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Treatment of Rare Metabolic Diseases

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Summary

- Description and Information on Metabolic Diseases
- Biodendrum products for each disease

Metabolic Diseases

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Inherited Metabolic Disorders

- Inherited Metabolic Disorders have their origin in specific enzymatic deficiencies, which affect a given metabolic pathway, leading to the accumulation of substrates – often toxic – and to reduced (or zero) production of a biologically important product. The enzyme deficit is the consequence of mutations in one or more genes coding for the respective metabolic step.
- In short, when there is a metabolic error, some reactions at the enzymatic level do not occur with the proper efficiency. This way, the compounds before the reaction accumulate and the later ones are not synthesized correctly.
- The Inherited Metabolic Disorders covered in our site are diagnosed through the neonatal heel prick or Guthrie test.

Metabolic Diseases

Aminoacidopathies:

- Phenylketonuria (PKU)
- Leucinosis or Maple Syrup Urine Disease (MSUD)
- Homocystinuria (HCU)
- Tirosinemia (TYR)

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Metabolic Diseases

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Organic Acidurias:

- Propionic (AP) and Methylmalonic (AMM) acidurias
- Isovaleric Aciduria (AIV)
- Glutaric Aciduria Type I (AGI)

Urea Cycle Diseases (DCU)

Bile Acid Synthesis Disorders

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Aminoacidopathies (Amino acid Metabolism Disorders)

- Aminoacidopathies (and organic acidurias) include inherited diseases of the metabolism of amino acids in different metabolic steps. These pathologies are characterized by signs and symptoms of acute and progressive intoxication due to accumulation of toxic metabolites upstream the enzyme block. Long-term treatment consists essentially at removing the toxic product from the diet, which in practice translates into a protein-restricted diet (hypoproteic diet).
- Why are amino acid formulas restricted in a given amino acid (or groups of amino acids) essential in these pathologies? Because these formulas guarantee an appropriate formation of proteins, indispensable for growth, and that otherwise would not be obtained naturally, due to the toxicity associated with the respective pathology.

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Phenylketonuria (PKU)

Brief description: Phenylketonuria (PKU) is an inherited disease of the amino acids' metabolism. It is characterized by a deficit in the activity of the enzyme that metabolizes the essential amino acid phenylalanine (Phe). This deficit leads to the accumulation of phenylalanine in blood in high concentrations that become toxic to the body, causing severe brain damage. There is the possibility of psychomotor delay, if treatment is not carried out in advance. Treatment includes a hypoprotein diet restricted in phenylalanine, supplemented with the remaining amino acids.

Phenylketonuria (PKU)

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- Phenylketonuria (PKU) is an autosomal recessive hereditary disease and the most common inborn error of amino acid metabolism in Europe. PKU is characterized by a deficiency of the liver enzyme phenylalanine hydroxylase which, in a healthy state, converts the essential amino acid phenylalanine (Phe) into tyrosine (Tyr). This enzyme deficit leads to an increase in the concentration of phenylalanine in all body fluids and tissues, and formation of abnormal metabolites that are excreted in the urine. If left untreated, the increase in the passage of phenylalanine through the blood-brain barrier causes brain damage, which conducts to severe motor and mental retardation, microcephaly and seizures.
- Thus, normal protein intake in patients with PKU produces a high amount of toxins that can lead to neurological damage. The treatment is, therefore, fundamentally based on a hypoprotein diet (vegetables, fruits and low-protein dietary foods), restricted in phenylalanine (liquid, powder or tablet formulas, without phenylalanine, and supplemented in the remaining amino acids, with carbohydrates, fats, micronutrients, vitamins and minerals). This type of hypoprotein diet restricted in phenylalanine, and supplemented with the remaining amino acids, guarantees good cognitive development, along with a good growth.

Keywords: Excess of phenylalanine; Deficit in the enzyme phenylalanine hydroxylase; Psychomotor delay; Hypoprotein diet restricted in phenylalanine

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Hyperphenylalaninemia (HPA)

- There is also moderate or benign Hyperphenylalaninemia (HPA) - a disease characterized by partial deficits in the enzyme phenylalanine hydroxylase, which also lead to increased plasma levels of the amino acid phenylalanine, but to a lesser extent than in the classic form of PKU. Hyperphenylalaninemia can manifest itself through attention deficit and sleep disorders. Treatment, when necessary, is superimposed on that of PKU.

KEYWORDS: EXCESS OF PHENYLALANINE; PARTIAL DEFICIT IN THE ENZYME PHENYLALANINE HYDROXYLASE; ATTENTION DEFICIT; HYPOPROTEIN DIET RESTRICTED IN PHENYLALANINE WHEN INDICATED

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Source

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Leucinosis or Maple Syrup Urine Disease (MSUD)

BRIEF DESCRIPTION: Leucinosis (MSUD) is a disease caused by the difficulty in metabolizing the branched chain amino acids leucine (Leu), isoleucine (I) and valine (Val), due to the deficit in the activity of the enzyme complex that metabolizes these 3 amino acids. The consequence is the increase in the concentration of these amino acids and the respective α-ketonic acids to toxic values for the organism, which cause a lack of appetite, seizures and severe neurological deterioration, sometimes fatal, in the absence of treatment. Nutritional treatment involves a hypoprotein diet, restricted in branched-chain amino acids, and supplemented with the remaining amino acids.

Leucinosis (MSUD)

- Leucinosis (MSUD) is a disease caused by the difficulty in metabolizing the branched-chain amino acids leucine (Leu), isoleucine (I) and valine (Val), due to the deficit in the activity of the oxidative decarboxylation enzymatic complex of these 3 amino acids. Consequently, there is an increase in blood and urinary concentrations of branched chain amino acids and their α-ketonic acids, which accumulate in toxic amounts. The name of the disease comes from the sweet smell in the urine of MSUD patients, reminiscent of maple syrup. After PKU, MSUD is the most common inherited disease of amino acid metabolism.
- Symptoms include neurological consequences, poor appetite and seizures. If treatment is not started immediately, severe neurological impairment, sometimes fatal (death or coma), can occur for the patient with MSUD. Note that leucine is considered one of the most neurotoxic branched-chain amino acids, and it is usually present in foods in higher concentrations than isoleucine and valine. The nutritional treatment for this disease therefore involves establishing a diet restricted in branched chain amino acids, supplemented with a mixture of the remaining amino acids, using liquid, powder or tablet formulas, in order to satisfy the nitrogen needs, allowing a normal growth, and preventing decompensation during metabolic stress situations.

Keywords: Excess of valine, leucine and isoleucine (3 branched chain amino acids) ; Deficit in the enzyme 2-keto acid-dehydrogenase; Neurological deterioration; Hypoprotein diet restricted in branched-chain amino acids

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Source

- 1. Sociedade Portuguesa de Pediatria. Consenso para o tratamento nutricional da leucinose. Acta Pediátrica Portuguesa, vol. 38, 3, p.120-128. 2007.


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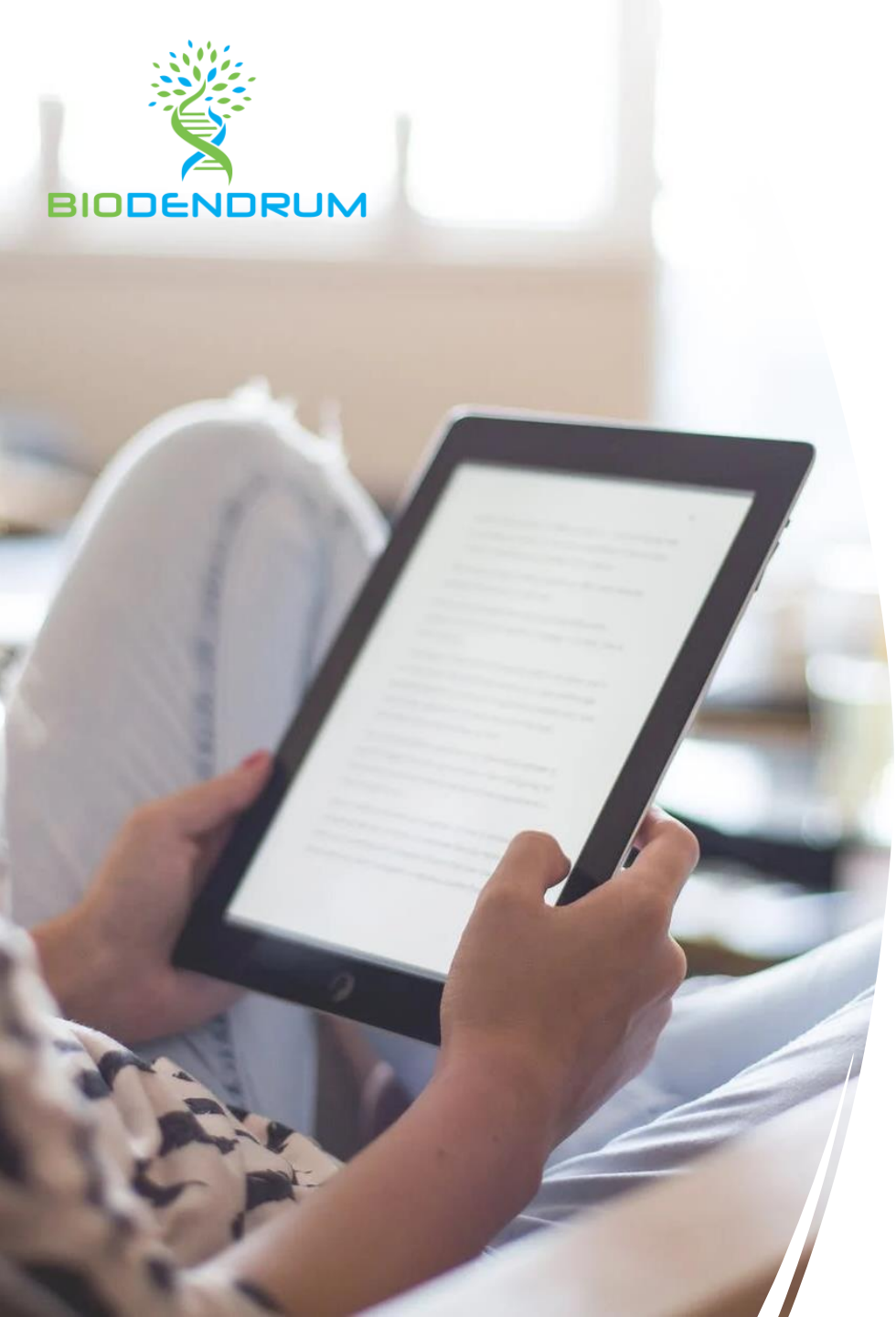

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Homocystinuria (HCU)

Brief description: Homocystinuria (HCU) is an inherited disease of methionine metabolism (Met), which occurs due to the deficiency of the enzyme involved in the sulfur cycle of this amino acid. This enzyme deficit results in the accumulation of homocysteine and methionine in toxic values for patients with HCU, causing damage to organs such as the eyes, brain, bones and blood vessels. Dietary treatment consists of implementing a hypoprotein diet restricted in homocysteine and methionine, and enriched in cystine, with supplementation in the remaining amino acids.

Homocystinuria (HCU)

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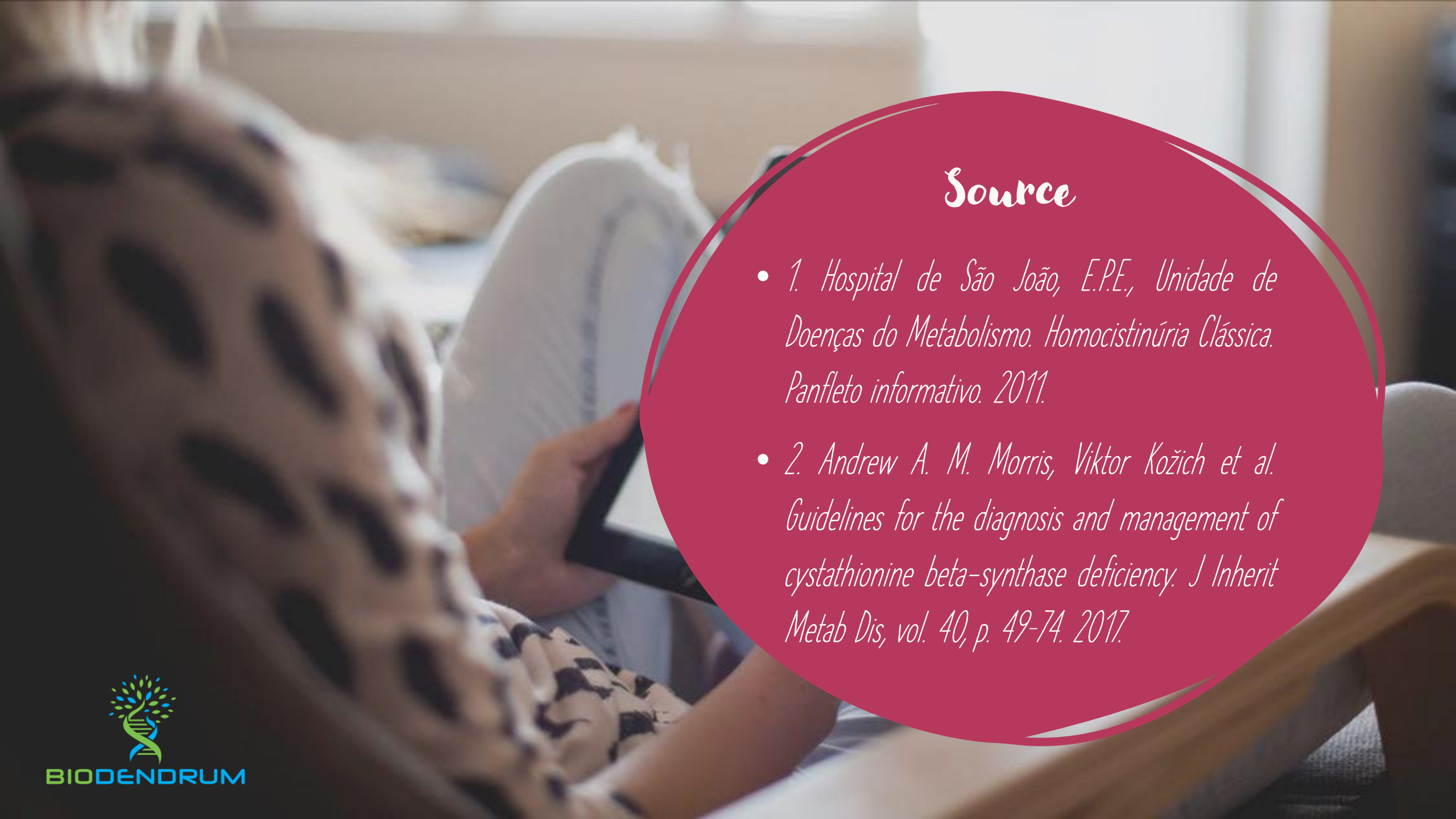
- Homocystinuria (HCU) is a hereditary disease of the metabolism of the amino acid methionine (Met), which occurs due to a deficiency of the enzyme cystathionine β-synthetase, responsible for the conversion of the amino acid homocysteine into cystathionine, and later into cysteine, in the trans-sulfurization pathway of the methionine cycle. In the absence of its activity, there is an accumulation of homocysteine and, consequently, methionine, and a reduction in the levels of cysteine and cystine, to toxic values for the organism.
- HCU translates into clinical and pathological abnormalities, essentially in four organs / systems: eyes (dislocation of the lens and myopia), skeleton (deformations in the skeletal structure and osteoporosis), central nervous system (mild cognitive delay) and vascular system (formation of blood clots in the arteries and veins).
- The treatment of this disease aims to lower the total homocysteine content and includes the use of medications, an adequate diet, or a combination of both. Dietary treatment is based on methionine and homocysteine restriction, and cystine enrichment for life. In certain cases, this diet needs to be supplemented with pyridoxine (a vitamin essential for the functioning of the damaged enzyme), folic acid, vitamin B12 or betaine (the latter 3 to stimulate the transformation of homocysteine into methionine, whose accumulation is less harmful).

Keywords: Excess of homocysteine and methionine; Decrease in cysteine and cystine; Deficit in the enzyme cystathionine β-synthase; Injuries in eyes, brain, bones and blood vessels; Hypoprotein diet restricted in methionine and homocysteine (and L-cystine supplements)



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HCU

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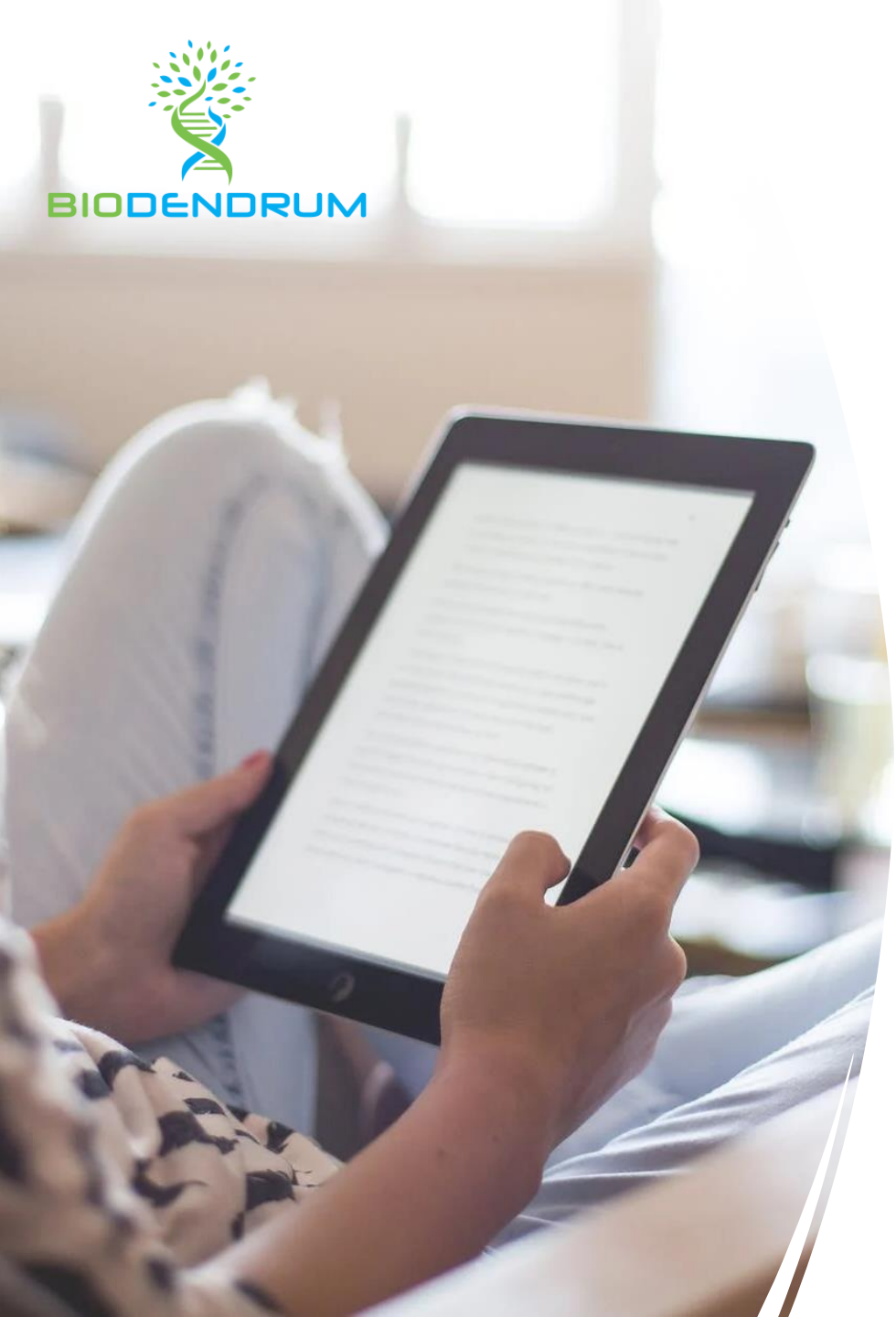


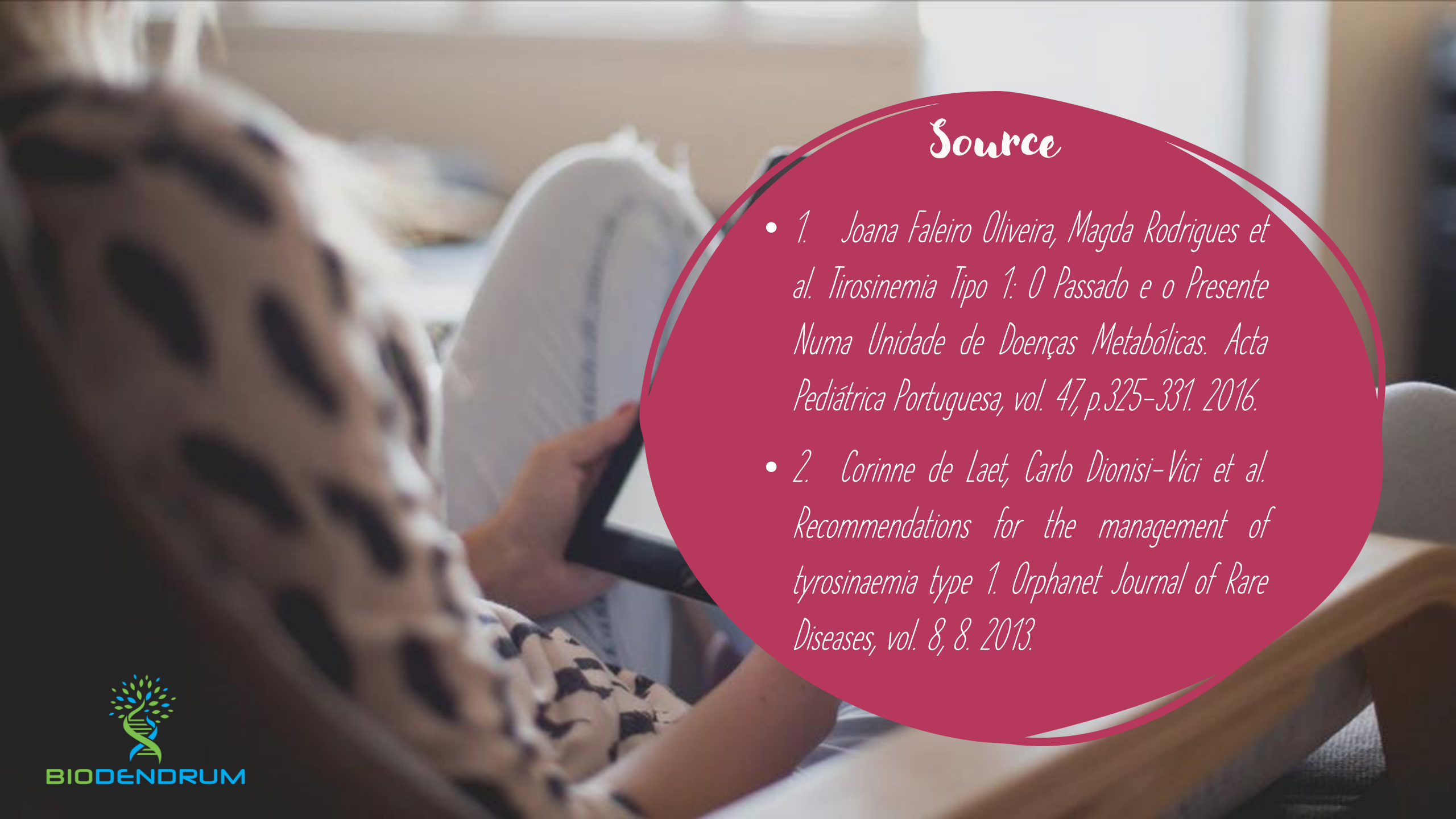
Tyrosinemia (TYR)

Brief description: : Tyrosinemia (TYR) is a disease caused by the malfunction of enzymes responsible for the degradation of the amino acid tyrosine (Tyr), which causes elevated levels of tyrosine and the formation of toxic metabolites. The long-term effect of these harmful substances causes liver and kidney damage, with the risk of hepatocellular carcinoma. The treatment entails a hypoprotein diet restricted in tyrosine and phenylalanine (tyrosine precursor), with supplementation in the remaining amino acids.

Tyrosinemia (TYR)

- Tyrosinemias (TYR) type I, II and III are inherited diseases of the metabolism caused by the deficiency of enzymes responsible for the degradation of the amino acid tyrosine (Tyr). In the case of Tyrosinemia I, the most severe of the 3 types, there is a defect in the final enzyme of the tyrosine degradation pathway – the fumarylacetoacetase enzyme. As a result of the metabolic block, elevation of tyrosine levels occurs, and toxic metabolites are formed, such as maleylacetoacetate, fumarylacetoacetate, succinylacetoacetate and succinylacetone, which accumulate in the hepatocytes and cells of the proximal bypassed tubules. This toxic accumulation results in hepatic and renal damage, with risk of hepatocellular carcinoma. In fact, the main organs affected by this pathology are the liver, kidneys and peripheral nerves.
- The clinical symptoms of Tyrosinemia type II (deficiency in tyrosine aminotransferase) are registered mainly in terms of changes in the skin and the eye, while neurological abnormalities are related to Tyrosinemia type III (deficiency in 4-hydroxy-phenylpyruvate dehydrogenase).
- The individualized diet plan, the hepatorenal transplantation and the nitisinone (or NTBC) are the main therapeutic strategies used. At dietary level, the treatment includes a hypoprotein diet restricted in tyrosine and phenylalanine (tyrosine precursor) for the three types of Tyrosinemia.

Keywords: Excess of tyrosine; Deficit in the fumarylacetoacetase enzyme; Progressive liver failure, renal tubular dysfunction and hepatocellular carcinoma; Hypoprotein diet restricted in tyrosine and phenylalanine



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TYR

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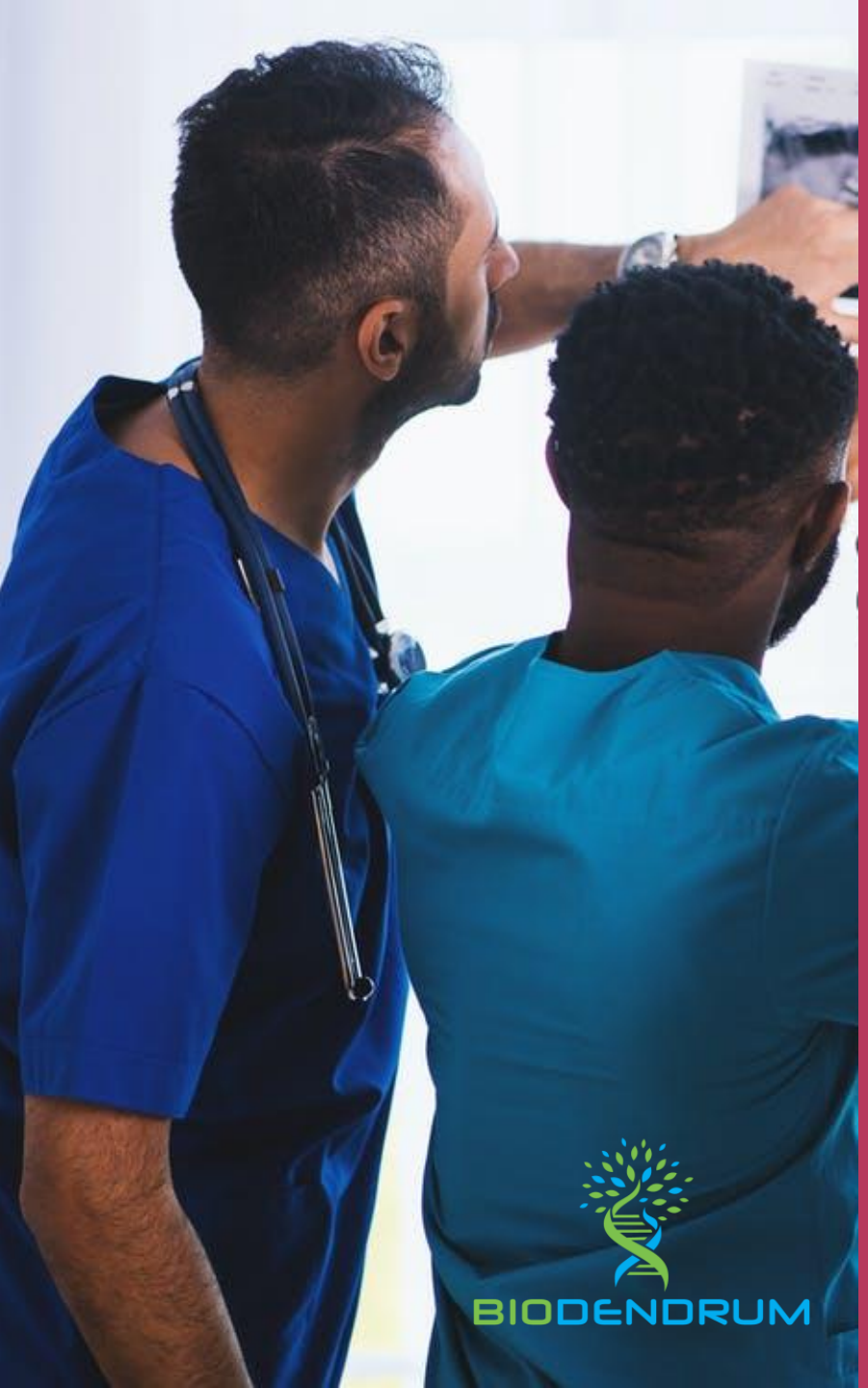

Organic Acidurias

- Organic acidurias are characterized by the accumulation in blood and urine of compounds derived from intermediate metabolism, which have a markedly acidic pH. These acids undergo conjugation in vivo with carnitine, either for later metabolization or to facilitate their excretion (via urine), giving rise to the respective acylcarnitins.

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Propionic (AP) and Methylmalonic (AMM) acidurias

BRIEF DESCRIPTION: Propionic (AP) and methylmalonic (AMM) Acidurias are inherited diseases of metabolism in which the body is unable to properly process the branched chain amino acids methionine (Met), threonine (T), isoleucine (I) and valine (Val). The enzymatic block responsible for these pathologies causes accumulation of organic acids – an increase in methylmalonic and propionic acid in concentrations toxic to the organism, in the case of AMM and AP, respectively. Refusal to eat, vomiting and weight loss are symptoms of these acidurias. If left untreated, they can develop into psychomotor development delay. The recommended treatment is the implementation of a hypoprotein diet restricted in methionine, threonine, isoleucine and valine, supplemented in the remaining amino acids, and in carnitine.

Propionic (AP) and Methylmalonic (AMM) acidurias

- Propionic (AP) and methylmalonic (AMM) Acidurias are inherited metabolic disorders in which the body is unable to properly process certain amino acids, including methionine (Met), threonine (T), isoleucine (I) and valine (Val), as well as some fatty acids in food. Both Acidurias result from an enzymatic block in the catabolism of branched-chain amino acids, which occurs due to a deficit in the activity of the methylmalonyl-CoA mutase (enzyme dependent on vitamin B12) and of the propionyl-CoA carboxylase (biotin-dependent mitochondrial enzyme), in the case of Methylmalonic and Proprionic Acidurias, respectively.
- These organic Acidurias are detected, essentially, through the excretion of organic acids through urine – increase of methylmalonic and propionic acid in toxic concentrations – as well as by the high serum concentrations of acylcarnitins. Symptoms such as refusal to eat, seizures, fatigue, vomiting, dehydration and progressive weight loss typically appear in childhood. If left untreated, these pathologies result in a long-term delay in psychomotor development.

Propionic (AP) and Methylmalonic (AMM) acidurias

- The nutritional treatment includes a low protein diet, with the administration of a mixture of essential amino acids, restricted in the amino acids methionine, threonine, isoleucine and valine, with supplementation of carnitine (helps in the excretion of toxics and prevents secondary deficit in this substance). The food plan should guarantee energy and nutritional needs, preventing the installation of catabolic states, and guaranteeing adequate physical and mental development. Fasting should be avoided.

Keywords: Excess of methylmalonic and propionic acids; Deficiency in methylmalonyl-CoA mutase and propionyl-CoA carboxylase enzymes; Refusal to eat, vomiting and weight loss; Hypoprotein diet restricted in methionine, threonine, isoleucine and valine

BIODENDRUM

Source

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AP e AMM

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Isovaleric Aciduria (AIV)

Brief description: Isovaleric Aciduria (AIV) is caused by a deficit in the activity of an enzyme responsible for the degradation of the amino acid leucine (Leu), resulting in the accumulation of toxic derivatives, such as isovaleric and 3-hydroxy-isovaleric acids, in blood. The symptoms of this pathology are like those of propionic and methylmalonic acidurias. Nutritional treatment involves following a hypoprotein diet, restricted in leucine, supplemented in the remaining amino acids, as well as in carnitine and glycine.

Isovaleric Aciduria (AIV)

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- Isovaleric Aciduria (AIV) is caused by a deficit in the activity of the enzyme dehydrogenase of isovaleryl-CoA, a mitochondrial flavoprotein responsible for the transport of electrons in the respiratory chain and that catalyzes the third step of the leucine (Leu) catabolism. This enzymatic deficit in the leucine degradation cascade leads to the accumulation of isovaleryl-CoA derivatives, including free isovaleric acid, which is highly toxic. This pathology is also known as Sweaty Feet Syndrome, since the accumulation of isovaleric acid causes the emission of an odor similar to sweat / foot odor.
- The symptoms of Isovaleric Aciduria are similar to those presented for Propionic and Methylmalonic Acidurias. The treatment of this pathology involves maintaining the absence of isovaleric and 3-hydroxy-isovaleric acids, as well as isovalerylglycine, in the blood and urine. For this, it is necessary to follow a hypoprotein diet, restricted in leucine, and supplemented with carnitine and glycine.

KEYWORDS: EXCESS OF ISOVALERIC ACID; DEFICIT IN THE ISOVALERYL-COA DEHYDROGENASE ENZYME; REFUSAL TO EAT, VOMITING AND WEIGHT LOSS; LEUCINE-RESTRICTED HYPOPROTEIN DIET

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Source

- 1. Sociedade Portuguesa de Pediatria. Consenso para o tratamento nutricional das acidúrias isovalérica, propiónica e metilmalónica. Acta Pediátrica Portuguesa, vol. 39, 1, p.30-40. 2008.

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AIV

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Glutaric Aciduria Type I (AGI)

Brief description: Glutaric aciduria type I (AGI) is an inherited disease of the metabolism of the amino acids lysine (Lys), hydroxylysine and tryptophan. The deficit in the activity of the enzyme involved in this activity causes accumulation of toxic metabolites such as glutaric acid and 3-hydroxyglutaric acid, whose toxicity is possibly responsible for the neurodegenerative changes seen in patients with AGI. The nutritional treatment includes a hypoprotein diet restricted in lysine and reduced in tryptophan, with supplementation in the remaining amino acids, as well as in carnitine.

Glutaric Aciduria Type I (AGI)

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- Glutaric aciduria type I (AGI) is an inherited disease of the metabolism of the amino acids lysine (Lys), hydroxylsine and tryptophan, caused by the deficit of glutaryl-CoA dehydrogenase (mitochondrial enzyme). This enzyme deficit results in the accumulation of glutaric acid, 3-hydroxyglutaric acid and glutaconic acid in body fluids, with excretion through the urine. The mechanism of this pathology is still poorly understood, however glutaric acid and, in particular, 3-hydroxyglutaric acid, appear to be responsible for the toxicity behind the neurodegenerative changes seen in patients with AGI. Secondarily, there is a decrease in carnitine concentrations, with urinary excretion of glutarylcarnitine, as also seen in propionic, methylmalonic and isovaleric acidurias. This secondary carnitine deficit appears to be the main cause of most metabolic crises, characterized by severe hypoglycemia and metabolic acidosis.

Glutaric Aciduria Type I (AGI)

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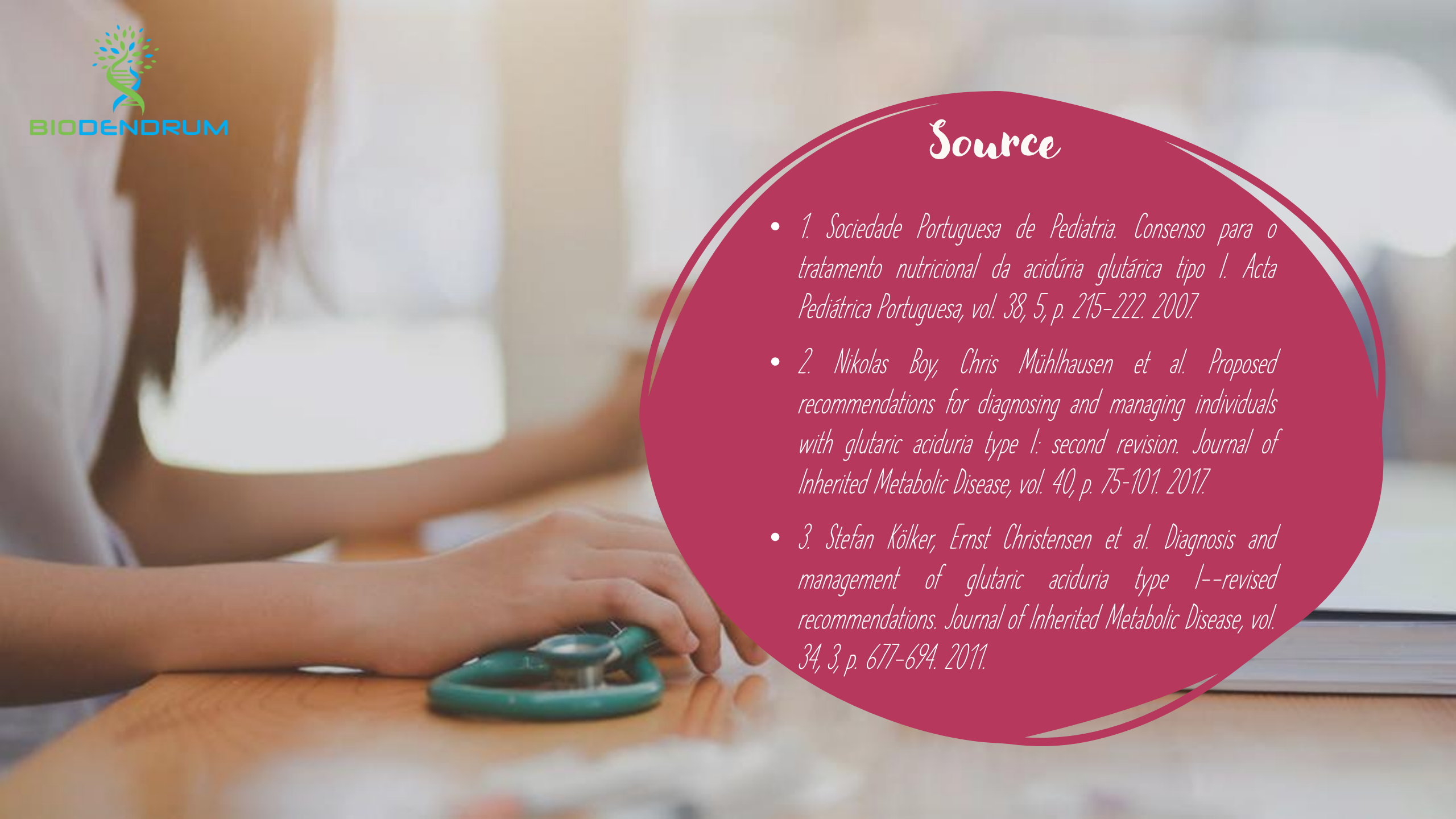
- This disease is characterized by an acute encephalopathic crisis, accompanied by fever and dehydration. This is followed by the installation of a neurological condition dominated by dystonia and axial hypotonia, with immediate loss of acquisitions and faculties. After the occurrence of neurological sequelae, the nutritional treatment proves to be ineffective in its reversion, so it should be implemented as soon as possible through a hypoprotein diet restricted in lysine and supplemented with carnitine. Supplementation in the remaining amino acids is done through liquid, powder or tablet formulas, which must satisfy the energy, amino acids and micronutrients needs, and which are used in all diseases hitherto covered by Biodendrum. The main objective of this treatment is to reduce the production of toxic organic acids, restricting the supply of lysine and tryptophan. During episodes of acute decompensation, treatment should be intensified, increasing the intake of carbohydrates, restricting natural proteins and doubling the dose of carnitine.

KEYWORDS: EXCESS OF GLUTARIC ACID; DEFICIT IN THE ENZYME DEHYDROGENASE OF GLUTARYL-COA; ACUTE ENCEPHALOPATHIC CRISIS; HYPOPROTEIN DIET RESTRICTED IN LYSINE AND REDUCED IN TRYPTOPHAN



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AGI

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Urea Cycle Diseases (DCU)

Brief description: Urea Cycle Diseases (DCU) are caused by an enzyme deficit in one of the six enzymes normally involved in the metabolic cycle of protein nitrogen excretion, which results in an elevated concentration of ammonia in the blood (hyperammonaemia) – toxic compound, especially at the neurological level. If treatment is not carried out on time and at long term, patients with DCU may suffer from variable encephalopathy (including psychiatric manifestations) and liver dysfunction. Dietary treatment involves a hypoprotein diet, supplemented in a mixture of essential amino acids, as well as in arginine.

Urea Cycle Diseases (DCU)

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- The Urea Cycle allows the body to transform the excess of nitrogen into urea and synthesize arginine (an amino acid that integrates all proteins). In this way, a series of cyclic enzymatic reactions convert ammonia into urea, which is easily eliminated in the urine. Note that urea is water-soluble, constituting a non-toxic way to eliminate nitrogen, in contrast to its precursors, such as ammonia, whose toxicity is high.
- Urea cycle diseases (DCU) are caused by an enzyme deficit in one of the six enzymes normally involved in this cycle. This deficit results in an increase of the ammonia concentration in blood - a condition called hyperammonaemia. These high levels are toxic especially at the neurological level. On the other hand, arginine will not be formed in sufficient quantity to allow the protein synthesis necessary for growth.
- DCU symptoms include refusal to eat, irritability, seizures, vomiting, prostration, encephalopathy, poor height-weight evolution, delayed psychomotor development, liver dysfunction and even coma.

Urea Cycle Diseases (DCU)

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- The main goals of the treatment are the correction of biochemical parameters, namely keeping ammonia and glutamine as close to normal levels as possible, together with an energy, protein, essential amino acids and other nutrients supply, in order to meet nutritional needs and allowing to optimize the patient's mental, neurological and physical development. Thus, the treatment consists of a restricted protein diet, supplemented with a mixture of essential amino acids, and L-arginine supplements, as well as possible use of ammonia chelating drugs, sodium benzoate and sodium phenylbutyrate, which create alternative nitrogen excretion pathways. The implementation of a hypoprotein diet is justified by the fact that the physiological production and excretion of urea increases linearly with protein intake. Therefore, by reducing protein intake, we are also reducing the accumulation of glutamine, alanine and ammonia.

KEYWORDS: AMMONIA EXCESS AND ARGININE DEFICIT; DEFICIT OF ENZYME INVOLVED IN THE UREA CYCLE; VARIABLE ENCEPHALOPATHY (INCLUDING PSYCHIATRIC MANIFESTATIONS) AND LIVER DYSFUNCTION; HYPOPROTEIN DIET SUPPLEMENTED WITH A MIXTURE OF ESSENTIAL AMINO ACIDS AND ARGININE

BIODENDRUM

Source

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DCU

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Primary bile acid synthesis disorders

BRIEF DESCRIPTION: Primary bile acid synthesis disorders (BASD) are genetic autosomal recessive diseases. There are usually present as cholestatic jaundice and/or liver failure. The two most frequent ones responsible for chronic liver disease are 3β-HSD deficiency and Δ4-3-oxoR deficiency. They correspond to a lack of one of the two enzymes, 3β-HSD or Δ4-3-oxoR, which are involved in the transformation of cholesterol into primary bile acids in liver cells. When they are missing, cholesterol transformation is incomplete which leads to the absence of production of primary bile acids and accumulation of toxic intermediates in the liver causing its deterioration. Early diagnosis of these disorders is essential.

Primary bile acid synthesis disorders

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- Primary BASD are associated with mutations in the coding genes for enzymes involved in the biosynthesis of primary bile acids (cholic acid and chenodeoxycholic acid). They are rare causes of liver disease in children that can occur at any age (from birth to adolescence). The two most frequent ones responsible for chronic liver disease are:

  - 3**β**-hydroxy-**Δ**5-C27-steroid oxidoreductase (or dehydrogenase/isomerase) deficiency; may also be called 3**β**-HSD deficiency, or BAS defect type 1.

  - **Δ**4-3-oxosteroid-5**β** reductase deficiency; may also be called **Δ**4-3-oxoR, or 5**β**-reductase deficiency, or BAS defect type 2.

- 3**β**-HSD and **Δ**4-3-oxoR are enzymes that play an important role in the primary bile acid synthesis pathway. If they are deficient, synthesis of primary bile acids, which is essential for promoting biliary secretion, is prevented leading to accumulation of toxic bile acid precursors in the liver. This results in cholestasis, then liver cirrhosis or progressive and irreversible liver failure.

Primary bile acid synthesis disorders

- These diseases may be suspected based on a combination of clinical and laboratory signs, and histological findings of the liver. Furthermore, since these diseases are inherited, it is important to look into the patient's family history: cases of unexplained liver problems (or even deaths) in young children in the family can help with the diagnosis of BASD.
- Diagnosis can be difficult because many diseases manifest as neonatal cholestasis or chronic liver disease, and there are no specific clinical features or biomarkers allowing the specific identification of BASDs. However, most patients with BASDs present with:
  - Normal or low total serum bile acid concentrations
  - Normal **γ**-glutamyl transpeptidase concentrations
  - No pruritus
- Early diagnosis is important because these disorders can be treated. Without treatment, there is a 50% mortality rate of **Δ**4-3-oxoR deficiency infants for whom diagnosis is delayed.

Primary bile acid synthesis disorders

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KEYWORDS: Block in the production of normal primary bile acids; Accumulation of unusual bile acids and toxic intermediate metabolites; Deficit of one of two enzymes involved in the transformation of cholesterol into primary bile acids (3β-HSD or Δ4-3-oxoR) ; Liver failure and neurological disease

BIODENORUM

Source

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Information Leaflets

Available on our website:

www.biodendrum.com

Example

XPhe Infant Mix LCP

Isento de Fenilalanina (Phe). Até aos 12 meses.

Descrição geral:

XPhe Infant Mix LCP é um suplemento proteico livre de fenilalanina (Phe) para o tratamento nutricional da Fenilcetonúria (PKU) ou Hiperfenilalaninemia (HPA). XPhe Infant Mix LCP é uma fórmula de aminoácidos em pó para preparação em biberão ou papa. Funciona como leite de início, para lactentes entre 0 a 1 ano de idade. Possui na sua constituição hidratos de carbono (maioritariamente lactose), minerais, vitaminas, gorduras, lípidos do tipo LC-PUFA (como no leite materno humano), L-aminoácidos purificados e micronutrientes em quantidades adequadas. Contém ácido docosahexaenóico (DHA).

Apresentação e Equivalente proteico (EP):

Lata com 500 g do produto em pó, com colher dosadora (3.7 g). 15 g do produto equivalem a 1.65 g de EP.

Informações importantes:

XPhe Infant Mix LCP deve ser tomado sob supervisão médica. Contém hidratos de carbono facilmente digeríveis. Em caso de intolerância à glicose e à galactose assegurar um controlo atento do metabolismo. Não é um alimento completo. Não administrar por via parentérica.

Dosagem e administração:

Dependa da idade, peso e condição clínica do paciente, sendo determinada pelo médico especialista. A quantidade diária é determinada individualmente e administrada juntamente com a quantidade calculada de leite materno ou outros alimentos à base de leite. A toma desta fórmula deverá ser dividida entre 3 a 5 doses diárias.

Preparação:

Diluição standard (15%) - Dissolver 4 medidas de fórmula (4 colheres dosadoras niveladas correspondem a 15 g do produto) em 90 ml de água a 40 °C de forma a obter 100 ml de biberão. Agitar bem, verificar a temperatura e consumir de imediato.

XPhe Infant Mix LCP misturado com água prepara um alimento isento de Phe, que pode ser consumido em forma líquida com biberão. Para preparar uma papa com baixo teor de Phe para lactentes, XPhe Infant Mix LCP deve ser misturado com hidratos de carbono e frutas, em proporção determinada pelo médico ou nutricionista. Em caso de uso prolongado, é necessária a suplementação com alimentos naturais (por exemplo, leite e alimentos à base de leite para lactentes).

Conservação:

Conservar em local seco e fresco. Fechar a tampa firmemente após utilização. Após a primeira abertura, consumir dentro de 4 semanas.

Produto	Tratamento de	Apresentação e EP	Idade	Preparação
XPhe Infant Mix LCP	PKU ou HPA	Fórmula de AA em pó, 500 g. 15 g = 1.65 g EP	0 – 1 ano	4 colheres em 90 ml de água a 40 °C

Produzido na Alemanha por mataX Institut für Diätetik GmbH
Comercializado em Portugal por Biodendrum Portugal
E-mail: info@biodendrum.com
Rua Joaquim António Aguiar 45 2º Esq.1070-150 Lisboa, Portugal

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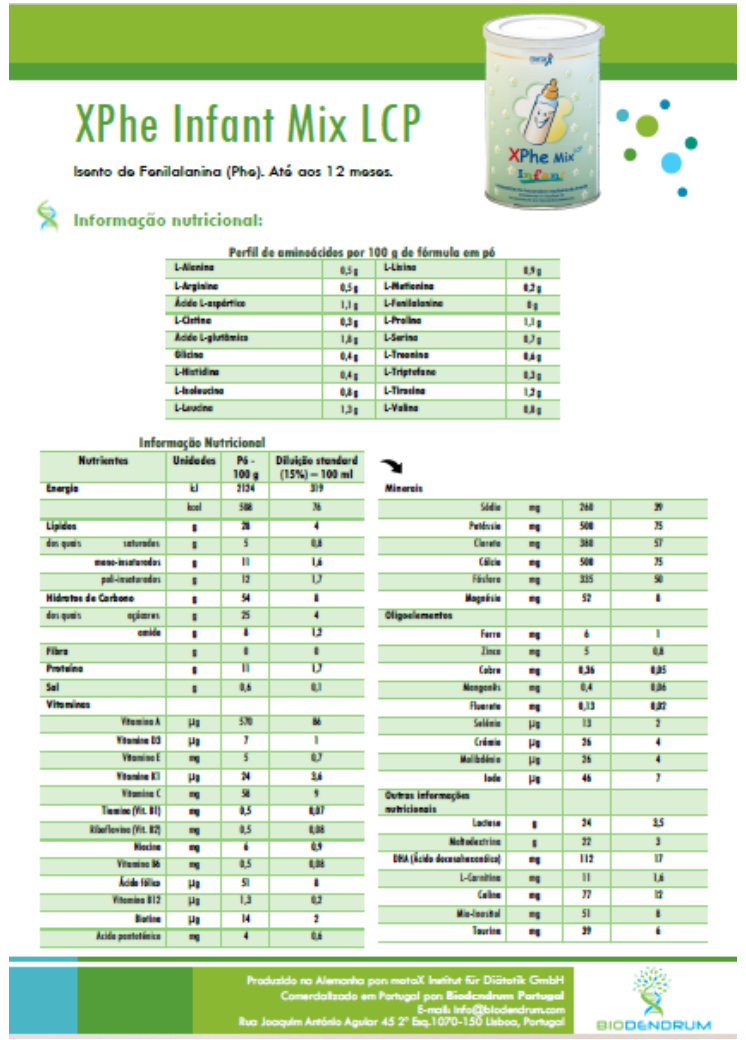

XPhe Infant Mix LCP

Isento de Fenilalanina (Phe). Até aos 12 meses.

Informação nutricional:

Perfil de aminoácidos por 100 g de fórmula em pó

L-Alanina	0,5 g	L-Lisina	0,9 g
L-Arginina	0,5 g	L-Metionina	0,2 g
Ácido L-aspártico	1,1 g	L-Fenilalanina	0 g
L-Cistina	0,3 g	L-Prolina	1,1 g
Ácido L-glutâmico	1,8 g	L-Serina	0,7 g
Glicina	0,4 g	L-Treonina	0,6 g
L-Histidina	0,4 g	L-Triptofano	0,3 g
L-Isoleucina	0,8 g	L-Tirosina	1,3 g
L-Leucina	1,3 g	L-Valina	0,8 g

Informação Nutricional

Nutrientes	Unidades	Pó - 100 g	Diluição standard (15%) – 100 ml
Energia	kJ	2124	319
	kcal	508	76
Lípidos	g	28	4
dos quais saturados	g	5	0,8
mono-insaturados	g	11	1,6
poli-insaturados	g	12	1,7
Hidratos de Carbono	g	54	8
dos quais açúcares	g	25	4
amido	g	8	1,2
Fibra	g	0	0
Proteína	g	11	1,7
Sal	g	0,6	0,1
Vitaminas			
Vitamina A	µg	570	86
Vitamina D3	µg	7	1
Vitamina E	mg	5	0,7
Vitamina K1	µg	24	3,6
Vitamina C	mg	58	9
Tiamina (Vit. B1)	mg	0,5	0,07
Riboflavina (Vit. B2)	mg	0,5	0,08
Niacina	mg	6	0,9
Vitamina B6	mg	0,5	0,08
Ácido fólico	µg	51	8
Vitamina B12	µg	1,3	0,2
Biotina	µg	14	2
Ácido pantoténico	mg	4	0,6

Minerais

Sódio	mg	260	39
Potássio	mg	500	75
Cloreto	mg	380	57
Cálcio	mg	500	75
Fósforo	mg	335	50
Magnésio	mg	52	8
Oligoelementos			
Ferro	mg	6	1
Zinco	mg	5	0,8
Cobre	mg	0,36	0,05
Manganês	mg	0,4	0,06
Fluoreto	mg	0,13	0,02
Selénio	µg	13	2
Crómio	µg	26	4
Molibdénio	µg	26	4
Iodo	µg	46	7
Outras informações nutricionais			
Lactose	g	24	3,5
Maltodextrina	g	22	3
DHA (Ácido docosahexaenóico)	mg	112	17
L-Carnitina	mg	11	1,6
Colina	mg	77	12
Mio-inositol	mg	51	8
Taurina	mg	39	6

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BIODENDRUM

Range of Products

Each metabolic disease has a specific associated packaging colour

Consult our Commercial Flyers!

PHENYLKETONURIA (PKU) OR HYPERPHENYLALANINEMIA (HPA)

Protein supplements free of Phenylalanine (Phe)

XPhe Infant Mix LCP

Powder. Up to 12 months. Neutral flavour.

XPhe minis

Tablets. From 7 years of age.

XPhe Energy K (Neutral)

Powder - sachets. From 1 to 6 years of age. Neutral flavour.

XPhe enjoy GMP (10 and 20 g PE)

Low content of Phe. Powder – sachets. From 3 years of age. Flavours – neutral, vanilla and chocolate.

XPhe JUMP (10 and 20 g PE)

Ready-to-drink formula. From 3 years of age. Flavours – neutral, cola, orange, tropical, vanilla and wild fruits.

XPhe smart A

Powder – tin or sachets (20 g PE). From 15 years of age. Flavours – neutral, lemon, wild fruits and vanilla.

HOMOCYSTINURIA (HCU)

ZeroMet minis

Free of Methionine (Met). Tablets. From 3 years of age.

TYROSINEMIA (TYR)

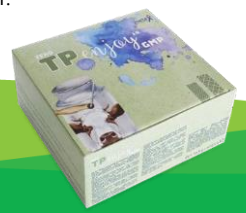
Protein supplements free of Tyrosine (Tyr) and Phenylalanine (Phe)

ZeroTP minis

Tablets. From 3 years of age.

ZeroTP enjoy[10] GMP (10 g PE)

Low content of TYR and Phe. Powder – sachets. From 3 years of age. Neutral flavour.



PE - Protein Equivalent

LEUCINOSIS (MSUD)

Protein supplements free of Valine (Val), Isoleucine (I) and Leucine (Leu). Neutral flavour

ZeroVIL Infant Mix LCP

Powder. Up to 12 months.

ZeroVIL Kid

Powder. From 4 months to 6 years of age.

ZeroVIL Junior

Powder. From 7 to 14 years of age.

ZeroVIL Advance

Powder. From 15 years of age.

ZeroVIL minis

Tablets. From 3 years of age.

PROPIONIC (AP) AND METHYLMALONIC (AMM) ACIDURIAS

ZeroTVMI minis

Free of Threonine (T), Valine (Val), Methionine (Met) and Isoleucine (I). Tablets. From 3 years of age.

GLUTARIC ACIDURIA TYPE I (AGI)

ZeroLys minis

Free of Lysine (Lys), reduced in Tryptophan and enriched in Arginine. Tablets. From 3 years of age.

ISOVALERIC ACIDURIA (AIV)

ZeroLeu minis

Free of Leucine (Leu). Tablets. From 3 years of age.

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UREA CYCLE DISORDERS (DCU)

PLUS8 minis

It contains all 8 essential amino acids. Tablets. From 3 years of age.

PRIMARY BILE ACID SYNTHESIS DISORDERS (DSABP)

Orphacol (cholic acid)

More info:

https://www.ema.europa.eu/en/medicines/human/EPAR/orphacol

Products available in your country may vary according to commercialization status

E-mail: info@biodendrum.com

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Questions
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Treatment of Rare Metabolic Diseases