

## **Lister-V® Product Information**

**Lister-V** capsules by oral administration. A specially formulated Medical Food product, consisting of a proprietary blend of amino acids and polyphenol ingredients in specific proportions, for the nutritional management of the metabolic processes associated with viral infection. 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 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 system 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. **Lister-V** has been developed, manufactured, and labeled in accordance with both the statutory and the FDA regulatory definition of a Medical Food. **Lister-V** must be used while the patient is under the ongoing care of a physician.

## **DISORDERS OF IMMUNE RESPONSE (IR)**

### **Disorders of Immune Response as a Metabolic Deficiency Disease**

A critical component of the definition of a Medical Food is the requirement for a distinctive nutritional deficiency. FDA scientists have proposed a physiologic definition of a distinctive nutritional deficiency 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 symptoms of influenza responds to arginine as a precursor to nitric oxide, by decreasing the severity and/or duration of symptoms, a deficiency of arginine is assumed to exist.

Patients with a compromised immune system are known to have nutritional deficiencies of arginine, choline, flavonoids, and certain antioxidants. **Lister-V** is a specially formulated Medical Food product designed to enhance immune function, activating the white blood cells to seek out and destroy viruses when they invade the body. Arginine serves as the substrate for the nitric oxide synthase enzyme, which catalyzes the oxidation of arginine to produce citrulline and nitric oxide (NO). Nitric oxide is a potent inhibitor of virus growth, particularly viruses that are responsible for the common cold including rhinoviruses, adenoviruses, and corona viruses. Delivery of nitric oxide to viruses in the nasal passages and lungs is likely to inhibit their growth thereby decreasing the duration of a common cold and certain types of virus induced illnesses.

Arginine and choline, precursors of nitric oxide and acetylcholine, combined with food-based potentiators, will produce nitric oxide in nasal passages. Echinacea increases white blood cell activity in the nasal passages and the lungs. The combination of nitric oxide production, acetylcholine production, and echinacea induced white blood cell increase, will reduce the duration and symptoms of a common cold. Echinacea extracts have been shown to stimulate the growth and activity of cells of the immune system (macrophages, natural killer cells, T-cells). Such activation of protective mechanisms is thought to increase the body's defenses to infection by viruses. Flavonoids are thought to be the primary immunostimulatory constituents in the various echinacea species. Grape seeds are a potent source of proanthocyanidins, a powerful antioxidant. The complex metabolic processes that are responsible for optimal functioning of the immune system involve the coordinated efforts of several types of white blood cells.

## **PRODUCT DESCRIPTION**

### **Primary Ingredients**

**Lister-V** 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 IR. The formulation consists of nonessential and essential amino acids, L-Arginine HCL, L-Glutamine, L-Histidine HCL, L-Leucine, L-Cysteine, Lecithin, Echinacea, Green Tea Extract, Cinnamon, Cocoa Extract, Whey Protein Isolate (Milk), Zinc, and Grape Seed Extract. These ingredients fall into the category of "Generally Regarded 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 **Lister-V** 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. Patients with a viral disease may require an increased amount of certain amino acids that cannot be obtained from normal diet alone. Choline, for example, is an essential amino acid. The body cannot make choline and must obtain choline from the diet. Choline is required to fully potentiate nitric oxide synthesis in the nasal passage and lungs. A deficiency of choline leads to reduced nitric oxide production in the nasal passage and lungs. Flavonoids potentiate the production of nitric oxide in the nasal passage and lungs. Choline deficient diets and diets deficient in flavonoid rich foods can result in inadequate flavonoid concentrations, impeding nitric oxide production. Provision of arginine, choline, and flavonoids with antioxidants, in specific proportions can restore the production of beneficial nitric oxide, thereby inhibiting viral growth.

### **Other Ingredients**

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

### **Physical Description**

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

## **CLINICAL PHARMACOLOGY**

### **Mechanism of Action**

**Lister-V** acts by providing the nutritional requirements that support the synthesis and physiological activities of neurotransmitters involved in IR. These nutrients include arginine, glutamine and histidine which support the balance of the neurotransmitters nitric oxide, GABA, and histamine, and acetylcholine that are associated with

disorders of the IR. 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 activities 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 deaminate 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 uptake 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, arginine, histidine and choline are considered nonessential because endogenous synthesis is sufficient to satisfy metabolic demand. When needs are altered due to increase demands as with disorders of IR, 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 *Lister-V* are primarily absorbed by the stomach and small intestines. All cells metabolize the amino acids in *Lister-V*. Circulating arginine and choline blood levels determine the production of nitric oxide and acetylcholine.

### Excretion

*Lister-V* 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

*Lister-V* is intended for the clinical nutritional management of the metabolic processes associated with viral infections, including common cold and influenza (flu) viruses.

### CLINICAL EXPERIENCE

Administration of *Lister-V* has demonstrated significant functional improvements of influenza symptoms when used for the nutritional management of the metabolic processes associated with certain viral infections. The administration of *Lister-V* results in increased production of white blood cells and a reduction in the severity and duration of symptoms associated with viral infections.

### PRECAUTIONS AND CONTRAINDICATIONS

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

### ADVERSE REACTIONS

Oral supplementation with L-arginine at high doses 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. Some patients may experience these symptoms at lower doses. The total combined amount of amino acids in each *Lister-V* capsule does not exceed 400 mg.

### DRUG INTERACTIONS

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

### OVERDOSE

There is a negligible risk of overdose with *Lister-V* as the total dosage of amino acids in a one month supply (60 capsules) is less than 25 grams. Overdose symptoms may include diarrhea, weakness, and nausea.

### POST-MARKETING SURVEILLANCE

Post-marketing surveillance has shown no serious or adverse reactions. Reported cases of mild rash and itching may have been associated with allergies to *Lister-V* flavonoid ingredients, including cinnamon, cocoa, and chocolate. The reactions were transient in nature and subsided within 24 hours.

### DOSAGE AND ADMINISTRATION

#### Recommended Administration

For the nutritional management of the metabolic processes associated with viral infections. *Lister-V* can be administered to ameliorate the symptoms and shorten the duration of a viral infection. At the first signs of viral infection take (3) capsules four times a day for five days or as directed by a physician. *Lister-V* may be used to enhance immune function after exposure to a viral disease. *Lister-V* may be taken by those susceptible to upper respiratory infections during airline travel. As with most amino acid formulations *Lister-V* should be taken without food to increase the absorption of key ingredients.

### HOW SUPPLIED

*Lister-V* is supplied in clear, size 0 capsules in bottles of 60 capsules.

### PHYSICIAN SUPERVISION

*Lister-V* is a Medical Food product available by prescription only and must be used 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%. *Lister-V* is supplied in a recyclable plastic bottle with a child-resistant cap.

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Manufactured for: Physician Therapeutics, a wholly owned subsidiary of Targeted Medical Pharma Inc.

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