



# Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration

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## ALSUntangled No. 54: "LEAP2BFIT"

### THE ALSUNTANGLED GROUP

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## RESEARCH ARTICLE

## ALSUntangled No. 54: “LEAP2BFIT”

## THE ALSUNTANGLED GROUP

ALSUntangled reviews alternative and off-label therapies on behalf of persons with ALS (PALS). Here we review the use of LEAP2BFIT for which we have received over 600 votes (1).

**Overview**

LEAP2BFIT is a supplement containing many ingredients (ref (2); Version 3.0 ingredients shown in Figure 1). It is sold as a powder that can be added to water or juice. It is marketed to the general population as a nutritional supplement to help: “boost energy levels and vitality, improve memory and mental clarity, quicken learning ability, strip away toxins that build up in the brain, arteries and organs ... ramp up your immune system, rebuild natural defenses against bacteria, viruses and toxins ... reduce body fat and increase lean muscle mass, eliminate unwanted weight gain, increase sexual stamina and drive, rejuvenate every organ, gland and tissue of your body including your skin’s elasticity and tone, put the brakes on aspects of the normal aging process” (3). To the best of our knowledge, there has never been a published scientific study on LEAP2BFIT for any condition. The manufacturer states that he derives these claims of benefit from reading research articles on the individual ingredients (3). Recently, testimonials describing benefits for PALS have appeared on social media (4) and at patient conferences (5).

**LEAP2BFIT ingredients**

In this section we summarize prior ALSUntangled reviews on ALS-relevant LEAP2BFIT ingredients.

For ingredients not previously reviewed, we briefly highlight some of their potential ALS-relevant mechanisms, pre-clinical data, cases, trials and risks. Of note, LEAP2BFIT does not provide the dosages of all of its ingredients which makes it difficult to predict potential benefits or risks.

ALSUntangled previously reviewed medium-chain triglycerides (6), curcumin (7), *L*-carnitine (8), resveratrol (9), and methylcobalamin (10); all 5 of these compounds can at least theoretically act on mechanisms that are relevant to ALS. Of these, we gave *L*-carnitine supplements and injected methylcobalamin “mechanistic plausibility” grades of “A” (8,10). Nanoparticle curcumin and high-dose injected methylcobalamin were each reported to modestly slow ALS disease progression in human studies for which we assigned “trials” grades of “C” (7) or “D” (10); however, neither have yet been reported to be beneficial in a well-conducted phase III clinical trial.

*Silymarin*

Silymarin is an extract from the milk thistle plant used in ancient Greek medicine and approved in some European countries as an antidote for ‘death cap mushroom’ (*Amanita phalloides*) poisoning (11). It likely has protective effects against liver injury and may have anti-inflammatory and antioxidant effects (12). Silymarin has not been studied in pre-clinical models of ALS and has not been studied in PALS. In the online community PatientsLikeMe (PLM), one PALS reported taking silymarin, but did not report their experience (13). In non-neurologic disease patient populations, the

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Note: This paper represents a consensus of those weighing in. The opinions expressed in this paper are not necessarily shared by every investigator in this group.

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1. MenaQ7 (a patented form of vitamin K)
2. Theracurmin (a patented form of curcumin)
3. Curcumin C3 complex (a patented form of curcumin)
4. Turmacin (a patented extract of turmeric)
5. SerinAid (a proprietary form of phosphatidylserine, an amino acid derivative)
6. AlphaSize (a patented form of alpha-glyceryl phosphoryl choline)
7. Quatrefolic (a patented form of folic acid)
8. SeleniumSelect (a patented form of the mineral selenium)
9. Several amino acids (*L*-leucine, *L*-lysine, *L*-isoleucine, *L*-valine, *L*-threonine, *L*-proline, *L*-glycine, *L*-arginine, *L*-cystine, *L*-histadine, *L*-phenylalanine, *L*-methionine, *L*-cysteine, *L*-tyrosine, *L*-tryptophan, *L*-carnitine, *L*-theanine)
10. Silymarin (milk thistle extract)
11. *trans*-resveratrol
12. Ginko Biloba
13. Medium-chain triglycerides
14. Chicory root
15. Vitamin C
16. Thiamine (Vitamin B1)
17. Niacin (Vitamin B3)
18. Pyridoxine (Vitamin B6)
19. Methylcobalamin (Vitamin B12)
20. Magnesium citrate
21. Taurine
22. Boron
23. Citric acid

Figure 1. List of Leap2Bfit Version 3.0 Ingredients. 1. MenaQ7 (a patented form of vitamin K). 2. Theracurmin (a patented form of curcumin). 3. Curcumin C3 complex (a patented form of curcumin). 4. Turmacin (a patented extract of turmeric). 5. SerinAid (a proprietary form of phosphatidylserine, an amino acid derivative). 6. AlphaSize (a patented form of alpha-glyceryl phosphoryl choline). 7. Quatrefolic (a patented form of folic acid). 8. SeleniumSelect (a patented form of the mineral selenium). 9. Several amino acids (*L*-leucine, *L*-lysine, *L*-isoleucine, *L*-valine, *L*-threonine, *L*-proline, *L*-glycine, *L*-arginine, *L*-cystine, *L*-histadine, *L*-phenylalanine, *L*-methionine, *L*-cysteine, *L*-tyrosine, *L*-tryptophan, *L*-carnitine, *L*-theanine). 10. Silymarin (milk thistle extract). 11. *trans*-resveratrol. 12. Ginko Biloba. 13. Medium-chain triglycerides. 14. Chicory root. 15. Vitamin C. 16. Thiamin (Vitamin B1). 17. Niacin (Vitamin B3). 18. Pyridoxine (Vitamin B6). 19. Methylcobalamin (Vitamin B12). 20. Magnesium citrate. 21. Taurine. 22. Boron. 23. Citric acid.

literature suggests the only side effect is occasional gastrointestinal discomfort (14–17).

#### *α*-GPC

Alpha-glycerolphosphorylcholine (*α*-GPC; also called choline alfoscerate) is a supplement that is thought to increase levels of the neurotransmitter acetylcholine (18). This mechanism may benefit cognitive symptoms of patients with Alzheimer's disease (19,20) but is unlikely to be of benefit in the type of dementia that is associated with ALS, i.e. frontotemporal dementia (21) because other neurotransmitter systems are primarily involved. Pilot ALS trials with drugs that increase acetylcholine have not been successful (22,23). In PLM, 1 PALS reported taking *α*-GPC. This single patient reported they could not tell if the supplement was effective and did not experience any side effects

(24). We could not find any other cases or clinical trials of PALS taking *α*-GPC. Safety data from other human populations suggests that *α*-GPC is generally safe (18,25). Supplementation has been associated with minor gastrointestinal distress and anxiety, presumably due to its cholinergic mechanism (25).

#### *Ginkgo biloba*

Pronounced 'gin-ko,' ginkgo is a tree native to East Asia. Products from this 'maidenhair tree' are used in China and Japan as food and traditional medicine. In Western countries, extracts from the leaves are commonly sold as a supplement. The exact composition of these extracts varies by manufacturer. Ginkgo extracts has been reported *in vitro* to be able to neutralize oxidative stress (26–28), which is theoretically of benefit in ALS

Table 1. Table of Evidence for Leap2BFIT.

	Grade	Explanation
Mechanism	C	LEAP2BFIT contains <i>L</i> -carnitine for which we previously assigned a mechanisms grade of A. It is theoretically possible that some of the other ingredients might act synergistically with <i>L</i> -carnitine.
Pre-Clinical	U	There have been no pre-clinical model studies of LEAP2BFIT.
Cases	B	There are 3 PALS with validated ALS diagnoses and validated improvements in motor function while taking supplement cocktails that included LEAP2BFIT.
Trials	U	There have been no clinical trials of LEAP2BFIT.
Risks	D	Given that (1) the dosages of the individual ingredients are unknown and (2) LEAP2BFIT has never been tested in any clinical trial, we cannot adequately assess the safety of this supplement in PALS. A D grade is warranted by several of the individual ingredients.

(29). In a single study with a mutant mouse model of ALS, a standardized extract of ginkgo (Egb 761), was shown to improve survival and slow lumbar-region motor neuron death (30). Twelve PALS in PLM reported taking ginkgo; the 2 that provided treatment reports stated that they could not tell if it had any efficacy (31). We could not find any other cases or clinical trials of PALS taking ginkgo. There are potential risks of ginkgo. In healthy rodents, ginkgo is reported to decrease lifespan, increase the risk of tumors, and to decrease reproductive function (32). It is unknown if these adverse effects are also true in humans. There are data in humans to suggest ginkgo raises the risk of seizures, ischemic stroke, and bleeding, as well as altering the blood levels of other drugs taken (32).

#### *Selenomethionine*

Selenomethionine is a special amino acid that provides the trace element selenium (33). Selenium is necessary in small quantities for normal human physiology (33) and may help protect against oxidative stress (34) but has many associated risks (see below). In PLM, 37 PALS reported taking selenium supplements. Of the 6 who provided treatment reports, 4 reported they could not tell if the supplement was effective and 2 perceived no effectiveness. None experienced any side effects (35). One small pilot trial of selenium in ALS showed no clear benefit on clinical outcome (36). There is substantial and compelling evidence that selenium supplementation increases the risk of developing type II diabetes mellitus in humans. Other possible adverse effects include gastrointestinal distress, hair loss and rash (37). Some

research suggests that chronic selenium exposure might even trigger ALS (38–43).

#### *Amino acids*

Some of the amino acids in LEAP2BFIT (*L*-leucine, *L*-valine, *L*-isoleucine and *L*-threonine) can potentially reduce glutamate and excitotoxicity, which gives them a plausible mechanism for slowing ALS progression (44). Unfortunately, multiple small trials of these amino acids in PALS have failed to show benefit (44).

#### *Vitamins*

B vitamins can decrease homocysteine levels (45), which are elevated in PALS and may contribute to oxidative stress and excitotoxicity (46). Unfortunately, published case reports showed no benefit of vitamin B6 (pyridoxine) on ALS progression (47,48). A single study in a transgenic SOD1 mouse model of ALS reported that vitamin B9 (folic acid) extended lifespan (49), but this has not been replicated and human trials have not been conducted. Vitamin C is an antioxidant (50). A small case series of an antioxidant cocktail including vitamin C found no benefit in PALS (51).

In summary, *L*-carnitine in LEAP2BFIT has an ALSUntangled “mechanisms” grade of A (8). Our “mechanisms” grade for LEAP2BFIT is based on whether all the other ingredients can add anything to *L*-carnitine. We conclude such a synergy is theoretically possible and so ALSUntangled assigns LEAP2BFIT a “mechanisms” grade of C (Table 1).

#### **Pre-Clinical models**

LEAP2BFIT has not been tested in any pre-clinical models relevant to ALS. Therefore, ALSUntangled assigns a TOE “pre-clinical models” grade of U (Table 1).

#### *Cases*

In the online community PatientsLikeMe (PLM), 5 PALS report taking LEAP2BFIT; of the 2 who submitted treatment evaluations, 1 perceived “slight” effectiveness and 1 perceived no effectiveness (52). A Facebook page reports “hundreds” of PALS “with positive results” (53). It is not clear how their diagnoses or reported benefits are being validated. Within the clinics of the ALSUntangled coauthors, at least 20 PALS have been self-experimenting with LEAP2BFIT for periods of 3–6 months; no clear benefits have yet been observed (54). Within the cohort of 47 “dramatic ALS reversals” validated at Duke University (55,56), 3 patients were taking LEAP2BFIT (as well as several other alternative and off-label treatments)

during their improvements. As we have previously stated, there are multiple possible explanations for these cases of ALS reversals (55).

Based on the above evidence, ALSUntangled assigns a TOE “cases” grade of B (Table 1).

### *Trials*

There have been no human trials of LEAP2BFIT, therefore ALSUntangled assigns a TOE “trials” grade of U (Table 1).

### *Risks*

It is impossible to know the safety of this specific combination of supplements in PALS without a carefully designed and placebo-controlled clinical trial. This is further complicated by not knowing the exact dosages of the individual supplements in a serving of LEAP2BFIT, nor whether there is any quality control to ensure that each can of LEAP2BFIT contains the same ingredients and the same dosages. Patients taking warfarin (a blood thinner) must talk with their doctor before starting or stopping LEAP2BFIT as it contains vitamin K. In a prior review, resveratrol, one of the ingredients in LEAP2BFIT, was given a “risks” grade of D. Based on available safety data (see “ingredients”), ginkgo biloba and selenomethionine would also receive a “risks” grade of D. Given that the safety profiles of several respective individual ingredients warrant a grade of D, ALSUntangled assigns a TOE “risks” grade of D (Table 1).

### *Dosing and costs*

LEAP2BFIT is exclusively available from the manufacturer’s website. The website recommended dosing for general health and wellness is 1 scoop (13 grams by weight) dissolved into liquid twice daily, on an empty stomach with doses at least 4 hours apart (57). It is not clear that any studies have been done to validate this dosing regimen. A container with 30 scoops costs \$50 USD plus shipping, so taking 2 scoops a day would cost around \$100 USD per month.

### **Conclusions**

Many ingredients contained within LEAP2BFIT could, at least in theory, be beneficial in ALS. Some of these ingredients have supporting animal or human studies. However, it is unknown if these ingredients are being provided in therapeutic quantities since the dosages are not disclosed. Furthermore, it is impossible to know the net positive or negative effect of so many ingredients without carefully testing the combination. Based on the above discussions, we do not currently recommend

LEAP2BFIT as a way to slow, stop, or reverse ALS.

### **Declaration of interest**

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