

SCIENCE IN FOCUS

Understanding B Vitamins in AMD

Nutritional Support: Intake, Safety and Practical Considerations

CLINICAL AREA	Age-related macular degeneration
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KEY TAKEAWAYS

- B vitamins support ocular-health pathways relevant to AMD, including homocysteine regulation, cellular metabolism and vascular function, and may complement the well-established AREDS2 nutrient approach.
- Preliminary clinical and epidemiologic evidence suggests potential relevance across the AMD continuum, including incident and early AMD, while prospective trials are needed to define the magnitude of incremental benefit.
- B vitamins have a favorable safety profile, with several having no established upper intake level and excess intake generally eliminated in urine; vitamins B3, B6 and B9 warrant closer interpretation, but their levels in PreserVision AREDS3™ remain below or within established tolerability thresholds.
- For most patients, coadministration of PreserVision AREDS3™ with a standard multivitamin is expected to remain within safety margins, but total supplement exposure should be reviewed in individual cases.

Established Nutrition Has Changed AMD Management

Few interventions in ophthalmology have shaped practice as durably as targeted nutritional supplementation in age-related macular degeneration (AMD). The original Age-Related Eye Disease Study enrolled 3640 participants across a range of AMD severity categories, randomly assigned to antioxidants (vitamin C 500 mg, vitamin E 400 IU, beta-carotene 15 mg), zinc 80 mg with copper 2 mg, both, or placebo. Among participants at higher risk of progression — principally those with intermediate AMD or advanced AMD in one eye — antioxidants plus zinc reduced the odds of progression to advanced AMD (odds ratio [OR] 0.72; 99% CI 0.52–0.98, and 0.66; 99% CI 0.47–0.91 once the lowest-risk categories were excluded) and of at least moderate visual acuity loss (OR 0.73; 99% CI 0.54–0.99) over an average of 6.3 years.¹

AREDS2 built on that foundation in 4203 participants with bilateral large drusen, or large drusen with advanced AMD in the fellow eye, testing whether lutein 10 mg and zeaxanthin 2 mg, omega-3 fatty acids, or both added benefit to the AREDS formulation. The primary analysis showed no significant reduction in progression to late AMD. Secondary and exploratory analyses were nonetheless informative. At 10 years, direct comparison of lutein and zeaxanthin with beta-carotene favored the carotenoid pair for progression to late AMD (hazard ratio 0.85; 95% CI 0.73–0.98), while beta-carotene nearly doubled the odds of lung cancer (OR 1.82; 95% CI 1.06–3.12) — together establishing lutein and zeaxanthin as the appropriate replacement.^{2,3}

A Cochrane review concluded that antioxidant vitamins plus zinc probably slow progression to late AMD and vision loss (moderate-certainty evidence),⁴ and current guidance recommends supplementation be considered in intermediate AMD, geographic atrophy, or other advanced AMD in one eye.⁵ That evidence base remains central to nutritional care for appropriate patients.

However, substantial residual risk of progression remains, creating an opportunity to address additional metabolic pathways that may contribute to retinal vulnerability.

Building Beyond Established Antioxidant Pathways: The Rationale for B Vitamins

AMD is multifactorial. Overlapping processes contribute to disease and progression: oxidative stress, inflammation, vascular and endothelial dysfunction, mitochondrial and metabolic health and nutritional status. Established AREDS2 ingredients address central elements of AMD biology, including antioxidant defense, zinc-dependent enzymatic function and macular pigment.

In addition, B vitamins offer a complementary approach through homocysteine regulation and vascular support. Homocysteine accumulation is a recognized underlying disease mechanism in cardiovascular disease and dementia, among others. Its clearance depends in part on vitamins B6, B9 and B12. AMD is associated with elevated total homocysteine and decreased vitamin B12 levels, indicating that homocysteine may act as a modulator of AMD risk.⁶

A randomized prospective clinical trial reported that daily supplementation of folic acid 2.5 mg, vitamin B6 50 mg and vitamin B12 1 mg was associated with fewer confirmed AMD cases and fewer visually significant AMD cases over a mean follow-up of more than 7 years. Additional prospective and long-term dietary evidence supports the same direction of association^{7–10}.

The current evidence should be interpreted with appropriate caution, as studies vary in the populations evaluated, the B vitamins and doses studied, and the clinical or epidemiologic outcomes reported, with some inconsistency in results. Prospective clinical trials will be essential to determine the magnitude of any incremental benefit and clarify which patient populations may be most likely to benefit.

Even so, the overall direction of the evidence suggests that B vitamins may offer a relevant extension of AMD nutritional support. The mechanistic basis for this rationale is discussed in detail in the companion Science in Focus article. From a practical perspective, eye care professionals may also need to consider how the B-vitamin content of PreserVision AREDS3™ fits within overall nutrient intake, safety considerations and use alongside other supplements.

Practicalities of B-Vitamin Supplementation: Intake, Status and Dose Interpretation

For eye care professionals, interpreting the B-vitamin content of PreserVision AREDS3™ requires consideration of recommended intake, upper intake levels, common suboptimal intake in older adults, and coadministration with multivitamins or other supplements. In routine AMD care, dose interpretation

matters because many patients may already be taking multivitamins or other dietary supplements. National dietary survey data add further context, showing that suboptimal intake of selected B vitamins remains common in 10–20% of adults not using multivitamins (reviewed in ¹¹).

Two distinct parameters generally define recommended doses of nutrients, the Recommended Dietary Allowance (RDA) and the Tolerable Upper Intake Level (UL). The RDA represents the average daily intake expected to meet the nutrient requirements of nearly all healthy individuals, whereas the UL represents the highest average daily intake unlikely to pose risk of adverse effects in the general population. A dose above the RDA should therefore not be interpreted as inherently unsafe. The UL includes a safety margin and is usually well below true toxicity levels; exceeding the UL does not mean toxicity will occur, only that risk begins to increase (reviewed in ¹²).

Notably, most B vitamins are water-soluble and excess intake is generally eliminated in urine, contributing to their favorable overall safety profile. In fact, vitamins B1, B2, B5, B7 and B12 have no established UL. However, for vitamin B3, the therapeutic range is more nuanced: toxicity concerns depend on the form and dose. Whereas the UL for niacin is 35 mg due to adverse event concerns, the niacinamide form of vitamin B3, used in the PreserVision AREDS3™ formulation, has been considered safe for healthy individuals at doses up to 1500 mg/day (reviewed in ¹²).

Regarding vitamin B6, the dose used in the PreserVision AREDS3™ formulation is below the adult UL and represents approximately 50% of that threshold. For folic acid, the UL was established due to the potential of folic acid supplementation to mask vitamin B12 deficiency. This risk is mitigated in formulations providing vitamin B12 as well. Importantly, the vitamin B6 and B12 doses in PreserVision AREDS3™ align with those evaluated in WAFACS, while the folic acid dose is lower than the 2.5 mg used in that study (reviewed in ¹²).

Coadministration With Multivitamins and Other Supplements

In clinical practice, dose interpretation also requires discussion of coadministration, as many patients may already be taking multivitamins or other dietary supplements alongside an AMD-specific formulation. This is not a new consideration in AMD care: in AREDS2, almost 90% of participants were already taking multivitamins at baseline, and participants in the AREDS clinical program were offered Centrum Silver to standardize non-study supplement use.

A practical approach is to ask patients whether they are already using a multivitamin, standalone B-complex supplement, vitamin B12 injections, or regularly consuming highly fortified products such as energy drinks.

For most patients using a standard multivitamin, total B-vitamin exposure is expected to remain within acceptable safety margins. Closer review is warranted for patients taking high-dose standalone B-complex products, those with renal impairment, or those who self-escalate supplement doses without guidance.

Further practical guidance on incorporating PreserVision AREDS3™ into clinical care is available in the recent article by Poteet et al. in *Optometry* 360¹².

Broadening Nutritional Support in AMD

AREDS2-based supplementation remains central to nutritional management for appropriate patients with AMD. The addition of B vitamins in PreserVision AREDS3™ reflects a scientifically grounded extension of this approach, supported by mechanistic, clinical and epidemiologic evidence linking B-vitamin-related pathways to AMD risk and progression.

Prospective clinical trials will be important to define the magnitude of incremental benefit and identify the patients most likely to benefit. In the meantime, PreserVision AREDS3™ can be viewed in the context of

what is already known about B vitamins: they support homocysteine regulation, cellular metabolism, vascular health and other pathways relevant to overall ocular health, while generally having a wide margin of safety. This is particularly relevant in older adults, among whom suboptimal intake of selected B vitamins remains common.

The available evidence suggests potential relevance across the AMD continuum, including preliminary data in incident and early AMD, while the safety profile supports consideration alongside established AREDS-based nutritional care in later stages when clinically appropriate. For eye care professionals, the practical task is therefore to interpret B-vitamin exposure using established safety benchmarks, consider coadministration with multivitamins or other supplements, and individualize counseling for patients with high-dose supplement use or relevant medical considerations.

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Author Disclosures

Authored and reviewed by Bausch + Lomb Global Medical and Scientific Affairs.

Availability Statement

PreserVision AREDS3™ is available in the US. However, it is not available worldwide. Contact us for further information about PreserVision AREDS3™ availability.

