

## **Percura™ PRODUCT INFORMATION**

**Percura** capsules by oral administration. A specially formulated Medical Food product, consisting of a proprietary blend of amino acids in specific proportions, for the dietary management of the metabolic processes associated with pain, inflammation and loss of sensation due to peripheral neuropathy. **Must be administered under physician supervision.**

### **Medical Foods**

Medical Food products are often used in hospitals (e.g., for burn victims or kidney dialysis patients) and outside of a hospital setting under a physician's care for the dietary management of diseases in patients with particular, unique or distinctive medical or metabolic needs due to their disease or condition. Congress defined "Medical Food" in the Orphan Drug Act and Amendments of 1988 as "a food which is formulated to be consumed or administered enterally [or orally] under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation." Medical Foods are complex formulated products, requiring sophisticated and exacting technology, and that are used only for a patient receiving active and ongoing medical supervision wherein the patient requires medical care on a recurring basis for, among other things, instructions on the use of the Medical Food. **Percura** has been developed, manufactured, and labeled in accordance with both the statutory definition of a Medical Food and FDA's regulatory labeling guidelines. **Percura** must be used while the patient is under the ongoing care of a physician.

### **NEUROPATHIC PAIN (NP)**

#### **NP as a Metabolic Deficiency Disease**

A critical component of the definition of a Medical Food is that the product must address the distinct nutritional requirements of a particular disease or condition. FDA scientists have proposed a physiologic definition of distinctive nutritional requirements as follows: "the dietary management of patients with specific diseases requires, in some instances, the ability to meet nutritional requirements that differ substantially from the needs of healthy persons. For example, in establishing the recommended dietary allowances for the general, healthy population, the Food and Nutrition Board of the Institute of Medicine National Academy of Sciences recognized that different or distinctive physiologic requirements may exist for certain persons with "special nutritional needs arising from metabolic disorders, chronic diseases, injuries, premature birth, other medical conditions and drug therapies. **Thus, the distinctive nutritional needs associated with a disease reflects the total amount needed by a healthy person to support life or maintain homeostasis, adjusted for the distinctive changes in the nutritional needs of the patient as a result of the effects of the disease process on absorption, metabolism and excretion.**" It was also proposed that in patients with certain disease states who respond to nutritional therapies, a physiologic deficiency of the nutrient is assumed to exist. For example, if a patient with neuropathic pain responds to a tryptophan formulation by decreasing perceived pain, then a deficiency of tryptophan is assumed to exist.

In **NP** neurons become unusually sensitive and there is abnormal excitability and heightened sensitivity to chemical, thermal and mechanical stimuli, called peripheral sensitization. In the complicated feedback loops and processes that lead to peripheral sensitization, there are increased demands and competition for nutrients involved with the pain receptors, response to afferent impulses and the development of nerve injury. Including arginine, choline, GABA, glutamine, histidine, tryptophan, and serine. These nutritional requirements are such that they cannot be achieved by the modification of the normal diet alone, or by supplementing the diet. **NP** involves degradation of pathways that increases the turnover rate of the precursors needed for neurotransmitters that results in a reduction in the level of production of neurotransmitters GABA, histamine, nitric oxide, serotonin, and acetylcholine. Research has also shown that a genetic predisposition to accelerated degradation can lead to increased precursor requirements in certain patients with neuropathic pain.

### **PRODUCT DESCRIPTION**

#### **Primary Ingredients**

**Percura** is a proprietary formulation of amino acids and other dietary factors to support induction, maintenance, and enhancement of the specific neurotransmitter activity involved in the physiology of neuropathic pain. The formulation consists of nonessential and essential amino acids L-Arginine HCL, L-Histidine HCL, L-Glutamine, L-Serine, L-Lysine, L-Oornithine, Acetyl L-Carnitine, L-Tyrosine, the nonstandard amino acid Gamma Aminobutyric Acid, Choline Bitartrate, Glucose, Inositol, Griffonia Extract griffonia simplicifolia (95% 5-HTP), and Creatinine. These ingredients fall into the classification of Generally Recognized as Safe (GRAS) as defined by the Food and Drug Administration (FDA) (Sections 201(s) and 409 of the Federal Food, Drug, and Cosmetic Act). A GRAS substance is distinguished from a food additive on the basis of the common knowledge about the safety of the substance for its intended use. The standard for an ingredient to achieve GRAS status requires not only technical demonstration of non-toxicity and safety, but also general recognition of safety through widespread usage and agreement of that safety by experts in the field. Many ingredients have been determined by the FDA to be GRAS, and are listed as such by regulation, in Volume 21 Code of Federal Regulations (CFR) Sections 182, 184, and 186.

#### **Amino Acids**

Amino Acids are the building blocks of protein and are GRAS listed as they have been safely ingested by humans for thousands of years. The formulations of the amino acids in **Percura** are equivalent to those found in the usual human diet. Patients with neuropathic pain may require an increased amount of certain amino acids that cannot be obtained from normal diet alone. Tryptophan, for example, is an essential amino acid. The body cannot make tryptophan and must obtain tryptophan from the diet. Tryptophan is needed to produce serotonin. Serotonin is required to reduce pain. Patients with neuropathic pain have altered serotonin metabolism.

#### **Other Ingredients**

**Percura** contains gelatin, silicon dioxide, vegetable magnesium stearate, microcrystalline cellulose, lac-resin and carmine.

#### **Physical Description**

**Percura** is a yellow to light brown powder encapsulated in a clear, dye-free capsule.

### **CLINICAL PHARMACOLOGY**

#### **Mechanism of Action**

The mechanism of action for **Percura** is not clearly understood.

#### **Metabolism**

Under usual physiological conditions, glutamine, arginine, serine, and choline are considered nonessential because endogenous synthesis is sufficient to satisfy metabolic demand. When needs are altered due to increase demands as with neuropathic pain, the usual rate of synthesis is no longer sufficient and these nutrients become conditionally essential, requiring that supplemental amounts be consumed. The amino acids in **Percura** are primarily absorbed by the stomach and small intestines. All cells metabolize the amino acids in **Percura**. Circulating tryptophan, arginine and choline blood levels determine the production of serotonin, nitric oxide, and acetylcholine.

#### **Excretion**

**Percura** is not an inhibitor of cytochrome P450 1A2, 2C9, 2C19, 2D6, or 3A4. These isoenzymes are principally responsible for 95% of all detoxification of drugs, with CYP3A4 being responsible for detoxification of roughly 50% of drugs. Amino acids do not appear to have an effect on drug metabolizing enzymes.

## INDICATIONS FOR USE

**Percura** is intended for the clinical dietary management of the metabolic processes of pain, inflammation and loss of sensation due to peripheral neuropathy.

## CLINICAL EXPERIENCE

Administration of the ingredients found in **Percura** has demonstrated significant reduction in symptoms of pain in patients with acute and chronic pain when used for the dietary management of the metabolic processes associated with pain, inflammation and loss of sensation due to peripheral neuropathy. Administration of **Percura** may result in the induction and maintenance of pain relief in patients with pain disorders related to peripheral neuropathy.

## PRECAUTIONS AND CONTRAINDICATIONS

**Percura** is contraindicated in an extremely small number of patients with hypersensitivity to any of the nutritional components of **Percura**.

## ADVERSE REACTIONS

Ingestion of L-Tryptophan, L-Arginine, or Choline at high doses of up to 15 grams daily is generally well tolerated. The most common adverse reactions of higher doses — from 15 to 30 grams daily — are nausea, abdominal cramps, and diarrhea. **Percura** contains less than 1 gram per dose of amino acids however, some patients may experience these symptoms at lower doses. The total combined amount of amino acids in each **Percura** capsule does not exceed 300 mg.

## DRUG INTERACTIONS

**Percura** does not directly influence the pharmacokinetics of prescription drugs. Clinical experience has shown that administration of the ingredients found in **Percura** may allow for lowering the dose of co-administered drugs under physician supervision.

## OVERDOSE

There is a negligible risk of overdose with **Percura** as the total amount of amino acids in a one month supply (120 capsules) is less than 30 grams. Overdose symptoms may include diarrhea, weakness, and nausea.

## POST-MARKETING SURVEILLANCE

One in five thousand patients may experience a skin rash after increased absorption of histamine. This rash is temporary and will subside within 24-hours.

## DOSAGE AND ADMINISTRATION

### Recommended Administration

For the dietary management of the metabolic processes associated with pain, inflammation and loss of sensation due to peripheral neuropathy. Take two (2) capsules twice daily or as directed by physician. As with most amino acid formulations **Percura** should be taken without food to increase the absorption of key ingredients.

### How Supplied

**Percura** is supplied in a clear, size 0 capsules in bottles of 120 capsules.

### Physician Supervision

**Percura** is a Medical Food product available by prescription only and may be used per FDA law, and product labeling only while the patient is under ongoing physician supervision.

### Storage

Keep tightly closed in a cool dry place 8-32° C (45-90° F), relative humidity below 50%. **Percura** is supplied in a recyclable plastic bottle with a child-resistant cap.

**US Patent 7,582,315; 7,585,523; 7,595,067; 7,601,369, Patents Pending.**

Manufactured for:

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