GABAdone® PRODUCT INFORMATION

GABAdone 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 nutritional management of the metabolic processes of sleep disorders (SD).
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. *GABAdone* has been developed, manufactured, and labeled in accordance with both the statutory and the FDA regulatory definition of a Medical Food. *GABAdone* must be used while the patient is under the ongoing care of a physician.

SLEEP DISORDERS (SD)

SD 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 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 reflect 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 sleep disorder responds to a tryptophan formulation by improving the duration and quality of sleep, a deficiency of tryptophan is assumed to exist.

Patients with sleep disorders are known to have increased nutritional requirements for tryptophan, GABA, choline, flavonoids, and certain antioxidants. Patients with sleep disorders frequently exhibit reduced plasma levels of tryptophan and have been shown to respond to oral administration of tryptophan or a 5-hydroxytryptophan formulation. Research has shown that tryptophan reduced diets result in a fall in circulating tryptophan. Patients with sleep disorders frequently experience activation of the tryptophan degradation pathway that increases the turnover rate of tryptophan leading to a reduced level of production of serotonin for a given tryptophan blood level. Research has also shown that a genetic predisposition to accelerated tryptophan degradation can lead to increased tryptophan requirements in certain patients with sleep disorders.

Choline is required to fully potentiate acetylcholine synthesis by brain neurons. A deficiency of choline leads to reduced acetylcholine production by the neurons. Flavonoids potentiate the production of acetylcholine by the neurons thereby inducing REM sleep. Low fat diets and diets deficient in flavonoid rich foods result in inadequate flavonoid concentrations, impeding acetylcholine production in certain patients with sleep disorders. Provision of tryptophan, choline, and flavonoids with antioxidants, in specific proportions can restore the production of beneficial serotonin and acetylcholine, thereby improving sleep quality.

PRODUCT DESCRIPTION

Primary Ingredients

GABAdone 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 SD. The formulation consists of nonessential and essential amino acids Choline Bitartrate, Gamma Aminobutyric Acid, Cocoa Extract, L-Glutamic Acid, Whey Protein Isolate (Milk), Griffonia Extract, Valerian Root, Acetyl L-Carnitine HCL, Ginkgo Biloba, and Grape Seed Extract in specific proportions. These ingredients fall into the category 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 U.S. Food and Drug Administration (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. All amino acids are GRAS listed as they have been ingested by humans for thousands of years. The doses of the amino acids in *GABAdone* are equivalent to those found in the usual human diet; however the formulation uses specific ratios of the key ingredients to elicit a therapeutic response. 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 induce sleep. Patients with sleep disorders have altered serotonin metabolism. Some patients with sleep disorders have a resistance to the use of tryptophan that is similar to the mechanism found in insulin resistance. Patients with sleep disorders cannot acquire sufficient tryptophan from the diet to establish normal sleep architecture without ingesting a prohibitively large amount of calories, particularly calories from protein.

Other Ingredients

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

Physical Description

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

CLINICAL PHARMACOLOGY

Mechanism of Action

GABAdone acts by providing the nutritional requirements that support the synthesis and physiological activities of neurotransmitters involved in SD. These nutrients include choline, GABA, glutamine, tryptophan and carnitine which support the balance of the neurotransmitters GABA, serotonin, and acetylcholine that are associated with SD. 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 and regulation of the sleep-wake cycle. 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, glutamine, serotonin and choline are considered nonessential because endogenous synthesis is sufficeint to satisfy metabolic demand. When needs are altered due to increase demands as with SD, 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 *GABAdone* are primarily absorbed by the stomach and small intestines. All cells metabolize the amino acids in *GABAdone*. Circulating tryptophan and choline blood levels determine the production of serotonin and acetylcholine.

Excretion
GABAdone 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
GABAdone is intended for the clinical nutritional management of the metabolic processes in patients with sleep disorders and sleep disorders associated with anxiety.

CLINICAL EXPERIENCE
Administration of *GABAdone* has demonstrated significant functional improvement when used for the dietary management of the metabolic processes related to general sleep disorders and sleep disorders associated with anxiety. The administration of *GABAdone* results in the induction and maintenance of sleep.

PRECAUTIONS AND CONTRAINDICATIONS
GABAdone is contraindicated in an extremely small number of patients with hypersensitivity to any of the nutritional components of *GABAdone*

ADVERSE REACTIONS
Ingestion of L-tryptophan, GABA 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. *GABAdone* contains less than 1 gram of amino acids per dose however, some patients may experience these symptoms at lower doses. The total combined amount of amino acids in each *GABAdone* capsule does not exceed 300 mg.

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

OVERDOSE
There is a negligible risk of overdose with *GABAdone* as the total amount of amino acids in a one month supply (60 capsules) is less than 20 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 *GABAdone* flavonoid ingredients, including Cocoa, Grape Seed Extract, and Griffonia Extract.

DOSAGE AND ADMINISTRATION
Recommended Administration
For the dietary management of the metabolic processes in patients with sleep disorders. Take (1) one or (2) capsules daily at bedtime, or as directed by physician. An additional dose of one or two capsules may be taken after awakenings during the night. As with most amino acid formulations *GABAdone* should be taken without food to increase the absorption of key ingredients.

How Supplied
GABAdone is supplied in clear, size 0 capsules in bottles of 60 capsules.

Physician Supervision
GABAdone is a Medical Food product available by prescription only and may be used per FDA law, and product labeling 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%. *GABAdone* 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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