Trepadone® *PRODUCT INFORMATION*

Trepadone capsules by oral administration. A specially formulated Medical Food product, consisting of a proprietary formulation of amino acids and polyphenol ingredients in specific proportions, for the dietary management of the metabolic processes associated with pain and inflammation related to joint disorders. (JD)
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. ***Trepadone*** has been developed, manufactured, and labeled in accordance with both the statutory definition of a Medical Food and FDA's regulatory labeling guidelines. ***Trepadone*** must be used while the patient is under the ongoing care of a physician.

PAIN & INFLAMMATION IN JOINT DISORDERS (JD)

JD 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 a pain and inflammation of the joints responds to a specific formulation by decreasing perceived pain, then a deficiency of tryptophan, histidine, Omega 3 Free Fatty Acids, and GABA is assumed to exist.

Patients with pain and inflammation of the joints are known to have increased nutritional requirements for glucosamine, chondroitin, tryptophan, arginine, histidine, GABA, flavonoids, and certain antioxidants. These nutritional requirements are such that they cannot be achieved by the modification of the normal diet alone, or by supplementing the diet. Patients with pain and inflammation of the joints frequently exhibit activation of the degradation pathways that increases the turnover rate of arginine, histidine, GABA, and tryptophan. Research has also shown that a genetic predisposition to accelerated degradation can lead to increased precursor requirements in certain patients with pain disorders and inflammatory conditions.

PRODUCT DESCRIPTION

Primary Ingredients

Trepadone is a proprietary formulation of of amino acids and other dietary factors to support induction, maintenance, and enhancement of the specific neurotransmitter activity involved in the physiology of JD. The formulation consists of Glucosamine Sulphate, Chondroitine Sulphate, L-Histidine HCL, Whey Protein Isolate, Omega 3 EFA (from Fish Oil), Grape Seed Extract, Cocoa Extract, and Gamma Aminobutyric Acid (GABA) in specific proportions. 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. Whey Protein Isolate contains all 22 amino acids essential for human metabolism including tryptophan, arginine and histidine.

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 ***Trepadone*** are equivalent to those found in the usual human diet. Patients with pain and inflammation of the joints may require an increased amount of certain amino acids that cannot be obtained from normal diet alone. Tryptophan, for example, is an obligatory 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 pain and inflammation of the joints have altered serotonin metabolism.

Other Ingredients

Trepadone contains the following "inactive" or other ingredients, as fillers, excipients, and colorings: Gelatin, vegetable magnesium stearate, silicon dioxide, lac-resin, carmine.

Physical Description

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

CLINICAL PHARMACOLOGY

Mechanism of Action

Trepadone acts by providing the nutritional requirements that supports the synthesis and physiological activities of neurotransmitters involved in JD. These nutrients which support the balance of the neurotransmitters that are associated with JD. Correcting nutritional deficiencies is critical to the physiological functions that must be balanced in the highly integrated and complex multiple feedback interactions that determine input to the brain. A balance is required between the activities of the excitatory and inhibitory neurotransmitters in the complex relationship between the various activities of the neurotransmitters. An imbalance in the intake of a nutrient or dietary factor which supports the synthesis or activity of any one neurotransmitter can influence the activites of the others, and negatively impact neurotransmitter-mediation. Metabolic efficiency requires an adequate supply of the precursors, delivery to targeted cells. Specific ratios, appropriate timing and uptake stimulation are required to reduce fractional absorption that would otherwise cause the liver to rapidly deaminates the absorbed nutrients.

Targeted Cellular Technology™ a patented integrated molecular system facilitates the uptake and utilization of neurotransmitter precursors by target cells in the nervous system. This 5-component system consists of (1) specific neurotransmitter precursors; (2) a stimulus for the neuronal update of the precursors by specific neurons; (3) an adenosine antagonist that blocks the inhibitory effect of adenosine on neuronal activity; (4) a stimulus to trigger the release of the required neurotransmitters from the targeted neurons, and (5) a mechanism to prevent attenuation of the precursor response.

Metabolism

Under usual physiological conditions, GABA and histidine are considered nonessential because endogenous synthesis is sufficeint to satisfy metabolic demand. When needs are altered due to increase demands as with JD, 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 *Trepadone* are primarily absorbed by the stomach and small intestines. All cells metabolize the amino acids in *Trepadone*.

Excretion

Trepadone 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

Trepadone is intended for the clinical dietary management of the metabolic processes of pain and inflammation of the joints

CLINICAL EXPERIENCE

Administration of *Trepadone* has demonstrated significant reduction in symptoms in patients with both acute and chronic conditions when used for the dietary management of the metabolic processes associated with pain and inflammation of the joints. Administration of *Trepadone* results in the induction and maintenance of pain relief in patients with pain and inflammation of the joints.

PRECAUTIONS AND CONTRAINDICATIONS

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

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. *Trepadone* contains less than 200mg per dose of amino acids however, some patients may experience these symptoms at lower doses. The total combined amount of amino acids in each *Trepadone* capsule does not exceed 100 mg. *Trepadone* contains Fish (Tuna), Shellfish (Shrimp, Crab, and Crayfish), and Milk (Whey Protein Isolate) ingredients.

DRUG INTERACTIONS

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

OVERDOSE

There is a negligible risk of overdose with *Trepadone* as the total amount of amino acids in a one month supply (90 capsules) is less than 9 grams. Overdose symptoms may include diarrhea, weakness, and nausea.

POST-MARKETING SURVEILLANCE

Post-marketing surveillance has shown no serious adverse reactions. Reported cases of mild rash and itching may have been associated with allergies to *Trepadone* flavonoid ingredients, including Cocoa, and Grape Seed Extract. These reactions were temporary and subsided within 24-hours.

DOSAGE AND ADMINISTRATION

Recommended Administration

For the dietary management of the metabolic processes associated with pain and inflammation of the joints. Take two (2) capsules four times per day or as directed by physician. As with most amino acid formulations *Trepadone* should be taken without food to increase the absorption of key ingredients.

How Supplied

Trepadone is supplied in clear, size 0 capsules in bottles of 90 and 120 capsules.

Physician Supervision

Trepadone 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 8-32º C (45-90º F), relative humidity below 50%. *Trepadone* 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.

Manufactured for:
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