

RHEUMATE®

Folate (1mg)
(as L-5-methyltetrahydrofolate)
Methylcobalamin (vitamin B-12) (1mg)
Curcuminoid turmerone complex (500mg)



When it Comes to Methotrexate Toxicity, Give Patients a Superior Folate

L-methylfolate:

- A high-quality, bioactive folate that is superior to folic acid because it does not need to be converted by the body²
- Unaffected by genetic MTHFR polymorphisms⁹

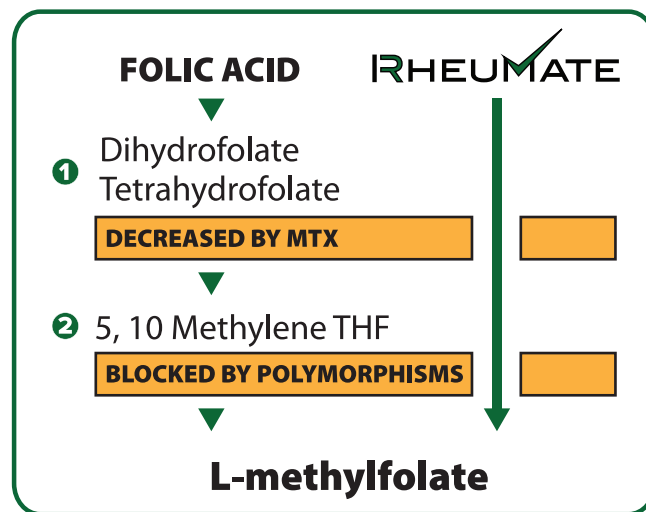
With the added benefit of:

Curcumin:

- Biocurcuma™ is seven times more bioavailable⁸
- Has an average ORAC (antioxidant value) of 13,500⁸
- Protects against methotrexate-induced liver damage^{3,4}
- Clinically shown to decrease joint tenderness and swelling¹⁰

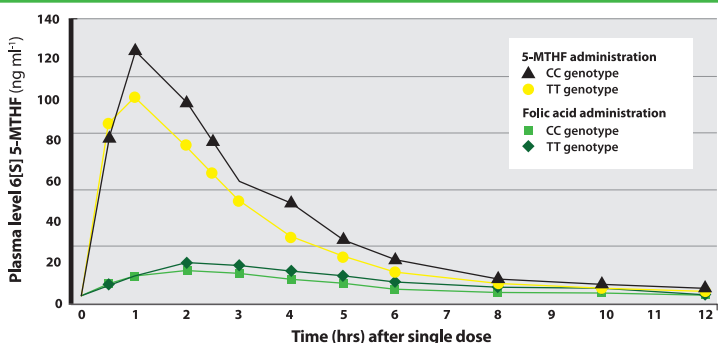
Vitamin B12:

- Methylcobalamin, the most bioavailable form of B12, avoids B12 insufficiency masked by folate therapy⁵
- Show to improve nerve function¹¹
- Bio-equivalent to intramuscular B12 at 12 weeks¹²



Clinical studies show that L-methylfolate is more biocompatible than traditional folic acid^{6,7}

5-MTHF plasma concentrations in patients with an MTHFR polymorphism (TT genotype) and normal individuals (CC genotype) after administration of either folic acid or 5-MTHF



Genotype and treatment: 6[S] 5-MTHF plasma concentration (ng ml⁻¹) in patients with MTHFR CC genotype or TT genotype following the administration of 6[R,S] 5-MTHF. 6[S] 5-MTHF plasma concentration (ng ml⁻¹) in patients with MTHFR CC genotype or TT genotype following the administration of folic acid.

According to the Centers for Disease Control and Prevention, nearly half of the US population has a MTHFR genetic polymorphism, which can block the conversion of folic acid into folate.⁹

MTHFR Polymorphisms by Race/Ethnicity

Race/Ethnicity	Genotype % (95% CI)					
	C677T			A1298C		
	C/C (Homozygous Normal)	C/T (Heterozygous Mutant)	T/T (Homozygous Mutant)	A/A (Homozygous Normal)	A/C (Heterozygous Mutant)	C/C (Homozygous Mutant)
Non-Hispanic White	46.4	42.1	11.5	48.2	41.3	10.5
Non-Hispanic Black	77.9	20.9	1.2	67.6	29.0	3.4
Mexican-American	30.7	49.4	19.9	66.0	30.5	3.5
	49.3	39.8	10.9	52.2	38.8	9.0



With Rheumate, Have Peace of Mind That You Are Protecting 100% of Your Patients from MTX Induced Side Effects⁹

Rx

Rheumate
#90 Sig. † QD or BID
Refill x11

DISPENSE AS WRITTEN



RHEUMATE®

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(as L-5-methyltetrahydrofolate)
Methylcobalamin (vitamin B-12) (1mg)
Curcuminoid turmerone complex (500mg)

RheumateRx.com

[†] The specific L-methylfolate (also commonly called L-5-methylfolate) in Rheumate is (6S)-5-methyltetrahydrofolic acid, glucosamine salt under license from Gnosis SpA as Quatrefolic®
1. Cronstein BN. Molecular therapeutics. Methotrexate and its Mechanism of Action. Arthritis and Rheumatism. Dec 1996;39(12):1951-1960. **2.** Toffoli G, De Mattia E. Pharmacogenetic Relevance of MTHFR Polymorphisms. Pharmacogenomics. Sep 2008;9(9):1195-1206. **3.** Hemeida RA, Mohafez OM. Curcumin Attenuates Methotrexate-induced Hepatic Oxidative Damage in Rats. J Egypt Natl Canc Inst. Jun 2008;20(2):141-148. **4.** Naik SR, Thakare VN, Patil SR. Protective Effect of Curcumin on Experimentally Induced Inflammation, Hepatotoxicity and Cardiotoxicity in Rats: Evidence of its Antioxidant Property. Exp Toxicol Pathol. Jul 2011;63(5):419-431. **5.** Smith AD. Folic Acid Fortification: The Good, The Bad, and the Puzzle of Vitamin B-12. Am J Clin Nutr. Jan 2007;85(1):3-5. **6.** Frank F, Willems, Godfried H.J. Boers, Henk J. Blom, Wim R.M. Aengevaeren, & Freek W.A. Verheugt. Pharmacokinetic study on the utilisation of 5-methyltetrahydrofolate and folic acid in patients with coronary artery disease. British Journal of Pharmacology (2004) 141, 825-830. **7.** Francesco Scaglione and Giscardo Panzavolta. Folate, folic acid and 5-methyltetrahydrofolate are not the same thing. Department of Medical Biotechnology and Translational Medicine, University of Milan, Milan, Italy. Xenobiotica, Early Online: 1-9, 2014 Informa UK Ltd. DOI: 10.3109/00498254.2013.845705. **8.** Data on file at Primus Pharmaceuticals. **9.** Centers for Disease Control and Prevention, U.S. Genome Variation Estimates MTHFR Allele and Genotype Frequencies. **10.** Binu Chandran and Ajay Goel. A Randomized, Pilot Study to Assess the Efficacy and Safety of Curcumin in Patients with Active Rheumatoid Arthritis. Phytotherapy Research (2012) **11.** Ming Zhang, Wenjuan Han, Sanjue Hu, and Hui Xu. Review Article: Methylcobalmin: A Potential Vitamin of Pain Killer. Hindawi Publishing Corporation, Neural Plasticity, Volume 2013, Article ID 424651 **12.** Christopher C Butler, Josep Vidal-Alaball, Oral vitamin B12 versus intramuscular vitamin B12 for vitamin B12 deficiency: a systematic review of randomized controlled trials.

Rheumate is a prescription medical food product for the clinical dietary management of the metabolic effects of methotrexate therapy. Rheumate is to be used under a physician's supervision. Full prescribing information is available at www.rheumaterx.com. ©2017 Primus Pharmaceuticals, Inc. All rights reserved. ISS. 1217 #18102