immediately. When necessary, the reconstituted product can be kept for up to 24 hours in the refrigerator and mixed well before use.

» STORAGE CONDITIONS Store the product in a cool and dry place, away from light and sources of direct heat. MMA/PA Medi 15 are single-dose sachets. Any prepared and unused product can be stored in the refrigerator and used within 24 hours. The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS MMA/PA Medi 15 must be taken only under medical supervision by individuals with known methymalonic acidemia/propionic acidemia. MMA/PA Medi 15 must not be used as one's only source of food. The product can result in health risks if taken by individuals who do not have the specific disorder for which it is indicated. Keep out of the reach of children.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g of powder	per 25 g (1 sachet)
Energy kJ/kcal	1550/365	388/91
Fats	0 g	0 g
of which saturated fatty acids	0 g	0 g
Carbohydrates	20 g	5 g
of which sugars	2.7 g	0.7 g
Protein equivalent	60 g	15 g
Salt	1.2 g	0.3 g

VITAMINS		
Biotin	188 µg	47 µg
Choline	600 mg	150 mg
Folic acid	400 µg	100 µg
Pantothenic acid	8.0 mg	2.0 mg
Niacin	24.8 mg	6.2 mg
Riboflavin (Vitamin B2)	2.3 mg	0.57 mg
Thiamine (Vitamin B1)	2.0 mg	0.50 mg
Vitamin A	832 µg (RE)	208 µg (RE)
Vitamin B12	4.8 µg	1.2 µg
Vitamin B6	2.8 mg	0.7 mg
Vitamin C	108 mg	27 mg
Vitamin D	13.2 µg	3.3 µg
Vitamin E	15.6 mg (αTE)	3.9 mg (αTE)
Vitamin K	100 µg	25 µg

MINERALS	per 100 g of powder	per 25 g (1 sachet)
Calcium	1196 mg	299 mg
Chloride	728 mg	182 mg
Chromium	88 µg	22 µg
Iron	21.6 mg	5.4 mg
Phosphorus	1068 mg	267 mg
Iodine	252 µg	63 µg
Magnesium	376 mg	94 mg
Manganese	3.2 mg	0.80 mg
Molybdenum	144 µg	36 µg
Potassium	940 mg	235 mg
Copper	2.2 mg	0.55 mg
Selenium	88 µg	22 µg
Sodium	508 mg	127 mg
Zinc	21.6 mg	5.4 mg

AMINO ACIDS		
L-Alanine	5.96 g	1494.0 mg
L-Arginine	6.19 g	1548.0 mg
Ac. L-Aspartate	9.93 g	2484.0 mg
L-Carnitine	66 mg	16.6 mg
L-Cystine	2.55 g	637.2 mg
L-Phenylalanine	4.00 g	1000.8 mg
Glycine	2.81 g	702.0 mg
L-Glutamine	7.29 g	1821.6 mg
L-Isoleucine	0.22 g	54.0 mg
L-Histidine	4.00 g	1000.8 mg
L-Leucine	9.47 g	2368.8 mg
L-Lysine	6.59 g	1648.8 mg
L-Methionine	– g	– mg
L-Proline	2.91 g	727.2 mg
L-Serine	4.22 g	1054.8 mg
Taurine	132 mg	33 mg
L-Tyrosine	4.00 g	1000.8 mg
L-Threonine	– g	– mg
L-Tryptophan	1.60 g	399.6 mg
L-Valine	– g	– mg

MMA/PA medimicro3H

440 g
4 per 110 g

MMA /PA
3+

Slow-release micro-tablets.
Amino acid mixture free of methionine, threonine, and valine, indicated for the dietary management of methymalonic acidemia/propionic acidemia.

SLOW-RELEASE TECHNOLOGY

» INDICATIONS

For the dietary management of subjects starting from three years of age with ascertained methymalonic acidemia/propionic acidemia. Microtablets are suitable for children from three years of age upwards, depending on their ability to swallow, as determined by the attending physician.

» DOSAGE AND ADMINISTRATION

According to the physician's prescription, taking into account age, body weight, the clinical condition of the subject, and the fact that the tablets are delayed-release. After being taken, MMA/PA Medimicro 3H releases the amino acids in the tablets over a three hour period. The cap of the jar contains about 13 g of micro-tablets (equal to approximately 8 g of protein equivalents).

» INSTRUCTIONS FOR USE

Take the prescribed amount with water or other allowed liquids. The micro-tablets have no taste; to retain this feature, it is recommended that they are not chewed, pulverized, or dissolved.

» STORAGE CONDITIONS

After use, close the container properly and store it in a cool and dry place, below 25°C, away from light and sources of direct heat. The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS

MMA/PA Medimicro 3H must only be taken under medical supervision by individuals with methymalonic acidemia/propionic acidemia. MMA/PA must not be used as one's only source of food. The product can result in health risks if consumed by individuals who do not have the specific disorder for which it is indicated. Keep out of the reach of children.

NUTRITIONAL INFORMATION

food for special medical purposes

	per 100 g of micro-tablets
Energy kJ/kcal	1628/389
Fats	2.6 g
of which saturated fatty acids	2.6 g
Carbohydrates	12 g
of which sugars	0 g
Protein equivalent	65 g
Fiber	10 g
Salt	1 g

AMINO ACIDS	
L-Aspartic acid	10.7 g
L-Alanine	6.4 g
L-Arginine	6.7 g
L-Cystine	2.8 g
L-Phenylalanine	4.3 g
Glycine	3 g
L-Glutamine	7.9 g
L-Isoleucine	0.23 g
L-Histidine	4.3 g
L-Leucine	10.2 g
L-Lysine	7.1 g
L-Proline	3.1 g
L-Serine	4.6 g
L-Tyrosine	4.3 g
L-Tryptophan	1.73 g
L-Methionine	– g
L-Threonine	– g
L-Valine	– g
Taurine	143 mg
L-Carnitine	71 mg

Protein and amino acid requirements

The primary dietary objective in patients with organic aciduria should remain the prevention of catabolism and allow normal growth, without causing obesity. Key dietary management principles are similar for patients with MMA and PA.

The quantity of natural proteins prescribed is determined by age, growth, metabolic stability, and severity of the condition. When natural proteins are exclusively used, FAO/WHO/UNU (2007) recommendations should be followed. Some metabolic centers supplement the diet with methionine, threonine, and valinefree amino acid mixes, with low isoleucine content. According to various publications, **the prescribed quantity varies between 15% and 50% of total protein requirements**. These amino acid mixes should be used when tolerance to natural proteins is below FAO/WHO/UNU (2007) safety levels.

(Baumgartner, M. R. et al. "Proposed Guidelines for the Diagnosis and Management of Methylmalonic and Propionic Acidemia." Orphanet Journal of Rare Diseases 9 (2014): 130. PMC. Web. 7 Mar. 2018).

NOTES

Protein-free products

In a normal dietary regime, consumption of protein-rich products provides noble proteins (e.g. from meat, fish, eggs, and milk) and non-noble proteins (e.g. from bread, pasta, and cookies). In particular conditions, it is necessary to partially or totally restrict protein intake (especially non-noble proteins).

Following a low-protein diet must not lead to abandoning one's eating habits or tasty meals. Today, there is a vast range of protein-free products with which it is possible to prepare delicious meals while retaining the pleasure of eating. Following a low-protein diet does not mean following a poor diet, but only reducing the content of protein and mineral salts (1).

Medifood protein-free products, with a protein content lower than 1 g per 100 g of product, and low in sodium, potassium, and phosphorus, are perfectly suited to the needs of those who suffer from limited kidney function and who must follow a diet with reduced amounts of the minerals mentioned. They thus provide an important contribution towards lowering the level of proteins in food without having to give up a healthy and tasty diet.

A protein-free diet is suited for patients affected by:

Chronic kidney disease (CKD)[2,3]; patients in conservative therapy, pre-dialysis, and post-transplant conditions

In CKD, a low-protein diet is useful to reach/increase calories and not affect the kidney load, delaying dialysis and controlling other complications due to CKD (hypertension, malnutrition, etc.).

Patients with CKD can thus:

- reduce protein intake, in order not to burden renal function;
- manage calorie intake to reach or maintain optimal weight;
- limit the intake of sodium, phosphorus, and potassium.

Parkinson's disease (treated with levodopa)[4,5]

In Parkinson's disease, levodopa is the medicinal product of choice. Carriers tasked with transporting levodopa to the circulation and from the circulation to the brain are the same used for amino acid transport, and thus a low-protein (and therefore low amino acid) diet improves absorption of levodopa, augmenting its clinical action.

Furthermore, in a high percentage of patients there may be a reduction in the levels of levodopa, especially when taken close to a low-protein lunch. Recent studies have demonstrated that low-protein diets in the first part of the day reduce the daily "OFF" periods, improving the patient's motor performance and well-being.

Metabolic aminoacidopathies (e.g. hyperphenylalaninemia, PKU, and tyrosinemia, etc)

In metabolic diseases affecting protein metabolism, with the need to limit the intake of natural proteins, a protein-free diet is necessary to allow the patient to have a varied, complete, and correct nutrition.

1. *Giancarlo Vanozzi, Gioachino Leandro – Lineamenti di dietoterapia e nutrizione clinica, II Edizione [TN: Foundations of diet therapy and clinical nutrition, II Edition], Il Pensiero Scientifico Editore*
2. *Michael T. Pedrini; Andrew S. Levey; Joseph Lau; Thomas C. Chalmers; and Ping H. Wang – The Effect of Dietary Protein Restriction on the Progression of Dia-betic and Nondiabetic Renal Diseases: A Meta-Analysis, Annals of Internal Medicine, 1996.*
3. *Lai S, Molfino A, Coppola B, De Leo S, Tommasi V, Galani A, Migliaccio S, Greco EA, Gnerre Musto T, Muscaritoli M. – Clinical Medicine Department, Rome Sapienza University – Effect of personalized dietary intervention on nutritional, metabolic and vascular indices in patients with chronic kidney disease, European Review for Medical and Pharmacological Sciences 2015.*
4. *Ismael Mena, George C. Cotzias – Protein Intake and Treatment of Parkinson's Disease with Levodopa, New England Journal of Medicine, 1975.*
5. *Emanuele Cereda; Michela Barichella; Giyears Pezzoli – Controlled-protein dietary regimens for Parkinson's disease, Nutritional Neuroscience, Volume 13, 2010.*

milco | milco ciock
milco cappuccino

500 ml
6 per 200 ml

Protein-free drink with milk ingredients, ready for use.

» INDICATIONS

Milco® has been conceived as a substitute for cow's milk in the nutritional management of various pathologies that require a low-protein diet with low phenylalanine content.

» DOSAGE AND ADMINISTRATION

The quantity to be taken during the day must be established by a physician taking into account the patient's age, weight, and clinical conditions.

» INSTRUCTIONS FOR USE

Milco® can be taken as is, with the addition of flavors, or with coffee. It can be used as a substitute for cow's milk in preparing various recipes. Shake well before use.

» STORAGE CONDITIONS

Store the product in a cool and dry place, at a temperature between 8 and 25°C, away from light and sources of direct heat. Once opened, the bottle must be stored in the fridge and the content consumed within 48 hours. The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS

Milco® is a food product for special medical purposes, and must be used under medical supervision. Milco® cannot be used as one's only source of food. Compared to cow's milk, the product has a low content of calcium. Keep out of the reach of children.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 ml
Energy kJ/kcal	272/65
Fats	3.6 g
of which saturated fatty acids	1.6 g
Carbohydrates	7.9 g
of which sugars	4.5 g
Protein	0.2 g
Salt	0.15 g
L-Phenylalanine	8 mg

MINERALS	
Sodium	0.058 g
Potassium *	38 mg
Phosphorus	7 mg
Calcium	10 mg
Chloride	53 mg
Osmolarity	250 mOsm/l

FATTY ACIDS	
Caprilic Acid	0.01 g
Capric Acid	0.03 g
Lauric Acid	0.04 g
Myristic acid	0.15 g
Palmitic acid	1.11 g
Stearic acid	0.21 g
Palmitoleic Acid	0.02 g
Oleic Acid	1.35 g
Linoleic Acid	0.30 g
Linolenic acid	0.07 g

AMINO ACIDS	per 100 ml
L-Isoleucine	12 mg
L-Leucine	20 mg
L-Lysine	16 mg
L-Methionine	5 mg
L-Cystine	4 mg
L-Phenylalanine	8 mg
L-Tyrosine	6 mg
L-Threonine	13 mg
L-Tryptophan	3 mg
L-Valine	13 mg
L-Arginine	6 mg
L-Histidine	5 mg
L-Alanine	8 mg
L-Aspartato	18 mg
L-Glycine	5 mg
L-Glutamate	34 mg
L-Proline	13 mg
L-Serine	10 mg

* Milco® Ciock: Potassium 59 mg

SINEAMIN

500 g
* 250 g

Protein-free
gluten-free pasta.

» INDICATIONS

For the dietary management of individuals with chronic kidney failure and metabolic aminoacidopathies. Sineamin® pasta is also indicated in protein-free and gluten-free diets, and has a low content of sodium, potassium, and phosphorus.

» COOKING SUGGESTIONS

Boil an abundant amount of water (at least a liter for each 100 g of pasta), add salt (only if approved by the physician), add the pasta, and stir energetically. Cook on a high flame for the time indicated on the package. In any event, cooking time can be modified according to individual preference: it is recommended that pasta is tasted to assess the desired level of cooking.

» STORAGE CONDITIONS

Store the product in a cool and dry place, away from light and sources of direct heat. The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS

Sineamin® must be used only under medical supervision. Sineamin® cannot be used as one's only source of food. The presence of safflower, of natural origin, in Sineamin® can lead to variation in color intensity between batches.

» FORMATS

Spaghetti, linguine, fusilli, penne rigate, pipe rigate, sedani lunghi, sedani corti, stelline, semolino, tagliatelle*, lasagne*, riso [TN: pasta types available].

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g of product	per 100 g of product (Sineamin i sorrisi)
Energy kJ/kcal	1550/364	1554/366
Fats	1.3 g	1.3 g
of which saturated fatty acids	0.3 g	0.2 g
Carbohydrates	87.4 g	88.1 g
of which sugars	0.3 g	0 g
Dietary fiber	1.0 g	0.3 g
Protein	0.5 g	0.4 g
Salt *	< 0.05 g	0.07 g
equal to sodium	< 0.02 g	28 mg
MINERALS		
Phosphorus	< 20 mg	22 mg
Potassium	< 20 mg	11 mg
Sodium	< 20 mg	28 mg
AMINO ACIDS		
Phenylalanine	< 10 mg	14 mg
Tyrosine	< 20 mg	

* The salt content is due exclusively to the sodium in the product.

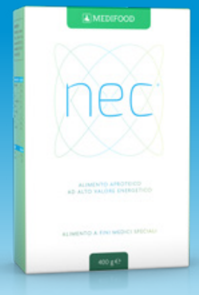
Special pediatric products

In a pediatric age, it is essential that the diet provides all the necessary nutrients for physical and psychological growth.

The following paragraph lists products for specific nutritional treatment of pathologies found in a pediatric age.

nec

400 g



Protein-free food
with high energy value.

» INDICATIONS

NEC is an alimentary product intended for special medical purposes. It is protein-free, low in electrolytes and has a high energy value. It should be used as indicated by a physician, for:

- diets requiring a high energy intake;
- low-protein diets with minimal electrolyte intake;
- as a dietary supplement in cases of acute and chronic kidney disease (low phosphorus intake).

» DOSAGE AND ADMINISTRATION

The quantity of product to be taken daily must be calculated according to the physician's judgement, taking into account the patient's age, body weight, caloric requirements, and clinical conditions. The measuring spoon in the package holds 5 g of product, equal to 25.4 kcal (106 kJ).

» INSTRUCTIONS FOR USE

Take the product together with any liquid or solid food product.

» STORAGE CONDITIONS

Store the product in a cool and dry place at a temperature between 8°C and 25°C, away from light and sources of direct heat. Once open, the product can be consumed within 4 weeks, if stored properly closed and away from sourced of heat. After use, close the box properly. The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS

NEC® must be used under medical supervision.
NEC® cannot be used as one's only source of food. Keep out of the reach of children.

NUTRITIONAL INFORMATION
food product for special medical purposes

	per 100 g of powder
Energy kJ/kcal	2139/512
Fats	23,7 g
of which saturated fatty acids	15,6 g
Carbohydrates	74,6 g
of which sugars	2,4 g
Protein	0 g
Salt *	0.06 g
MINERALS	
Phosphorus	19.2 mg
Potassium	1.6 mg
Sodium	25.3 mg
FATS (MCT 50%)	
Caprilic acid	4.2 g
Capric acid	3.3 g
Lauric acid	3.1 g
Myristic acid	1.2 g
Palmitic acid	1.3 g
Palmitoleic acid	0.02 g
Stearic acid	0.4 g
Oleic acid	3 g
Linoleic acid	4.7 g
α-linolenic acid	0.04 g
10% Osmolality	52.7 mOsm/kg
10% Osmolarity	54.1 mOsm/l

* The salt content is due exclusively to the sodium in the product.

Medigel

100 g

Plant-based thickening powder with carob seed flower.
Medigel is a completely taste-free food product for special medical purposes.

» INDICATIONS

Medigel is indicated for infants, children, and adults.
As anti-regurgitation:
- in milk-based diets.

As thickening/gelling agent:
- for liquid or semi-liquid food products in the case of problems swallowing (dysphagia);
- in patients with reflux problems.

» DOSAGE AND INSTRUCTIONS FOR USE

According to the physician's prescription, taking into account age, body weight, and clinical condition of the subject.
As anti-regurgitation:
- pour 3 g (1 measuring spoon) of product in water (100 ml) and heat on a low flame until a gel is obtained, which can be stored in the fridge for 24 hours;
- in the case of breastfeeding, the gel should be given to the infant before feeding (1-2 spoons depending on the requirements);
- in the case of bottle feeding, take the necessary quantity and dissolve it in the artificial milk, shaking the milk bottle.

As thickening agent:
- use the 3 g measuring spoon present in the package to remove the quantity suggested in the table (page 133);
- slowly add to liquid or semi-liquid foods, either hot or cold;
- mix with a fork or a kitchen beater until complete dissolution or mix in a closed container (e.g. a shaker). Alternative, use a low-speed electric mixer for 5-10 seconds.

» STORAGE CONDITIONS

Store in a cool and dry place, away from light and sources of direct heat. The reconstituted product can be stored in the refrigerator and used within 24 hours.

» IMPORTANT WARNINGS

Medigel must be used under medical supervision. Medigel must not be used as one's only source of food. Keep out of the reach of children. GLUTEN-FREE.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g
Energy kJ/kcal	1175/282
Fats	0.6 g
of which saturated fatty acids	0.0 g
Carbohydrates	40.9 g
of which sugars	38.5 g
Protein	4.2 g
Dietary fiber	48.27 g
Sodium	0.125 g

Food products 100 ml	Desired consistency		
Fruit juice	–	½ of the 3 g measuring spoon	1 measuring spoon (3 g)
Vegetable purée	–	½ of the 3 g measuring spoon	1 measuring spoon (3 g)
Milk - Orange juice Water - Tea Chamomile - Coffee	½ of the 3 g measuring spoon	1 measuring spoon (3 g)	2 of the 3 g measuring spoons

rubrojunior

7 per 10 ml

Supplement ready for use with B-group vitamins, Zinc and Lactoferrin.

» INDICATIONS

Coadjuvant for infants, children, and adults:

- with fevers or colds
- in a child's delayed growth
- in all cases where it is necessary to increase immune defences
- in emergencies
- during infectious diseases
- during recovery from illness
- when nutritionally deficient
- during therapy with aciclovir

» DOSAGE AND INSTRUCTIONS FOR USE

One vial per day away from meals, for an average duration of 2-3 weeks. The treatment can be repeated in cycles.
The dose can be increased up to two vials per day in the most demanding cases.

» STORAGE CONDITIONS

Store at room temperature (15-30°C); avoid exposure to localized sources of heat, sun, and contact with water. The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS

Do not exceed the recommended daily dose. Keep out of reach of children under three years of age. Food supplements should not be intended as substitutes for a varied and balanced diet and a healthy lifestyle. The product does not contain gluten.

NUTRITIONAL INFORMATION
food supplement

	per 100 ml	per 10 ml	VNR %
Lactoferrin	500 mg	50 mg	
Thiamine	5.5 mg	0.55 mg	50%
Riboflavin	7 mg	0.7 mg	50%
Vitamin B6	7 mg	0.7 mg	50%
Vitamin B12	0.025 mg	0.0025 mg	100%
Niacin	80 mg	8 mg	50%
Folic acid	2 mg	0.2 mg	100%
Zinc	50 mg	5 mg	50%

MCT Oil

1000 ml
240 ml

30 per
10 ml

Medium chain triglycerides mix (MCT) mostly obtained from coconut.

» INDICATIONS

Indicated for supportive therapy in cases of:

- Short bowel syndrome
- Pancreatopathy
- Cystic fibrosis
- Hypercatabolic states (malnutrition, burns, sepsis)
- Lymphedema
  - improves lymph composition
  - does not overload the lymphatic system
- Oxidative disorders of long-chain fatty acids: LCHAD, VLCAD
- MCT-based ketogenic diet, used in the treatment of drug-resistant epilepsy, GLUT-1 deficiency, PDHD deficiency
- Chylothorax
- Other diseases that alter the functionality of chyliferous vessels

» DOSAGE AND INSTRUCTIONS FOR USE

Following medical instructions, taking into account age, weight, and clinical conditions, the caloric portion indicatively provided by MCT should represent around 55% of the fat-derived caloric share. Normally in split doses of 15-20 ml (3-4 teaspoons).
MCT Oil can be consumed both raw and heated (T°<150- 160°C, to prevent thermal degradation).

» STORAGE CONDITIONS

Store in a cool and dry place. The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS

MCT Oil must be taken following medical instruction and monitoring. MCT Oil must not be used as one's only source of food. Keep out of the reach of children.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g
Energy kJ/kcal	3470/830
Fats	100 g
of which saturated fatty acids	100 g
of which caprilic acid (C8:0)	55 g
of which capric acid (C10:0)	43 g
of which caproic acid (C6:0)	0.5 g
of which lauric acid (C12:0)	0.9 g
of which myristic acid (C14:0)	0.6 g
Carbohydrates	0 g
of which sugars	0 g
Protein	0 g
Salt	0 g
Dietary fiber	0 g

DENSITY

1 ml of Chiloil corresponds to 0.95 g

Chiloil

30 per 10 ml

Medium chain triglycerides (MCT) mixture, mainly obtained from coconut, enriched with selenium and vitamins A, D3, and E.

» INDICATIONS

Indicated for supportive therapy in cases of:

- Short bowel syndrome
- Pancreatopathy
- Cystic fibrosis
- Hypercatabolic states (malnutrition, burns, sepsis)
- Lymphedema
  - improves lymph composition
  - does not overload the lymphatic system
- Oxidative disorders of long-chain fatty acids: LCHAD, VLCAD
- MCT-based ketogenic diet, used in the treatment of drug-resistant epilepsy, GLUT-1 deficiency, PDHD deficiency
- Chylothorax
- Other diseases that alter the functionality of chyliferous vessels

» DOSAGE AND INSTRUCTIONS FOR USE

Following medical instructions, taking into account age, weight, and clinical conditions, the caloric portion indicatively provided by MCT should represent around 55% of the fat-derived caloric share. Normally in split doses of 15-20 ml (3-4 teaspoons).
Chiloil can be consumed both raw and heated (T°<150-160°C, to prevent thermal degradation).

» STORAGE CONDITIONS

Store in a cool and dry place. The expiry date refers to the product in an unopened, correctly stored package.

» IMPORTANT WARNINGS

Chiloil must be taken following medical instructions and monitoring. Chiloil must not be used as one's only source of food. Keep out of the reach of children.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g	x sachet
Energy kJ/kcal	3331/797	317/76
Fats	96 g	9 g
of which saturated fatty acids	96 g	9 g
of which caprilic acid (C8:0)	53 g	5 g
of which capric acid (C10:0)	41 g	4 g
of which caproic acid (C6:0)	0.5 g	0.1 g
of which lauric acid (C12:0)	0.9 g	0.1 g
of which myristic acid (C14:0)	0.6 g	0.1 g
Carbohydrates	0 g	0 g
of which sugars	0 g	0 g
Protein	0 g	0 g
Salt	0 g	0 g
Vitamin A	4000 μg RE	400 μg RE
Vitamin E	200 mg	20 mg
Vitamin D3	80 μg	8 μg
Selenium	250 μg	25 μg

DENSITY

1 ml of Chiloil corresponds to 0.95 g

DHA Medi Oil

30 ml

DHA-based special medical food indicated for the dietary management of individuals with established cystic fibrosis.

» INDICATIONS

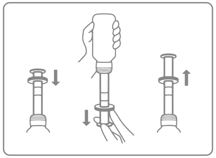
DHA Medi Oil is a DHA-based food for special medical purposes indicated for the dietary management of individuals with established cystic fibrosis.

» DOSAGE AND ADMINISTRATION

Following the physician's prescription, taking into account age, body weight and clinical conditions of the patient.

» DOSAGE AND INSTRUCTIONS FOR USE

Take 1 ml once or twice a day. Shake before use. Take the prescribed amount with the 2 ml dosing syringe included in the pack. The product can be administered directly or dissolved in water, fruit juice, milk or other liquids.



» STORAGE CONDITIONS

Store in a cool and dry place, away from heat, in a controlled temperature that does not exceed 25°C. The expiry date refers to the correctly stored, unopened product. Once open, store in the fridge and use within 30 days.

» IMPORTANT WARNINGS

Use under medical supervision. The product must not be used as a primary food source. The product should not be administered parenterally. Keep out of the reach of children. Due to the presence of ingredients of natural origin, different production batches may have slightly different colours, which in no way affects the quality of the finished product.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 1 ml	per 2 ml	per 100 ml
Energy kJ/kcal	19/5	37/9	1856/451
Fats	0.50 g	1 g	50 g
of which saturated fatty acids	<0.01 g	<0.01 g	<1 g
of which monounsaturated fatty acids	0 g	0 g	0 g
of which polyunsaturated fatty acids	0.25 g	0.5 g	25 g
Carbohydrates	0 g	0 g	0 g
of which sugars	0 g	0 g	0 g
Protein	0 g	0 g	0 g
Salt	0 g	0 g	0 g
DHA (from algal oil tit. to 50% in DHA)	250 mg	500 mg	25000 mg

AF
(Antisecretory Factor)

Antisecretory Factor (AF) is a protein that modulates the transport of water and ions. Its discovery dates to 1984. At that time, researchers observed that AF could inhibit hypersecretion of liquids and electrolytes within the intestinal lumen caused by cholera toxin.

Antisecretory factor is present in cells of all tissues, but it is particularly abundant in the intestinal mucosa. It acts by blocking chloride channels, which, when excessively activated, cause hypersecretion in the intestinal lumen.

The activation of antisecretory factor can take place within the intestinal lumen in the presence of:

- Pathogenic agents (bacteria, viruses, parasites, helminths);
- Hypertonic solutions (e.g. solution with a high quantity of sugars and/or amino acids, concentrated and absorbed within substrates such as cereals).

Its activation reflects a natural defence mechanism from causative agents of, for example, diarrhea, thus contributing to a favorable clinical outcome and resolution of the illness.

Specific dietary approaches lead to increasing AF levels, such as specially processed cereals (SPCs). The administration of SPCs to patients suffering from intestinal inflammatory disease, gastroenteritis, and Ménière's disease improves symptoms and the quality of life. Furthermore, AF-enriched egg yolk powder improves health status in children suffering from acute and chronic diarrhea, reducing the frequency and increasing the volume of feces.

References:

Annals of Otology, Rhinology & Laryngology, 2013 122(10):619-624. Antisecretory Factor–Inducing Therapy Improves Patient-Reported Functional Levels in Meniere's Disease. Samuel C. Leong, MPhil, FRCS(ORL-HNS); Surya Narayan, MS, DLO, FRCS(ORL-HNS); Tristram H. Lesser, MS, FRCS

FEBS Letters, 1984; 177:104-107. "Purification and characterization of a hormone-like factor which inhibits cholera secretion". Lonnroth I, Lange S.

Int. J. Neurosci., 1989; 46: 93-95." Further studies on the effect of ASF factor on chloride permeability across the Deiters' neuron plasma membrane". Rapallino MV, Cupello A, Lange S, Lonnroth I, Hydèn H.

Acta Physiol. Scand., 2003; 179: 367- 371. "Antisecretory factor peptide derivatives specifically inhibit [3H]-γ-amino-butyric acid/ 36chloride out>in permeation across the isolated rabbit Deiters' neuronal membrane". Rapallino MV, Cupello A, Lange S, Lonnroth I.

Nutr Res Rev. 2010 Dec;23(2):300-13. Antisecretory factor as a potential health-promoting molecule in man and animals. Ulgheri C, Paganini B, Rossi F.

SPC-flakes

450 g

Hydrothermally treated oat flakes to increase endogenous production of antisecretory protein (antisecretory factor) and increase the balance of cellular liquids.

›› INDICATIONS

Dietary management in children over 3 years of age and in adults in the case of hydrops or Ménière's disease.

›› DOSAGE AND INSTRUCTIONS FOR USE

It is recommended to take 1 g/kg/ day in 2-3 daily doses, following the physician's prescription.
SPC-Flakes can be taken as is, or mixed in water or yoghurt. SPC-Flakes can also be cooked and eaten as broth or vegetable or legume soup, or added to pasta or any other food. It can also be used in the preparation of oven-baked products such as bread, focaccias, or cookies. The product as is cannot be toasted.

›› STORAGE CONDITIONS

Store in a cool and dry place.
The expiry date refers to the product correctly stored in a cool and dry place.

›› IMPORTANT WARNINGS

Use under medical supervision.
SPC-flakes must not be used as one's only food source.
Contains gluten.
SPC-flakes are GMO-free.
Keep out of the reach of children.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g of flakes
Energy kJ/kcal	1580/375
Fats	10 g
of which saturated fatty acids	1.5 g
Carbohydrates	59 g
of which sugars	3 g
Fiber	7.5 g
Protein	12 g
Salt *	35 mg
VITAMINS	
Biotin	16 µg
Folic acid	166 µg
Niacin	2.7 mg
Pantothenic acid	1.7 mg
Riboflavin	1.3 mg
Thiamine	0.6 mg
Vitamin B6	0.1 mg
Vitamin B12	0.3 µg
Vitamin E	0.7 mg
Vitamin K	1.6 µg
MINERALS	
Calcium	88 mg
Chloride	86 mg
Chromium	14 µg
Iron	4.4 mg
Phosphorus	400 mg
Iodine	0.5 µg
Magnesium	130 mg
Manganese	3.1 mg
Molybdenum	130 µg
Potassium	310 mg
Selenium	8 µg
Sodium	14 mg
Zinc	2.4 mg

* The salt content is due exclusively to the sodium in the product.

Salovum

25 per 4 g
6 per 4 g

Pasteurized egg yolk with high antisecretory protein (antisecretory factor) content to improve the balance of cellular liquid.

›› INDICATIONS

Dietary management in children over 3 years of age and in adults in the case of hydrops or Ménière's disease.

›› DOSAGE AND INSTRUCTIONS FOR USE

Unless prescribed otherwise, as a general guideline it is recommended to take one sachet three times a day. Mix the contents of a sachet in a small amount of fresh water, fruit juice, or other allowed liquids, not hot.

›› STORAGE CONDITIONS

Store the product in a cool and dry place, away from light and sources of direct heat. The expiry date refers to the product in an unopened, correctly stored package.

›› IMPORTANT WARNINGS

Use under medical supervision.
Salovum must not be used as one's only source of food.
Keep out of the reach of children.
Salovum is GMO-free.

NUTRITIONAL INFORMATION
food for special medical purposes

	per 100 g	per 4 g
Energy kJ/kcal	2740/660	110/26
Fats	59 g	2.4 g
of which saturated fatty acids	20 g	0.8 g
Carbohydrates	0 g	0 g
of which sugars	0 g	0 g
Fiber	2 g	0.08 g
Protein	33 g	1.3 g
Salt *	350 mg	14 mg
VITAMINS		
Biotin	148 µg	5.92 µg
Folic acid	330 µg	13.2 µg
Niacin	0.1 mg	0.004 mg
Pantothenic acid	9 mg	0.36 mg
Thiamine	0.43 mg	0.017 mg
Vitamin A	3400 µg	136 µg
Vitamin B6	0.11 mg	0.004 mg
Vitamin B12	10 µg	0.4 µg
Vitamin D	7 µg	0.28 µg
Vitamin E	32 mg	1.28 mg
MINERALS		
Calcium	280 mg	11.2 mg
Chloride	1160 mg	46.4 mg
Chromium	6 µg	0.24 µg
Iron	9.9 mg	0.4 mg
Fluorine	200 mg	8 mg
Phosphorus	960 mg	38.4 mg
Iodine	110 µg	4.4 µg
Magnesium	23 mg	0.92 mg
Manganese	0.28 mg	0.011 mg
Molybdenum	14 µg	0.56 µg
Potassium	190 mg	7.6 mg
Selenium	96 µg	3.84 µg
Sodium	140 mg	5.6 mg
Zinc	7.1 mg	0.28 mg

* The salt content is due exclusively to the sodium in the product.

LARN 2014 - REFERENCE INTAKE LEVELS FOR THE ITALIAN POPULATION: AVERAGE ENERGY REQUIREMENTS (ARS) IN THE 6-12 MONTH AGE RANGE

Age months	**Body weight** kg	**Growth rate** (g/day)	**TEE** (kcal/day)	**Energy** (kcal/day)	**Energy requirement** (kcal/day)	**Energy requirement** (kcal/day)
MALES						
6	7.9	14.0	581	39	620	78
7	8.3	11.9	618	18	640	77
8	8.6	10.5	646	15	660	77
9	8.9	9.5	674	14	690	77
10	9.2	8.6	702	23	730	79
11	9.4	8.1	720	22	740	79
12	9.6	7.9	739	21	760	79
FEMALES						
6	7.3	13.3	525	49	570	79
7	7.6	11.5	553	20	580	75
8	7.9	10.4	581	18	600	76
9	8.2	9.1	609	16	630	76
10	8.5	8.2	637	19	640	77
11	8.7	7.8	655	18	660	77
12	8.9	7.6	674	18	690	78

TEE: Total energy expenditure. Energy requirement values rounded to 10 kcal/day. Age is considered as chronological age; for example, 9 months refers to the period between the ninth and tenth month of age. Body weight as 50th body weight percentile by age from the WHO document (2006) tables. Growth rate calculated based on body weight data from the WHO document (2006) tables. TEE (kcal/day) calculated with Butte's equations (Butte, 2005). Energy deposited calculated as energy content of newly formed tissues x growth rate. Energy requirements obtained as TEE + energy needed. The values shown are exemplary and do not have regulatory meaning.

LARN 2014 - REFERENCE INTAKE LEVELS FOR THE ITALIAN POPULATION: AVERAGE ENERGY REQUIREMENTS (AR) IN THE 1-17 YEAR AGE RANGE

Age years	**Body weight** kg	**BM** (g/day)	**Energy requirements for a PAL of**		
			25th pct	median	75th pct
MALES					
1	10.9	620	840	870	890
2	14.0	800	1090	1130	1160
3	16.3	880	1260	1390	1490
4	18.5	930	1330	1470	1580
5	20.8	980	1400	1550	1670
6	23.3	1030	1480	1640	1770
7	26.2	1100	1580	1750	1880
8	29.5	1180	1690	1870	2010
9	33.2	1260	1810	2000	2150
10	37.2	1320	2210	2300	2460
11	41.7	1400	2340	2440	2610
12	46.9	1490	2490	2600	2780
13	52.7	1590	2670	2780	2970
14	58.7	1700	2840	2960	3170
15	63.5	1780	2990	3110	3330
16	66.6	1840	3080	3210	3430
17	68.2	1860	3130	3260	3480
FEMALES					
1	10.2	560	770	790	810
2	13.4	750	1020	1050	1080
3	15.7	800	1150	1280	1370
4	18.0	850	1220	1350	1450
5	20.5	900	1290	1430	1540
6	23.3	960	1380	1520	1640
7	26.4	1020	1470	1620	1740
8	29.6	1090	1560	1720	1860
9	33.2	1160	1660	1840	1980
10	37.5	1190	2000	2090	2230
11	42.7	1260	2120	2210	2360
12	48.4	1340	2250	2340	2500
13	52.5	1390	2340	2440	2610
14	54.6	1420	2390	2490	2660
15	55.4	1430	2400	2510	2680
16	55.7	1440	2410	2510	2690
17	55.8	1440	2410	2510	2690

BM: basal metabolism; PAL: physical activity level; pct: percentile. BM values and energy requirement values rounded to 10 kcal/day. Age is considered as chronological age; for example, 4 years refers to the period between the fourth and fifth birthday. Body weight according to median values by age published by Cacciari et al. (2006). For 1.5 years, the data was calculated by interpolation. BM was estimated with the equation of Schofield et al. (1985). LAF values (25th percentile - median – 75th percentile) chosen according to the expected distribution in the population of growing age (SACN, 2011) and equal to: <3 years 1.35 - 1.39 - 1.43; 3-9 years 1.42 - 1.57 - 1.69; 10-18 years 1.66 - 1.73 - 1.85. Energy requirement obtained by increasing EET by 1% to take into account the energy deposited in the newly-synthesized tissues. The values shown are exemplary and do not have regulatory meaning.

CALCULATION OF BASAL METABOLISM ACCORDING TO THE EQUATION BY HARRIS BENEDICT

Man (BMR) = 66.5 + (13.75 x kg) + (5.003 x cm) - (6.775 x age)

Woman (BMR) = 655.1 + (9.563 x kg) + (1.850 x cm) - (4.676 x age)

LARN 2014 - REFERENCE INTAKE LEVELS FOR THE ITALIAN POPULATION: AVERAGE ENERGY REQUIREMENTS (AR) IN ADULTS.

Height m	Body weight kg	BM Basal Metabolism kcal/day (kcal/kg)	Energy requirement (kcal/day) for one PAL (level of physical activity) of:			
			1,45	1,6	1,75	2,1
MALES 18-29 YEARS						
1.5	50.6	1450	2110	2330	2540	3050
1.6	57.6	1560	2260	2490	2730	3270
1.7	65	1670	2420	2670	2920	3510
1.8	72.9	1790	2590	2860	3130	3760
1.9	81.2	1910	2780	3060	3350	4020
MALES 30-59 YEARS						
1.5	50.6	1450	2110	2330	2540	3050
1.6	57.6	1530	2220	2450	2680	3220
1.7	65	1620	2350	2590	2830	3400
1.8	72.9	1710	2480	2730	2990	3590
1.9	81.2	1800	2620	2890	3160	3790
FEMALES 18-29 YEARS						
1.5	50.6	1240	1790	1980	2160	2600
1.6	57.6	1340	1940	2140	2340	2810
1.7	65	1450	2100	2320	2540	3040
1.8	72.9	1570	2270	2510	2740	3290
1.9	81.2	1690	2450	2700	2960	3550
FEMALES 30-59 YEARS						
1.5	50.6	1260	1820	2010	2200	2640
1.6	57.6	1310	1900	2100	2300	2760
1.7	65	1370	1990	2200	2400	2880
1.8	72.9	1440	2080	2300	2520	3020
1.9	81.2	1510	2180	2410	2630	3160

LARN 2014 - REFERENCE INTAKE LEVELS FOR THE ITALIAN POPULATION: PROTEINS

	Body weight	AR average requirements		PRI Intake recommended for the population		SDT Objective nutritional for the prevention	
	(kg)	(g/kg×day)	(g/day)	(g/kg×day)	(g/day)	(g/kg×day)	(g/day)
INFANTS							
6-12 months	8.6	1.11	9	1.32	11		
ADOLESCENTS							
1-3 years	13.7	0.82	11	1.00	14		
4-6 years	20.6	0.76	16	0.94	19		
7-10 years	31.4	0.81	25	0.99	31		
ADOLESCENTS - MALE							
11-14 years	49.7	0.79	39	0.97	48		
15-17 years	66.6	0.79	50	0.93	62		
ADOLESCENTS - FEMALE							
11-14 years	50.7	0.77	39	0.95	48		
15-17 years	55.7	0.72	40	0.90	50		
ADULTS - MALE							
18-29 years	70.0	0.71	50	0.90	63		
30-59 years	70.0	0.71	50	0.90	63		
60-74 years	70.0					1.1	77
≥75 years	70.0					1.1	77
ADULTS - FEMALE							
18-29 years	60.0	0.71	43	0.90	54		
30-59 years	60.0	0.71	43	0.90	54		
60-74 years	60.0					1.1	66
≥75 years	60.0					1.1	66
PREGNANCY							
First trimester			+0.5		+1		
Second trimester			+7		+8		
Third trimester			+21		+26		
BREAST-FEEDING							
First semester			+17		+21		
Second semester			+11		+14		

AR, PRI, and SDT correspond to the average daily value over a reasonable time interval. Age ranges are based on chronological age; for example, 4-6 years refers to the period between the fourth and seventh birthday. 6-12 month corresponds to the second semester of life. Indicated body weight is exemplary and does not represent a standard value for the population. AR, PRI, and SDT are corrected based on the protein quality ascribed to the Italian diet. For pregnancy, a total weight increase of 12 kg is considered. AR and PRI refer to the increase in dietary requirements during gestation (in relation to women with normal weight; see also Table 8). For breastfeeding women, milk production equal to 0.81 L/day is considered for the first semester and 0.58 L/day thereafter. Scientific evidence does not allow the maximum tolerable intake level to be defined (UL) for any of the groups studied.

LARN 2014 – REFERENCE INTAKE LEVELS FOR THE ITALIAN POPULATION: VITAMINS RECOMMENDED INTAKE FOR THE POPULATION (PRI IN BOLD) AND ADEQUATE INTAKE (AI IN ITALICS): VALUES ON A DAILY BASIS

	Vit. C mg	Thiamine mg	Riboflavin mg	Niacin mg	Ac. pantotenico mg	Vit. B6 mg	Biotin µg	Folates µg	Vit.B12 µg	Vit. A µg	Vit. D µg	Vit. E mg	Vit. K µg
INFANTS													
6-12 months	*35*	*0.3*	*0.4*	*5*	*2*	*0.4*	*7*	*110*	*0.7*	*450*	*10*	*4*	*10*
ADOLESCENTS													
1-3 years	**35**	**0.4**	**0.5**	**7**	*2*	**0.5**	*10*	**140**	**0.9**	**300**	**15**	*5*	*50*
4-6 years	**45**	**0.5**	**0.6**	**8**	*2.5*	**0.6**	*15*	**170**	**1.1**	**350**	**15**	*6*	*65*
7-10 years	**60**	**0.8**	**0.8**	**12**	*3.5*	**0.9**	*20*	**250**	**1.6**	**500**	**15**	*8*	*90*
ADOLESCENTS - MALE													
11-14 years	**90**	**1.1**	**1.3**	**17**	*4.5*	**1.2**	*25*	**350**	**2.2**	**600**	**15**	*11*	*130*
15-17 years	**105**	**1.2**	**1.6**	**18**	*5*	**1.3**	*30*	**400**	**2.4**	**700**	**15**	*13*	*140*
ADOLESCENTS - FEMALE													
11-14 years	**80**	**1**	**1.2**	**17**	*4.5*	**1.2**	*25*	**350**	**2.2**	**600**	**15**	*11*	*130*
15-17 years	**85**	**1.1**	**1.3**	**18**	*5*	**1.3**	*30*	**400**	**2.4**	**600**	**15**	*12*	*140*
ADULTS - MALE													
18-29 years	**105**	**1.2**	**1.6**	**18**	*5*	**1.3**	*30*	**400**	**2.4**	**700**	**15**	*13*	*140*
30-59 years	**105**	**1.2**	**1.6**	**18**	*5*	**1.3**	*30*	**400**	**2.4**	**700**	**15**	*13*	*140*
60-74 years	**105**	**1.2**	**1.6**	**18**	*5*	**1.7**	*30*	**400**	**2.4**	**700**	**15**	*13*	*170*
≥75 years	**105**	**1.2**	**1.6**	**18**	*5*	**1.7**	*30*	**400**	**2.4**	**700**	**20**	*13*	*170*
ADULTS - FEMALE													
18-29 years	**85**	**1.1**	**1.3**	**18**	*5*	**1.3**	*30*	**400**	**2.4**	**600**	**15**	*12*	*140*
30-59 years	**85**	**1.1**	**1.3**	**18**	*5*	**1.3**	*30*	**400**	**2.4**	**600**	**15**	*12*	*140*
60-74 years	**85**	**1.1**	**1.3**	**18**	*5*	**1.5**	*30*	**400**	**2.4**	**600**	**15**	*12*	*170*
≥75 years	**85**	**1.1**	**1.3**	**18**	*5*	**1.5**	*30*	**400**	**2.4**	**600**	**20**	*12*	*170*
PREGNANCY													
	100	**1.4**	**1.7**	**22**	*6*	**1.9**	*35*	**600**	**2.6**	**700**	**15**	*12*	*140*
BREAST-FEEDING													
	130	**1.4**	**1.8**	**22**	*7*	**2**	*35*	**500**	**2.8**	**1000**	**15**	*15*	*140*

LARN 2014 – REFERENCE INTAKE LEVELS FOR THE ITALIAN POPULATION: MINERALS RECOMMENDED INTAKE FOR THE POPULATION (PRI IN BOLD) AND ADEQUATE INTAKE (AI IN ITALICS): VALUES ON A DAILY BASIS

	Ca mg	P mg	Mg mg	Na g	K g	Cl g	Fe mg	Zn mg	Cu mg	Se µg	I µg	Mn mg	Mo µg	Cr µg	F mg
INFANTS															
6-12 months	*260*	*275*	*80*	*0.4*	*0.7*	*0.6*	*11*	*3*	*0.2*	*20*	*70*	*0.4*	*10*	*4*	*0.4*
ADOLESCENTS															
1-3 years	**700**	**460**	**80**	*0.7*	*1.7*	*1*	**8**	**5**	**0.3**	**19**	*100*	*0.6*	*15*	*7*	*0.7*
4-6 years	**900**	**500**	**100**	*0.9*	*2.4*	*1.4*	**11**	**6**	**0.4**	**25**	*100*	*0.8*	*20*	*10*	*1*
7-10 years	**1100**	**875**	**150**	*1.1*	*3*	*1.7*	**13**	**8**	**0.6**	**34**	*100*	*1.2*	*30*	*14*	*1.6*
ADOLESCENTS - MALE															
11-14 years	**1300**	**1250**	**240**	*1.5*	*3.9*	*2.3*	**10**	**12**	**0.8**	**49**	*130*	*1.9*	*50*	*25*	*2.5*
15-17 years	**1300**	**1250**	**240**	*1.5*	*3.9*	*2.3*	**13**	**12**	**0.9**	**55**	*130*	*2.7*	*60*	*33*	*3.5*
ADOLESCENTS - FEMALE															
11-14 years	**1300**	**1250**	**240**	*1.5*	*3.9*	*2.3*	**10/18**	**9**	**0.8**	**48**	*130*	*1.9*	*50*	*21*	*2.5*
15-17 years	**1200**	**1250**	**240**	*1.5*	*3.9*	*2.3*	**18**	**9**	**0.9**	**55**	*130*	*2.3*	*60*	*23*	*3*
ADULTS - MALE															
18-29 years	**1000**	**700**	**240**	*1.5*	*3.9*	*2.3*	**10**	**12**	**0.9**	**55**	*150*	*2.7*	*65*	*35*	*3.5*
30-59 years	**1000**	**700**	**240**	*1.5*	*3.9*	*2.3*	**10**	**12**	**0.9**	**55**	*150*	*2.7*	*65*	*35*	*3.5*
60-74 years	**1200**	**700**	**240**	*1.2*	*3.9*	*1.9*	**10**	**12**	**0.9**	**55**	*150*	*2.7*	*65*	*30*	*3.5*
≥75 years	**1200**	**700**	**240**	*1.2*	*3.9*	*1.9*	**10**	**12**	**0.9**	**55**	*150*	*2.7*	*65*	*30*	*3.5*
ADULTS - FEMALE															
18-29 years	**1000**	**700**	**240**	*1.5*	*3.9*	*2.3*	**18**	**9**	**0.9**	**55**	*150*	*2.3*	*65*	*25*	*3*
30-59 years	**1000**	**700**	**240**	*1.5*	*3.9*	*2.3*	**18/10**	**9**	**0.9**	**55**	*150*	*2.3*	*65*	*25*	*3*
60-74 years	**1200**	**700**	**240**	*1.2*	*3.9*	*1.9*	**10**	**9**	**0.9**	**55**	*150*	*2.3*	*65*	*20*	*3*
≥75 years	**1200**	**700**	**240**	*1.2*	*3.9*	*1.9*	**10**	**9**	**0.9**	**55**	*150*	*2.3*	*65*	*20*	*3*
PREGNANCY															
	1200	**700**	**240**	*1.5*	*3.9*	*2.3*	**27**	**11**	**1.2**	**60**	*200*	*2.3*	*65*	*30*	*3*
BREAST-FEEDING															
	1000	**700**	**240**	*1.5*	*3.9*	*2.3*	**11**	**12**	**1.6**	**70**	*200*	*2.3*	*65*	*45*	*3*

CONVERSION FACTORS

VITAMINS

Vitamin D 1 μg = 40 International Units (IU)

Vitamin A 1 μg = 3.33 International Units (IU)

Vitamin E 1 mg (α-tocopherol equivalent) = 1.49 International Units (IU)

AMINO ACIDS

Molecular weight (MW) of phenylalanine and tyrosine, and conversion formul (μmol/L < > mg/dl)

- Phenylalanine (MW) = 165.19
- Tyrosine (MW) = 181.19

Formulas

$$\mu mol/L = \frac{mg / dl \times 10^4}{MW} \qquad Mg/dl = \frac{MW \times \mu mol/L}{10^4}$$

AMINO ACIDS

Protein < > phenylalanine empirical conversion factor
1 g of protein = 50 mg of phenylalanine

PROTEINS

1 g of proteins = 1.2 g di amino acids = 4 Kcal (17KJ)
1 g of nitrogen = 6.25 g of proteins

VALUES SELECTED FROM FAO/WHO/UNU SAFETY LEVELS RELATIVE TO PROTEIN INTAKE AND ENERGY REQUIREMENTS OF CHILDREN AND ADULTS, AS WELL AS IN PREGNANCY AND BREASFEEDING FOR A HEALTHY POPULATION

PROTEIN INTAKE		ENERGY REQUIREMENTS				
AGE	INTAKE	AGE	FEMALES	MALES	FEMALES	MALES
months	g/kg pc/day	years	kj/kg pc/day		kcal/kg pc/day	
1	1.77	0.5	340	335	81.3	80.0
2	1.50	2.5	334	348	79.8	83.2
3	1.36	5.0	305	315	72.9	75.3
6	1.31	10	248	275	59.3	65.7
12	1.14	15	193	230	46.1	55.0
YEARS		ADULTS. MODERATE LEVEL OF ACTIVITY - BODY WEIGHT 70 KG				
1.5	1.03					
2	0.97					
3	0.90	18-29	159	183	38.0	43.7
4-6	0.87	30-59	148	175	35.4	41.8
7-10	0.92					

YEARS	FEMMINE	MALES	ADULTS. MODERATE LEVEL OF ACTIVITY - BODY WEIGHT 50 KG				
11	0.90	0.91	18-29	180	212	43.0	50.7
12	0.89	0.90	30.59	183	212	43.7	50.7
13	0.88	0.90					
14	0.87	0.89					
15	0.85	0.88					
16	0.84	0.87					
17	0.83	0.86					
18	0.82	0.85					
>18	0.83	0.83					

PREGNANCY: TOTAL EXTRA PROTEIN INTAKE		EXTRA TOTAL ENERGY REQUIREMENTS DURING PREGNANCY		
trimester	g/day	trimester	kJ/day	kcal/day
1st	1	1st	375	90
2nd	10	2nd	1200	287
3rd	31	3rd	1950	466

BREAST-FEEDING : TOTAL EXTRA PROTEIN INTAKE		EXTRA TOTAL ENERGY REQUIREMENTS DURING BREAST-FEEDING		
months	g/day	months	kJ/day	kcal/day
1-6	19	1-6	2800	669
>6	13	>6	1925	460

pc= body weight

NOTES

SPECIALIZED CLINICAL NUTRITION
MEDIFOOD®
A DIVISION OF PIAM

Registered brand owned by PIAM FARMACEUTICI

PIAM
Pharma &
Integrative Care

PIAM FARMACEUTICI S.p.A.
Via Fieschi 8, 16121 - Genova - ITALY
www.piamfarmaceutici.com

Code 6100000752 March 2023