Description:

The hypodopaminergic conditions or states can occur when systemic dopamine concentrations on a normal diet are not enough, low, inadequate, depleted, deficient, deficit, or suboptimal.

Mucuna Medical Food™ (MMF™) is a specially formulated and processed medical food not available as a naturally occurring foodstuff for patients with a hypodopaminergic condition. MMF powder™ can achieve systemic dopamine concentrations higher than normal diets. MMF powder is for the partial feeding of a patient via a powder taken orally. The ingredients in MMF powder are for administration in a daily dosing range determined by medical evaluation. R&R™ is a specially formulated static dosed (one size fits all) medical food. Concomitant administration of R&R with MMF powder is needed to address the ability of MMF powder to induce hyposerotonergic and glutathionemia conditions. R&R also provides the necessary cofactors to address relative nutritional deficiencies associated with hypodopaminergic, hyposerotonergic, and glutathionemia conditions.[1,2,3,4,5,6,7,8,9,10,11,12]

Intended Use:

The formulation of MMF powder is a medical food administered enterally under a healthcare professional's supervision for hypodopaminergic conditions or states' specific dietary management.

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[3] Ritvo E. et al. Effects of L-dopa in autism Journal of Autism and Developmental Disorders Volume 1, Number 2 / June, 1971 190-205

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[8] ScienceDirect. Competitive inhibition article. Available at https://www.sciencedirect.com/topics/neuroscience/competitive-inhibition.

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[12] Kato Y, Peskin AV, Dickerhof N, Harwood DT, Kettle AJ. Myeloperoxidase catalyzes the conjugation of serotonin to thiols via free radicals and tryptamine-4,5-dione. Chem Res Toxicol. 2012 Nov 19;25(11):2322-32. doi: 10.1021/tx300218f. Epub 2012 Oct 10. PMID: 23009681.

Examples of hypodopaminergic condition etiologies faced by patients on a normal diet include but are not limited to nutrient-induced competitive inhibition depletion at the aromatic amino acid enzyme[13,14]; drug-induced dopamine depletion[15]; aromatic amino acid decarboxylase deficiency[16]; tetrahydrobiopterin (BH4) deficiency[17]; age-related suboptimal dopamine concentrations[18]; dysfunction of dopamine regulated transporter function or decrease in dopamine transporter activity[19]; loss of dopaminergic neurons[20]; disease-associated low dopamine idiopathic etiology; low dopamine associated with Parkinson's disease[21]; dopamine associated post-traumatic stress disorder[22]; dopamine-related suicide risk[23]; bipolar type 1 associated low dopamine;[24] dopamine-related depression;[25] and low dopamine related to ADHD[26]

DOSAGE, ADMINISTRATION, INGREDIENTS

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

Dosing

The recommended starting dose of MMF powder is 2.4 grams in three divided daily doses. Based on medical evaluation, the caregiver may increase MMF powder's daily dosing weekly by 1.8 grams or 2.4 grams per day to achieve the optimal dose for control of hypodopaminergic condition symptoms. Weekly evaluation via in-office visits or telemedicine is associated with optimal results. Optimal control of hypodopaminergic conditions may occur in one week or may require many weekly visits as determined by medical evaluation. Concomitant administration of MMF powder with R&R is needed as one tablet twice a day to provide cofactors and address the ability of MMF powder to

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[15] Lam R. et al. Effects of Alpha-Methyl-Para-Tyrosine-Induced Catecholamine Depletion in Patients with Seasonal Affective Disorder in Summer Remission NEUROPSYCHOPHARMACOLOGY 2001 VOL 25 NO S5
[16] 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.
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[20] Segura-Aguilar J. On the role of endogenous neurotoxins and neuroprotection in Parkinson's disease. Neural Regen Res. 2017;12(6):897-901. doi:10.4103/1673-5374.208560
[21] Kish S. et al. Brain dopamine neurone 'damage': methamphetamine users vs. Parkinson's disease–a critical assessment of the evidence European Journal of Neuroscience, Vol. 45, pp. 58–66
[22] Drury S. et al. The Role of the Dopamine Transporter (DAT) in the Development of PTSD in Preschool Children J Trauma Stress. 2009 December ; 22(6): 534–539. doi:10.1002/jts.20475.
[23] Rydling E. et al. The role of dopamine and serotonin in suicidal behaviour and aggression Progress in Brain Research Volume 172, 2008, Pages 307-315
[24] Moriera T. et al. Impulse control loss rapidly reversed by aripiprazole in a patient with concomitant bipolar disease type I and posttraumatic frontal lobe lesions BMJ Case Reports 2011; doi:10.1136/bcr.09.2011.4756
[25] Belujon P. et al. Dopamine System Dysregulation in Major Depressive Disorders International Journal of Neuropsychopharmacology (2017) 20(12): 1036–1046
[26] Barone H. et al. Tyrosinemia Type 1 and symptoms of ADHD: Biochemical mechanisms and implications for treatment and prognosis Am J Med Genet.2020;183B:95–105

induce hyposerotonergic and glutathionemia conditions. Caregiver adjustment of the R&R daily dosing may be needed if side effects caused by serotonin-dopamine imbalance develop. Administering greater than three pills of R&R per day for side effect management is not recommended.

Ingredients
MMF powder is a white mucuna pruriens powder that requires weighing the daily dosing value on a weight scale with a minimum of 0.01 gram (one-one hundredth of a gram) accuracy. Active ingredients include:

- Mucuna Pruriens (active ingredient 40% L-dopa)

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

CONTRAINDICATIONS
Administering MMF powder to patients with known hypersensitivity is contraindicated.

PREGNANCY
No studies demonstrate the active ingredients in MMF powder 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 MMF powder.

ADVERSE REACTIONS
This nutritional combination's side effects are nausea, vomiting, loss of appetite, lightheadedness, lowered blood pressure, confusion, and dyskinesia,[27]

Drug Interactions
The medical food MMF powder can increase systemic dopamine 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.

[27] L-dopa side effects, Parkinson Organization Website, https://www.parkinson.org/Understanding-Parkinsons/Treatment/Prescription-Medications/Levodopa

CLINICAL PHARMACOLOGY

When a hypodopaminergic condition exists on a normal diet, dietary modification is not effective. Management of the hypodopaminergic condition while on a normal diet requires the immediate aromatic amino acid precursor of dopamine (mucuna pruriens active ingredient L-dopa) and vitamin B6, which activates AADC (EC 4.1.1.28).[28]

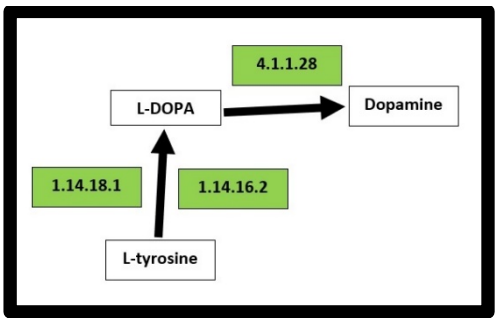

Figure 1: On a normal diet, the synthesis of L-dopa, the precursor of dopamine, is dependent on L-tyrosine.[29] Metabolism of L-tyrosine to L-dopa is rate limited by the tyrosine hydroxylase enzyme. No matter how great the L-tyrosine dosage is, there is a hard limit to dopamine synthesized. Metabolism of L-dopa to dopamine is without regulation. L-dopa administration can increase dopamine concentrations above concentrations achieved with L-tyrosine or L-phenylalanine from the normal diet.

As highlighted in Figure 1, the optimal activation of AADC (EC 4.1.1.28) depends on pyridoxine's (PLP, vitamin B6) adequate availability. The metabolism of L-tyrosine by tyrosine hydroxylase (EC 1.14.16.2) is rate limited. See Figure 1. No matter how much L-tyrosine is in the normal diet, there is a maximum limit to the amount of dopamine the body can synthesize from L-tyrosine. On a normal diet, L-dopa is a transient intermediate between L-tyrosine and dopamine, which is typically not found in substantial systemic concentrations or significant amounts in the normal diet, even with increasing intake of L-tyrosine containing foods. When the dopamine concentrations required by the body are higher than can be established on a normal diet, because of tyrosine hydroxylase rate-limitation, a hypodopaminergic condition exists. [30,31 ,32,33]

Increases in 5-HTP, L-dopa, serotonin, or dopamine may induce or exacerbate a glutathionemia caused by a glutathione-related RND on a normal diet. The special

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[28] EC 4.1.1.28.

[29] Kyoto Encyclopedia of Genes and Genomes. Tyrosine metabolism - Homo sapiens (human). Available at: https://www.genome.jp/kegg-bin/show_pathway?hsa00350

[30] Brun L, Ngu LH, Keng WT, Ch'ng GS, Choy YS, Hwu WL, Lee WT, Willemsen MA, Verbeek MM, Wassenberg T, Régal L, Orcesi S, Tonduti D, Accorsi P, Testard H, Abdenur JE, Tay S, Allen GF, Heales S, Kern I, Kato M, Burlina A, Manegold C, Hoffmann GF, Blau N. Clinical and biochemical features of aromatic L-amino acid decarboxylase deficiency. Neurology. 2010 Jul 6;75(1):64-71. doi: 10.1212/WNL.0b013e3181e620ae. Epub 2010 May 26. Erratum in: Neurology. 2010 Aug 10;75(6):576. Dosage error in article text. PMID: 20505134.

[31] Di Salvo ML, Fesko K, Phillips RS, Contestabile R. Editorial: PLP-Dependent Enzymes: Extraordinary Versatile Catalysts and Ideal Biotechnological Tools for the Production of Unnatural Amino Acids and Related Compounds. Front Bioeng Biotechnol. 2020 Feb 11;8:52. doi: 10.3389/fbioe.2020.00052. PMID: 32117932; PMCID: PMC7026007.

[32] Di Salvo ML, Fesko K, Phillips RS, Contestabile R. Editorial: PLP-Dependent Enzymes: Extraordinary Versatile Catalysts and Ideal Biotechnological Tools for the Production of Unnatural Amino Acids and Related Compounds. Front Bioeng Biotechnol. 2020 Feb 11;8:52. doi: 10.3389/fbioe.2020.00052. PMID: 32117932; PMCID: PMC7026007.

[33] Knappskog P. et al. Recessively inherited L-DOPA-responsive dystonia caused by a point mutation (Q381K) in the tyrosine hydroxylase gene Human Molecular Genetics, 1995, Vol. 4, No. 7 1209-1212

formulation of R&R addresses the specific static daily dosing needs of a nutrient-induced glutathionemia condition.[35,36,37,38,39,40,41]

HOW SUPPLIED

MMF powder is in bottles of 90 pills (a one-month supply).

STORAGE

Store MMF powder at room temperature; avoid storage in temperatures above 100 degrees Fahrenheit.

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