Description:

The etiology of hyposerotonergic conditions or states is when systemic serotonin concentrations on normal diet are not enough, low, inadequate, depleted, deficient, deficit, or suboptimal.

Administration of enteral R&R™ occurs under the supervision of a physician or other licensed caregiver for the dietary management of hyposerotonergic conditions or states, for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation. The special formulation of R&R meets the distinctive nutritional requirements induced by hyposerotonergic conditions and states. The hyposerotonergic condition or state has an increased requirement for serotonin precursor 5-HTP or vitamin B6 to prevent serotonin-related symptoms or functional dysregulation. A modification of the normal diet cannot manage these unique nutritional requirements. The unique formulation of R&R provides necessary 5-HTP and vitamin B6 while being formulated to address the undesirable ability of aromatic amino acid precursors to induced hypodopaminergic or glutathionemia conditions or states.

Intended Use:

The formulation R&R is a medical food administered enterally under the supervision of a healthcare professional, for the specific dietary management of hyposerotonergic conditions or states.

Examples of hyposerotonergic condition etiologies while on a normal diet which may require R&R based on medical evaluation, to include but are not limited to: drug-induced serotonin depletion[1,2,3,4,5], competitive inhibition serotonin depletion at the aromatic amino acid enzyme[6,7], aromatic amino acid decarboxylase deficiency[8], tetrahydrobiopterin (BH4) Deficiency[9], genetic polymorphism G-T and G/A involving introne 6[10], genetic serotonin transporter variance[11], suboptimal serotonin concentrations, age-related serotonin suboptimal

[1] Renoux C. et al. Association of Selective Serotonin Reuptake Inhibitors With the Risk for Spontaneous Intracranial Hemorrhage AMA Neurol. 2017;74(2):173-180
[2] Schultz J. et al. Serotonergic agents increase the incidence of gastrointestinal bleeds in patients with continuous-flow left ventricular assist devices. International Society for Heart Transplantation, 05 Jan 2016, 35(6):823-824
[3] Wagner A. et al. Effects of fluoxetine treatment of platelet 3H-imipramine binding, 5-HT uptake and 5-HT content in major depressive disorder Journal of Affective Disorders Volume 20, Issue 2, October 1990, Pages 101-113
[4] Maurer-Spurej E. et al. The influence of selective serotonin reuptake inhibitors on human platelet serotonin Thromb Haemost 2004; 91: 119-28
[5] Gagne, J. et al. Selective Serotonin Reuptake Inhibitor Use and Perioperative Bleeding and Mortality in Patients Undergoing Coronary Artery Bypass Grafting: A Cohort Study Drug Safety volume 38, pages1075–1082 (2015)
[6] Stansley, B., Yamamoto B. L-Dopa and Brain Serotonin System Dysfunction Toxics 2015, 3, 75-88
[7] Garcia N. et al. Chronic oral L-DOPA increases dopamine and decreases serotonin excretions Am J Physiol Regulatory Integrative Comp Physiol 277:1476-1480, 1999.
[8] Hyland K., Inherited Disorders Affecting Dopamine and Serotonin: Critical Neurotransmitters Derived from Aromatic Amino Acids Journal of Nutrition, Volume 137, Issue 6, June 2007, Pages 1568S–1572S
[9] Federal Register Vol. 84, No. 130 July 8, 2019 p. 32268
[10] I. Paclt1, J. Koudelová, A. Křepelová, P. Uhlíková, M. Gazdíková & P. Bauer Biochemical markers and genetic research of ADHD Neuroendocrinol Lett 2005; 26(4):423–430
[11] Offenbaecher M. et al. Possible association of fibromyalgia with a polymorphism in the serotonin receptor gene regulatory region, Arthritis & Rheumatism Vol. 42, No. 11, November 1999, pp 2482–2488

serotonin concentrations[12], decreased serotonin transporter activity[13], increased numbers (and activity) of SERT (serotonin transporters) or a loss of serotonergic neurons[14], low serotonin associated with Parkinson's disease[15], low serotonin associate with Post-traumatic stress disorder[16], low serotonin associated with chronic tension headache and migraine[17], low serotonin associated with fibromyalgia[18], and neurotoxin-induced hyposerotonergic condition[19]

DOSAGE, ADMINISTRATION, INGREDIENTS

NOTICE: THIS PRODUCT'S INTENDED USE OCCURS ONLY UNDER THE DIRECT SUPERVISION OF A PHYSICIAN OR OTHER LICENSED HEALTHCARE PRACTITIONER.

Dosing

Take as directed by your caregiver. The recommended adult daily dosing of R&R™ is two pills three times a day.

Nausea

If nausea develops during the first week of the R&R™ administration, contact the prescribing caregiver. If nausea occurs when taking the first dose within one to two hours of waking, move the first dose of the day to noon (4 to 5 hours after waking).

Ingredients

R&R is a white 1.9 cm non-scored round white pill with 2.948-grams of active ingredients. Active ingredients includes:

- L-cysteine
- L-tyrosine
- Vitamin C (ascorbic acid)
- Mucuna Pruriens (active ingredient 40% L-dopa)
- 5-hydroxytryptophan
- Calcium citrate
- Vitamin B6 (pyridoxine hydrochloride)
- Folate
- Selenium

[12] Nitkita L. et al. The impact of protein supplementation on cognitive performance in frail elderly Eur J Nutr 2014 Apr;53(3):803-12.
[13] Shih-Hsien L. et al. Serotonin and Mental Disorders: A Concise Review on Molecular Neuroimaging Evidence Clinical Psychopharmacology and Neuroscience 2014;12(3):196-202
[14] Hess S. et al. Advances in vivo imaging of serotonergic neurons in neuropsychiatric disorders Neuroscience and Biobehavioral Reviews 28 (2004) 547–563
[15] Tan S. et al. Serotonin-dependent depression in Parkinson's disease: A role for the subthalamic nucleus Neuropharmacology 61 (2011) 387e399
[16] DeBellis M. et al. Biologic Findings of Post-traumatic Stress Disorder and Child Maltreatment Current Psychiatry Reports 2003, 5:108–117
[17] Anthony, M. Plasma serotonin in patients with chronic tension headaches Journal ofNeurology, Neurosurgery, and Psychiatry 1989;52:182-184
[18] Amin O. et al. Clinical association of vitamin D and serotonin levels among patients with fibromyalgia syndrome Neuropsychiatric Disease and Treatment 2019:15 1421–1426
[19] McCann U. et al. Positron emission tomographic evidence of toxic effect of MDMA ("Ecstasy") on brain serotonin neurons in human beings Lancet 1998; 352: 1433–37

Discontinuation of R&R
There are no known adverse events or reactions associated with the abrupt stopping of R&R.

CONTRAINDICATIONS
Administering R&R to patients with known hypersensitivity to any of the components contained in this product is contraindicated.

PREGNANCY
No studies demonstrate the active ingredients in R&R cause pregnancy problems or are safe.

WARNINGS AND PRECAUTIONS

Renal or hepatic impairment

There has been no documented elevation of renal or hepatic enzymes attributed to the nutrients found in R&R.

ADVERSE REACTIONS
Side effects for this nutritional combination is dry mouth, insomnia, headache, nausea, dizziness, constipation.

Drug Interactions
The medical food R&R is intended to increase systemic serotonin concentrations beyond the ability of the normal diet. As can occur at any point during drug administration, a side effect may occur.

OVERDOSE
Overdose symptoms may include diarrhea, weakness, and nausea. Should poisoning concerns arise, contact the local poison control.

CLINICAL PHARMACOLOGY
A relative nutritional deficiency occurs when a normal diet does not meet the needs of the system. When systemic serotonin concentrations are not enough, low, inadequate, depleted, deficient, deficient, or suboptimal on a normal diet, the hyposerotonergic condition or state caused by a serotonin-related relative nutritional deficiency exists.

On a normal diet, L-tryptophan is the primary amino acid precursor metabolized to serotonin. A limitation of the amount of serotonin synthesized is regulated by the enzyme tryptophan hydroxylase, which restricts (limits) the metabolism of L-tryptophan to 5-hydroxytryptophan (5-HTP). When adequate cofactor (vitamin B6) activated enzyme concentrations exist, the only substance which can increase serotonin concentrations higher than can be achieved with L-tryptophan from the optimized normal diet is 5-HTP, the immediate amino acid precursor of

serotonin.[20,21,22,23]

The R&R medical food, through its special formulation, addresses the ability of 5-HTP to induce or exacerbate hypodopaminergic conditions (dopamine-related relative nutritional deficiency) secondary to competitive inhibition between immediate precursors of serotonin and dopamine at the aromatic amino acid decarboxylase.[24,25,26] Through its special formulation, R&R addresses the ability of serotonin concentrations increasing to induce or exacerbate hypoglutathionemia conditions (glutathione-related relative nutritional deficiency) secondary to conjugation between glutathione with 5-HTP, L-dopa, serotonin, and dopamine.[27,28,29,30,31,32]

HOW SUPPLIED
R&R supplied in bottles of 180 pills (a one month supply).

STORAGE
R&R should be stored at room temperature, avoid storage in temperatures above 100 degrees Fahrenheit.

[20] Hyland, K. Inherited Disorders Affecting Dopamine and Serotonin: Critical Neurotransmitters Derived from Aromatic Amino Acids, J. Nutr. 137: 1568S–1572S, 2007.
[21] Federal Register, Vol. 84, No. 130, Monday, July 8, 2019, Rules and Regulations, page 32,268
[22] Derek, M. et. al. Serotonin paracrine signaling in tissue fibrosis Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease Volume 1832, Issue 7, July 2013, Pages 905-910
[23] Cattaneo, M. et. al. Nicotine Stimulates a Serotonergic Autocrine Loop in Human Small-Cell Lung Carcinoma, Cancer research 53, November 15, 1993, 5566-5568
[24] KEGG Tryptophan metabolism pathway, https://www.genome.jp/kegg-bin/show_pathway?org_name=hsa&mapno=00380&scale=&orgs=&auto_image=&nocolor=&show_description=hide Accessed April 29, 2020
[25] KEGG Enzyme 4.12.1.28 https://www.genome.jp/dbget-bin/www_bget?ec:4.1.1.28 Accessed April 29, 2020
[26] Competitive inhibition definition https://www.chem.wisc.edu/deptfiles/genchem/netorial/modules/biomolecules/modules/enzymes/enzyme5.htm University of Wisconsin Department of Chemistry website, Last accessed October 25, 2019
[27] Oxford Dictionary, the definition of conjugation. https://books.google.com/books?id=anecAQAAQBAJ&pg=PA369&lpg=PA369&dq=%22toxic+compounds+eliminated+from+the+body+by+conjugation+with+glutathione%22&source=bl&ots=T_kB8xpHEP&sig=ACfU3U21d3ExNWrBLxGKmMQLGROBkSotFg&hl=en&sa=X&ved=2ahUKEwievKTFso7pAhXWWc0KHZ7PDh8Q6AEwAXoECA0QAQ#v=onepage&q=%22toxic%20compounds%20eliminated%20from%20the%20body%20by%20conjugation%20with%20glutathione%22&f=false Accessed April 29, 2020
[28] Ballatori, N. et. al. Glutathione dysregulation and the etiology and progression of human diseases, Biol Chem. 2009 March; 390(3): 191–214
[29] Lu, S. Regulation of glutathione synthesis, Mol Aspects Med. 2009; 30(1-2): 42–59.
[30] Johnson, C. et. al. Vitamin C Elevates Red Blood Cell Glutathione in Healthy Adults, Am J Clin Nutr. 1993 Jul;58(1):103-5.
[31] Waly, M. et. al. Low Nourishment of Vitamin C Induces Glutathione Depletion and Oxidative Stress in Healthy Young Adults, Prev. Nutr. Food Sci. 2015;20(3):198-203
[32] Selenium-glutathione peroxidase EC 1.11.1.9, https://www.genome.jp/dbget-bin/www_bget?ec:1.11.1.9 Accessed April 29, 2020