A PATIENT GUIDE FROM BELLYMD

Benfotiamine: What the evidence shows.

A plain-language look at a well-absorbed form of vitamin B1, how the body uses thiamine in nerves and energy metabolism, why the form on the label changes how much gets in, and what the published research does and does not support.

About this guide. Benfotiamine is the vitamin B1 in *MGB+ Calm*, dosed at 100 mg. It is a fat-soluble derivative of thiamine, chosen because ordinary thiamine is absorbed only in small, capped amounts. One point of confusion worth settling up front: benfotiamine and allithiamine are *different* compounds. Calm uses benfotiamine, not allithiamine. Both are better-absorbed forms of B1, but they are built from different chemistry, covered in the first chapter. This handout walks through the published evidence on thiamine and on benfotiamine specifically, so you can read it yourself and decide what makes sense for you.

CHAPTER ONE

What is benfotiamine?

> *Benfotiamine is a man-made version of vitamin B1 built to solve one specific problem: ordinary B1 is hard to absorb in any meaningful quantity. Benfotiamine gets around that limit.*[1,2]

Vitamin B1, also called thiamine, is an essential vitamin. Your body cannot make it and has to get it from food. It is a water-soluble vitamin, which means the body does not store much of it, so a steady daily intake matters. Thiamine sits at the center of how cells turn food into usable energy, and nerve and muscle tissue, which burn a lot of energy, are the first to feel it when thiamine runs low.[5,14]

Why ordinary thiamine hits a ceiling

The standard form of B1 in most multivitamins is thiamine hydrochloride or thiamine mononitrate. These are water-soluble salts, and the gut absorbs them through a dedicated transport system that works like a turnstile with a fixed speed limit. Once that system is saturated, taking more does not get more in. Studies of high oral doses of plain thiamine show that blood levels plateau, because the turnstile can only move so fast no matter how much you swallow.[3] This is the core reason a different form was developed.

How benfotiamine is built differently

Benfotiamine is chemically named S-benzoylthiamine O-monophosphate. The useful part is what its structure does: it is an open-ring, fat-compatible derivative of thiamine that does not depend on the saturable turnstile. It crosses the gut lining more freely, and once inside the body it is converted back into active thiamine.[1,2,7] Head-to-head pharmacokinetic studies in people found that benfotiamine produced substantially higher blood and tissue thiamine levels than equivalent doses of the water-soluble salts.[1,2] In short, more of what you take actually reaches the cells that need it.

Benfotiamine is not allithiamine

This is the distinction the cover flagged, and it is worth being precise about because the two are often lumped together. Both benfotiamine and allithiamine belong to a family of better-absorbed thiamine derivatives, but they are built differently.[2,8]

Benfotiamine is an S-acyl derivative: a benzoyl group and a phosphate are attached to an opened thiamine ring. **Allithiamine** is a disulfide derivative, originally identified in garlic, where the thiamine ring is opened and capped with an allyl disulfide group instead. The allithiamine-type compounds (the disulfide family) cross cell membranes through their fat-soluble disulfide chemistry; benfotiamine works through its S-acyl phosphate structure. They are cousins, not the same molecule, and they are not interchangeable on a label. MGB+ Calm uses benfotiamine.[2,8]

THE SHORT VERSION

Vitamin B1 (thiamine) is an essential, water-soluble vitamin that powers energy metabolism in nerves and muscle. Ordinary thiamine is absorbed through a saturable transporter, so swallowing more eventually stops adding more. Benfotiamine is an open-ring, fat-compatible derivative that bypasses that ceiling and delivers far higher thiamine levels. It is a distinct compound from allithiamine, a different better-absorbed B1 derivative built from disulfide chemistry. Calm uses benfotiamine.

CHAPTER TWO

How it works in your body

> *Thiamine is an energy vitamin and a nerve vitamin at the same time, because nerves are among the most energy-hungry tissue in the body. That overlap is why a B1 derivative shows up in a formula aimed at the gut-brain connection.*

It is a required helper in energy metabolism

Inside cells, thiamine is converted to its active form, thiamine pyrophosphate, which acts as a required helper, called a cofactor, for several key enzymes that break down sugars and branched-chain amino acids for energy.[5,6] Two of these enzymes, pyruvate dehydrogenase and alpha-ketoglutarate dehydrogenase, sit at chokepoints in the main energy-production pathway. When thiamine is short, those chokepoints slow down, and tissues that run hot, the brain and the nerves in particular, lose energy supply first.[5,14] This is the basic biology behind why classic thiamine deficiency, called beriberi, shows up as nerve and heart problems.[5]

It feeds the transketolase pathway

A third thiamine-dependent enzyme, transketolase, deserves its own mention because it is central to benfotiamine's most-studied mechanism. Transketolase shunts excess sugar metabolites down a safer side road instead of letting them pile up and form damaging byproducts.[4,6] In a landmark 2003 study in *Nature Medicine*, Hammes and colleagues showed that benfotiamine strongly activates transketolase and, by doing so, blocks three of the major pathways through which high blood sugar damages small blood vessels and nerves.[4] This is a documented mechanism in laboratory and animal models. It explains why most benfotiamine research has been done in the setting of diabetes, where those damaging pathways are most active.

The gut-brain and autonomic connection

The upper gut does not move on its own. It is paced by nerves, including the vagus nerve and the gut's own enteric nervous system, that signal the stomach to relax, fill, and empty in order. These nerves are part of the autonomic system, the automatic wiring that runs digestion without conscious effort.[14,16]

Because these nerves depend on steady energy metabolism, and because thiamine is what keeps that metabolism running, B1 status is part of the background chemistry that keeps autonomic and gut nerve signaling normal. When thiamine is genuinely deficient, the consequences can include autonomic and gastrointestinal disturbance: nausea, early fullness, and sluggish stomach emptying have been described in thiamine-deficiency states, a pattern sometimes called gastrointestinal beriberi.[16] The honest framing is that benfotiamine supplies the body with well-absorbed B1 so this nerve and energy machinery has what it needs. It supports normal function. It does not override or treat a gut disorder.

Why a better-absorbed form is the point

All of the above is true of thiamine in general. The reason benfotiamine specifically is used is delivery. The nerves and tissues that need thiamine can only benefit from what actually reaches them, and the saturable absorption of ordinary thiamine caps how much that is.[1,3] Benfotiamine's value is that it raises thiamine levels in blood and tissue well past what the water-soluble forms can manage, so the underlying biology has more to work with.[1,2]

WHY THIS MATTERS IN CALM

MGB+ Calm pairs benfotiamine with magnesium glycinate as its nervous-system base. Thiamine powers the energy metabolism that the autonomic nerves pacing the upper gut depend on, and benfotiamine is the form chosen so that B1 actually reaches those tissues rather than hitting the absorption ceiling of ordinary thiamine. This is foundational nerve-and-energy support, framed as supporting normal function, not as a treatment for any condition.

CHAPTER THREE

What the studies show

Benfotiamine has a real research literature, but the strength of the evidence is very uneven. The absorption advantage and the laboratory mechanism are well established. The human clinical trials are smaller, mostly in diabetes, and the results are mixed. Here is an honest breakdown, area by area.

Absorption and bioavailability

STRONG EVIDENCE · HUMAN PHARMACOKINETICS · WELL CHARACTERIZED

This is the firmest part of the benfotiamine story. Pharmacokinetic studies in people, including work by Loew and by Schreeb and colleagues, consistently show that benfotiamine raises blood and tissue thiamine levels several-fold higher than equivalent doses of the water-soluble thiamine salts.[1,2] Separate work on high-dose plain thiamine confirms the other half of the picture: ordinary thiamine plateaus because its absorption is saturable.[3]

What this means: the claim that benfotiamine is a better-absorbed form of B1 is well supported. This is the part of the label that the evidence backs most directly. It is a delivery advantage, not a disease claim.

The transketolase and AGE mechanism

STRONG PRECLINICAL · LANDMARK MECHANISM · LAB AND ANIMAL MODELS

The 2003 *Nature Medicine* study by Hammes and colleagues is the most influential benfotiamine paper. It demonstrated that benfotiamine activates the transketolase enzyme and blocks three major pathways of high-sugar damage, preventing experimental diabetic retinopathy in animals.[4] Later mechanistic reviews by Thornalley, Beltramo, Balakumar, and Raj built on this, mapping how benfotiamine interferes with the formation of advanced glycation end products, the harmful byproducts of chronically high blood sugar.[5,6,7,8]

What this means: the mechanism is well documented, but it is largely laboratory and animal work, and it is rooted in diabetes biology. It explains why researchers expect benfotiamine to do something. It is not, by itself, proof of a clinical benefit in people, and it is not a gut-brain finding.

Diabetic neuropathy

SMALL RCTS · MODEST AND MIXED

This is the most-studied human application. The BEDIP study by Haupt and colleagues, a small three-week randomized controlled trial, reported improvement in nerve-related symptom scores with benfotiamine versus placebo.[9] The larger BENDIP trial by Stracke and colleagues found a benefit on a neuropathy symptom score at the higher dose, but the results were modest and not significant on every measure.[10]

What this means: there is a genuine but modest signal in diabetic nerve symptoms, from small and short trials. It is worth knowing, but it is diabetes-specific and the evidence is not strong enough to generalize. MGB+ is a daily-support supplement, not a treatment for neuropathy.

Endothelial and autonomic function

SMALL HUMAN TRIALS · MIXED RESULTS

Stirban and colleagues ran two relevant trials in people with type 2 diabetes. The first showed that a single benfotiamine regimen blunted the blood-vessel dysfunction that follows a meal rich in advanced glycation end products.[11] A later six-week crossover trial, however, did not find a significant effect of benfotiamine on postprandial blood-vessel function or on measures of autonomic nerve function.[12]

What this means: an early positive finding was not confirmed by a longer, better-controlled follow-up. This is a useful reminder that short-term mechanism studies do not always translate into sustained clinical effects. The honest reading here is mixed.

Cognition and the gut-brain axis

EARLY-STAGE · PILOT TRIALS · EMERGING

Thiamine has a long-recognized link to brain function, and severe deficiency causes well-known neurological syndromes.[14] Animal work by Pan and colleagues found that benfotiamine reduced amyloid deposition and cognitive impairment in a mouse model of Alzheimer's disease.[13] A 2020 randomized placebo-controlled phase IIa trial by Gibson and colleagues tested benfotiamine in people with mild cognitive impairment or early Alzheimer's and reported encouraging but preliminary signals on cognitive and clinical measures.[15]

What this means: this is an active and interesting research area, but it is early. A single phase IIa trial and animal data are a starting point, not an established benefit. It is included here for an honest picture, not as a claim.

Thiamine deficiency and the gut

CASE-LEVEL · MECHANISM PLAUSIBLE · NOT A SUPPLEMENT CLAIM

The clearest link between B1 and the digestive system comes from deficiency. Thiamine-deficiency states can produce gastrointestinal and autonomic symptoms, including nausea, early fullness, and sluggish stomach emptying, a presentation described in the literature as gastrointestinal beriberi.[16]

What this means, and an honest distinction: this shows what happens when B1 is genuinely missing, which is rare in well-fed people. It does not show that extra benfotiamine improves digestion in someone who is not deficient. The supportable framing is that adequate B1 keeps the gut's nerve machinery supplied, not that benfotiamine treats a gut problem.

The honest summary

WHERE BENFOTIAMINE SITS IN THE EVIDENCE HIERARCHY

Benfotiamine has a clear, well-documented strength and a set of honest limits.[1,4,8]

The firmest claims are about delivery and mechanism: benfotiamine genuinely raises thiamine levels past the ceiling of ordinary B1, and it genuinely activates the transketolase pathway in the lab. The human clinical trials are smaller, almost entirely in diabetes, and mixed, with some positive neuropathy results and a notable negative follow-up on vascular and autonomic function. The cognition work is early. The gut connection rests mostly on what deficiency does, not on benefit in well-nourished people.[9,10,11,12,15,16]

> **READ THIS BEFORE THE MARKETING**
>
> Benfotiamine's best-supported property is that it is a better-absorbed form of vitamin B1, and that claim is solid. Most of its disease-area research is in diabetes, the human trials are small and mixed, and the gut-brain rationale is built on the role of thiamine in nerve energy metabolism rather than on trials showing benfotiamine improves digestion. The role in Calm is to supply well-absorbed B1 to the nerve-and-energy machinery, framed as supporting normal function. Anyone reading this brief deserves to know where the strong evidence ends and the reasonable inference begins.

CHAPTER FOUR

About dose and timing

> *Thiamine is one of the safest vitamins there is, because the body simply clears any excess of the water-soluble forms. The reason to care about the form, benfotiamine versus plain thiamine, is absorption, not a worry about overdose.*

The RDA and where supplements fit

The recommended dietary allowance for thiamine is small, roughly 1.1 to 1.2 mg per day for adults, and most people meet it easily from food: whole grains, pork, legumes, and fortified products are the common sources.[5,17] The doses used in benfotiamine supplements and studies are far above that RDA, commonly in the range of about 150 to 600 mg per day in the diabetes trials, because the goal in those studies was to drive thiamine levels high enough to push the transketolase mechanism, not simply to prevent deficiency.[9,10]

MGB+ Calm uses 100 mg of benfotiamine. That is well above the amount needed to cover the basic vitamin requirement and is squarely in the range used as a daily supportive dose, while sitting at the lower end of the higher therapeutic doses studied in diabetes.[9,10]

Why benfotiamine is dosed differently than plain B1

WHAT THE LABEL SAYS	WHAT IT ACTUALLY MEANS	WHY IT MATTERS
Thiamine HCl or mononitrate	The standard water-soluble form. Absorbed through a saturable transporter that caps how much gets in at once.[3]	A large number on the label does not mean a large amount is absorbed.
Benfotiamine	The open-ring, fat-compatible derivative. Bypasses the saturable transporter and reaches several-fold higher thiamine levels.[1,2]	More of the labeled dose actually reaches blood and tissue.
Allithiamine	A different better-absorbed B1 derivative, built from disulfide chemistry. Related to benfotiamine but not the same compound.[2,8]	Do not read the two as interchangeable. Calm uses benfotiamine.

How to read that table

The practical point is that the form drives how much B1 you actually get, not the milligram number alone. Benfotiamine's advantage is delivery: it clears the absorption ceiling that limits ordinary thiamine.[1,2,3] A sensible supplemental dose, like the 100 mg in Calm, is meant to keep the nerve-and-energy machinery well supplied with a form that genuinely arrives, not to chase a megadose.

Timing

Benfotiamine does not need tight timing and can be taken with or without food. Because it is the better-absorbed form, it does not depend on an empty-stomach window the way some nutrients do. As with most foundation nutrients, the realistic expectation is steady daily intake rather than a single dose producing a noticeable change.[1,5]

Who should be cautious

Thiamine and benfotiamine have a strong safety record. Because thiamine is water-soluble, the body excretes what it does not use, and no upper intake limit has been set for it precisely because toxicity is not seen at the doses people take.[5,17] That said, anyone who is pregnant, nursing, managing a medical condition, or taking prescription medication should run any new supplement past their physician or pharmacist first, as a matter of general good practice.[17]

THE HONEST DOSE FRAMING

Benfotiamine is dosed for absorption, not to hit a therapeutic target for any disease. The 100 mg in Calm is well above the basic vitamin requirement and at the low end of the higher doses studied in diabetes, delivered in a form that genuinely reaches tissue. It has a strong safety record because excess water-soluble thiamine is simply cleared. As always, anyone on medication or managing a condition should check with their clinician first.

CITATIONS

References

All references are real, PubMed-indexed publications or recognized clinical resources. PMID numbers are listed where assigned. DOIs are included where available for direct linking.

1. Loew D. Pharmacokinetics of thiamine derivatives especially of benfotiamine. *Int J Clin Pharmacol Ther.* 1996;34(2):47-50. *PMID: 8929745*
2. Schreeb KH, Freudenthaler S, Vormfelde SV, Gundert-Remy U, Gleiter CH. Comparative bioavailability of two vitamin B1 preparations: benfotiamine and thiamine mononitrate. *Eur J Clin Pharmacol.* 1997;52(4):319-320. *PMID: 9248773*
3. Smithline HA, Donnino M, Greenblatt DJ. Pharmacokinetics of high-dose oral thiamine hydrochloride in healthy subjects. *BMC Clin Pharmacol.* 2012;12:4. *PMID: 22305197. doi:10.1186/1472-6904-12-4*
4. Hammes HP, Du X, Edelstein D, Taguchi T, Matsumura T, Ju Q, Lin J, Bierhaus A, Nawroth P, Hannak D, Neumaier M, Bergfeld R, Giardino I, Brownlee M. Benfotiamine blocks three major pathways of hyperglycemic damage and prevents experimental diabetic retinopathy. *Nat Med.* 2003;9(3):294-299. *PMID: 12592403. doi:10.1038/nm834*
5. Thornalley PJ. The potential role of thiamine (vitamin B1) in diabetic complications. *Curr Diabetes Rev.* 2005;1(3):287-298. *PMID: 18220605. doi:10.2174/157339905774574383*
6. Beltramo E, Berrone E, Tarallo S, Porta M. Effects of thiamine and benfotiamine on intracellular glucose metabolism and relevance in the prevention of diabetic complications. *Acta Diabetol.* 2008;45(3):131-141. *PMID: 18581039. doi:10.1007/s00592-008-0042-y*
7. Balakumar P, Rohilla A, Krishan P, Solairaj P, Thangathirupathi A. The multifaceted therapeutic potential of benfotiamine. *Pharmacol Res.* 2010;61(6):482-488. *PMID: 20188835. doi:10.1016/j.phrs.2010.02.008*
8. Raj V, Ojha S, Howarth FC, Belur PD, Subramanya SB. Therapeutic potential of benfotiamine and its molecular targets. *Eur Rev Med Pharmacol Sci.* 2018;22(10):3261-3273. *PMID: 29863274. doi:10.26355/eurrev_201805_15089*
9. Haupt E, Ledermann H, Köpcke W. Benfotiamine in the treatment of diabetic polyneuropathy, a three-week randomized, controlled pilot study (BEDIP study). *Int J Clin Pharmacol Ther.* 2005;43(2):71-77. *PMID: 15726875. doi:10.5414/cpp43071*
10. Stracke H, Gaus W, Achenbach U, Federlin K, Bretzel RG. Benfotiamine in diabetic polyneuropathy (BENDIP): results of a randomised, double blind, placebo-controlled clinical study. *Exp Clin Endocrinol Diabetes.* 2008;116(10):600-605. *PMID: 18473286. doi:10.1055/s-2008-1065351*
11. Stirban A, Negrean M, Stratmann B, Gawlowski T, Horstmann T, Götting C, Kleesiek K, Mueller-Roesel M, Koschinsky T, Uribarri J, Vlassara H, Tschoepe D. Benfotiamine prevents macro- and microvascular endothelial dysfunction and oxidative stress following a meal rich in advanced glycation end products in individuals with type 2 diabetes. *Diabetes Care.* 2006;29(9):2064-2071. *PMID: 16936154. doi:10.2337/dc06-0531*
12. Stirban A, Pop A, Tschoepe D. A randomized, double-blind, crossover, placebo-controlled trial of 6 weeks benfotiamine treatment on postprandial vascular function and variables of autonomic nerve function in type 2 diabetes. *Diabet Med.* 2013;30(10):1204-1208. *PMID: 23701274. doi:10.1111/dme.12240*
13. Pan X, Gong N, Zhao J, Yu Z, Gu F, Chen J, Sun X, Zhao L, Yu M, Xu Z, Dong W, Qin Y, Fei G, Zhong C, Xu TL. Powerful beneficial effects of benfotiamine on cognitive impairment and beta-amyloid deposition in amyloid precursor protein/presenilin-1 transgenic mice. *Brain.* 2010;133(Pt 5):1342-1351. *PMID: 20385653. doi:10.1093/brain/awq069*
14. Gibson GE, Hirsch JA, Fonzetti P, Jordan BD, Cirio RT, Elder J. Vitamin B1 (thiamine) and dementia. *Ann N Y Acad Sci.* 2016;1367(1):21-30. *PMID: 26971083. doi:10.1111/nyas.13031*
15. Gibson GE, Luchsinger JA, Cirio R, Chen H, Franchino-Elder J, Hirsch JA, Bettendorff L, Chen Z, Flowers SA, Gerber LM, Grandville T, Schupf N, Xu H, Stern Y, Habeck C, Jordan B, Fonzetti P. Benfotiamine and cognitive decline in Alzheimer's disease: results of a randomized placebo-controlled phase IIa clinical trial. *J Alzheimers Dis.* 2020;78(3):989-1010. *PMID: 33074237. doi:10.3233/JAD-200896*
16. Tjong E, Dimri M, Mohiuddin SS. Gastrointestinal beriberi and Wernicke's encephalopathy triggered by one session of heavy drinking. *Case Rep Neurol.* 2019;11(1):124-131. *PMID: 31543793. doi:10.1159/000499601*
17. National Institutes of Health, Office of Dietary Supplements. Thiamin: Fact Sheet for Health Professionals. Bethesda (MD): NIH ODS. *ods.od.nih.gov/factsheets/Thiamin-HealthProfessional*