

Scientific Evidence & Safety Dossier GLP-1 Muscle Guard



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β -Hydroxy- β -Methylbutyrate (HMB)

Clinical Trial Evidence & References

INTRODUCTION

HMB (β -Hydroxy- β -Methylbutyrate) is a leucine metabolite with strong scientific evidence supporting its role in muscle preservation. This document summarizes high-quality clinical trials, meta-analyses, and references relevant for endocrinology practice.

MECHANISM OF ACTION HMB reduces muscle protein breakdown via inhibition of the ubiquitin-proteasome pathway and caspase activity, while stimulating muscle protein synthesis through mTOR signaling. This dual mechanism supports muscle preservation in catabolic and aging-related conditions.

KEY META-ANALYSES

1. American Journal of Clinical Nutrition (2019): Meta-analysis of 15 RCTs (n=2137) showed significant improvement in muscle strength (SMD=0.31, p=0.001) and modest increase in muscle mass. (Bear DE, Langan A, Dimidi E, Wandrag L, Harridge SDR, Hart N, Connolly B, Whelan K. β -Hydroxy- β -methylbutyrate and its impact on skeletal muscle mass and physical function in clinical practice: a systematic review and meta-analysis. Am J Clin Nutr. 2019 Apr 1;109(4):1119-1132. doi: 10.1093/ajcn/nqy373. PMID: 30982854.)
2. Su et al., 2024: Meta-analysis in sarcopenia patients showed significant improvement in handgrip strength (+1.26 kg, p=0.004). (Su H, Zhou H, Gong Y, Xiang S, Shao W, Zhao X, Ling H, Chen G, Tong P, Li J. The effects of β -hydroxy- β -methylbutyrate or HMB-rich nutritional supplements on sarcopenia patients: a systematic review and meta-analysis. Front Med (Lausanne). 2024 Jul 12;11:1348212. doi: 10.3389/fmed.2024.1348212. PMID: 39071082; PMCID: PMC11272589.)

RANDOMIZED CONTROLLED TRIALS

1. 12-week RCT in sarcopenic older adults showed improved handgrip strength (+4.61 kg, $p < 0.001$) and gait speed. (Yang C, Song Y, Li T, Chen X, Zhou J, Pan Q, Jiang W, Wang M, Jia H. Effects of Beta-Hydroxy-Beta-Methylbutyrate Supplementation on Older Adults with Sarcopenia: A Randomized, Double-Blind, Placebo-Controlled Study. *J Nutr Health Aging*. 2023;27(5):329-339. doi: 10.1007/s12603-023-1911-1. PMID: 37248756.)
2. Pre-frail elderly RCT (Whey protein + 3g HMB) demonstrated increased thigh muscle CSA and improved physical performance. (Peng LN, Cheng YC, Yu PC, Lee WJ, Lin MH, Chen LK. Oral Nutritional Supplement with β -hydroxy- β -methylbutyrate (HMB) Improves Nutrition, Physical Performance and Ameliorates Intramuscular Adiposity in Pre-Frail Older Adults: A Randomized Controlled Trial. *J Nutr Health Aging*. 2021;25(6):767-773. doi: 10.1007/s12603-021-1621-7. PMID: 34179932.)
3. Post-hospitalization sarcopenia RCT showed improved SPPB scores and sustained strength benefits. (Meza-Valderrama D, Sánchez-Rodríguez D, Messaggi-Sartor M, Muñoz Redondo E, Morgado-Pérez A, Tejero-Sánchez M, De Jaime-Gil E, Leiva-Banuelos N, Marco E. Supplementation with β -hydroxy- β -methylbutyrate after resistance training in post-acute care patients with sarcopenia: A randomized, double-blind placebo-controlled trial. *Arch Gerontol Geriatr*. 2024 Apr;119:105323. doi: 10.1016/j.archger.2023.105323. Epub 2023 Dec 27. PMID: 38171034.)

CLINICAL RELEVANCE FOR ENDOCRINOLOGY

HMB is particularly relevant for patients on GLP-1 receptor agonists, elderly patients with sarcopenia, individuals undergoing weight loss, and patients with diabetes or insulin resistance where muscle preservation is critical.

DOSAGE USED IN TRIALS

Most clinical trials use 3 g/day of Calcium HMB for at least 12 weeks. This dose is well tolerated and consistently associated with clinical benefits.

SAFETY

Clinical trials report no significant adverse effects on liver, kidney, glucose, or lipid parameters. HMB is considered safe for long-term use in the elderly and metabolic patients.

