

# Risks Associated with Ocular Vitamin and General Multivitamin Regimens in Patients with Age-Related Macular Degeneration

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## Introduction

Age related macular degeneration (AMD) is the leading cause of vision loss in patients over 50 years of age<sup>1</sup>. The National Eye Institute developed the Age-Related Eye Disease Study (AREDS) to study risk factors associated with AMD. The AREDS study examined the use of various types of vitamins and minerals that may reduce the risk of AMD in specific clinical scenarios and promulgated recommendation for the use of vitamins and minerals as a means to reduce AMD risk. As a result, non-prescription vitamin and mineral use is widely recommended by clinicians who demonstrate early AMD retinal findings<sup>2</sup>. However, many older adults self-medicate with multivitamins even prior to use of eye vitamins and therefore may be subject to increased levels of vitamins and minerals that may increase risk for toxicity. The goal of this study was to provide recommendations for safe and appropriate vitamin and mineral supplementation regimens for patients with age-related macular degeneration (AMD) who seek to add ocular vitamins to their general multivitamin regimen.

## Methods

A systematic review of the literature was performed using secondary literature databases. The reference search allowed for compilation of primary and tertiary sources. The evidence was compared to common ocular supplement and Centrum multivitamin ingredients; multivitamins and ocular vitamins were also directly compared. Upper limits of each vitamin or mineral examined was determined using total upper intake limit (TUIL) set by the Institutes of Medicine (IOM). The vitamins and minerals assessed in the ocular and multivitamin include: vitamins A, B<sub>2</sub>, C, zinc, copper, lutein, selenium, calcium, omega-3 fatty acids, and zeaxanthin

## Vitamins

Table 1. Ocular vitamin and mineral supplements analyzed in this study.

Brand	Product	Formula	Dose
Bauch & Lomb	Preservision	Eye Vitamin with Lutein Formula Soft Gels	1 gel, twice daily
		Soft Gel	2 tablets, twice daily
		Tablet	1 gel, twice daily
		AREDS 2 Soft Gels	1 gel, twice daily
	Ocuvite	Adult 50+, Soft Gel	1 soft gel daily
Alcon	iCaps	Tablet	2 tablets, twice daily
		Eye Vitamin with Lutein and Zeaxanthin Tablet	1 tablet, twice daily
		Eye Vitamin with Lutein and Omega-3 Tablet	1 tablet daily
		AREDS Formula Coated Tablets	2 tablets, twice daily
		AREDS Formula Soft Gels	1 gel, twice daily
Veterans Affairs	Ocular vitamin	I-Vite Protect Tablets	1 tablet, twice daily
		I-Vite Tablets	1 tablet, twice daily

Table 2. Daily multivitamin and mineral supplements analyzed in this study

Brand	Product	Formulation	Dose	
Centrum	Silver	Adults 50+, Tablet	1 tablet daily	
		Women's, Tablet	1 tablet daily	
		Men's, Tablet	1 tablet daily	
		Ultra	Women's, Tablet	1 tablet daily
			Men's, Tablet	1 tablet daily
	Flavor Burst Chews	Grape	4 chews daily	
		Mixed Fruit	4 chews daily	
		Specialist	Energy Tablet	1 tablet daily
	Multivitamin		Tablet	1 tablet daily
			Liquid	15mL daily
Veterans Affairs	Multivitamin	Tablet	1 tablet daily	

## Results

Results from the systematic review found relevant data regarding the ingredients present in both ocular supplements and daily multivitamin formulations. Cumulative levels of vitamin A and zinc were found to surpass the established TUIL.

Zinc levels reached a high of 99.6 mg with concurrent use of iCaps ocular multivitamin and Men's or Women's Centrum Ultra Silver, 2.49 times the TUIL. Zinc intake above the TUIL when combined with all multivitamins analyzed were seen with PreserVision Eye Vitamin with Lutein formula and AREDS 2 soft gel formula, and Ocuvite Eye Vitamin with Lutein (except in combination with VA multivitamin).

Among products examined, levels of vitamin A reached a high of 32,140 IU between the combination of Preservision Lutein, iCaps AREDS formulas, and the VA I-Vite Protect ocular vitamins in combination with Men's or Women's Centrum Ultra Silver. Patients taking this combination would be taking 3.21 times TUIL. There was an increase in vitamin A above TUIL in combinations of iCaps Eye Vitamin with Lutein and Omega-3 formula with all multivitamin formulations.

There were inconsistent results when assessing the combination of VA I-Vite tablet formulation with multivitamin formulas assessed. While an increase in zinc was seen with all combinations involving I-Vite, amounts of vitamin A above the TUIL were seen in the following vitamins: Centrum Multivitamin tablets, Ultra Men's and Women's tablets, Silver Men's and Women's tablets, and Specialist Energy tablet formulations.

No amounts of any vitamins or minerals above the recommended TUIL were seen when comparing the Ocuvite Eye Vitamin for Adults 50+ soft gel formula to all of the multivitamins assessed.

### Vitamin A:

Substantial data exists on the adverse effects of high vitamin A intakes. Acute toxicity can manifest as signs and symptoms of nausea, vomiting, headache, increased cerebrospinal fluid pressure, vertigo, blurred vision, muscular incoordination.<sup>3</sup> These are usually transient effects involving single or short-term large doses of greater than or equal to 150,000 µg in adults and proportionately less in children.<sup>4</sup> Chronic and excessive vitamin A intake has been shown to cause bone density loss in animals.<sup>5</sup> Additionally, alcohol intake has been shown to potentiate heptatotoxicity.<sup>6</sup>

### Zinc:

Adverse effects associated with chronic and excessive zinc intake include signs and symptoms of epigastric pain, nausea, vomiting, loss of appetite, abdominal cramps, diarrhea, and headaches.<sup>7,8</sup> Specific effects associated with increased zinc intake include immune response suppression, decreases in high-density lipoprotein cholesterol, and reduced copper.<sup>9</sup>

## Conclusion

- In many combination regimens vitamin A and zinc levels surpassed tolerable upper intake levels.
- Patients with comorbidities, such as those with diabetes and complicating renal disease are susceptible to toxicity and should also take caution when adding an ocular vitamin to their daily multivitamin therapy<sup>10-12</sup>
- Select combinations regimens keep nutrients at safe levels. Eye care professionals should be knowledgeable of harmful combinatory effects when adding ocular vitamins to established daily multivitamin regimens and recommend regimens that avoid interactions.

## Results

Table 3. Amounts of zinc in ocular vitamins, daily multivitamins, and combined levels. Amounts of zinc were taken from the product label of the respective ocular vitamin or daily multivitamin. Numbers highlighted in red represent the combined amounts of zinc that are above the daily total upper intake limit of 40 mg established by the Institutes of Medicine.

		Zinc (mg)	Centrum									Veterans Affairs	
			Adults under 50		Flavor Burst		Ultra		Silver			Specialist	
			Tablet	Liquid	Grape	Mixed Fruit	Men's	Women's	Men's	Women's	Adults 50+	Energy	Multivitamin
Preservision	Eye Vitamin with Lutein Formula, Soft Gels	69.6	80.6	72.6	74.6	74.6	80.6	77.6	84.6	84.6	80.6	80.6	69.6
	Soft Gel	69.9	80.9	72.9	74.9	74.9	80.9	77.9	69.9	69.9	69.9	69.9	69.9
	Tablet	69.6	80.6	72.6	74.6	74.6	80.6	77.6	84.6	84.6	80.6	80.6	69.6
	AREDS 2, Soft Gels	80	91	83	85	85	91	88	95	95	91	91	80
Ocuvite	Adult 50+, Soft Gel	9	20	12	14	14	20	17	24	24	20	20	9
	Eye Vitamin with Lutein, Tablet	40	51	43	45	45	51	48	55	55	51	51	40
iCaps	Tablet	84.6	95.6	87.6	89.6	89.6	95.6	92.6	99.6	99.6	95.6	95.6	84.6
	Eye Vitamin with Lutein and Zeaxanthin Tablet	60	71	63	65	65	71	68	75	75	71	71	60
	Eye Vitamin with Lutein and Omega-3, Tablet	7	18	10	12	12	18	15	22	22	18	18	7
	AREDS Formula Coated Tablets	69.6	80.6	72.6	74.6	74.6	80.6	77.6	84.6	84.6	80.6	80.6	69.6
	AREDS Formula Soft Gels	69.6	80.6	72.6	74.6	74.6	80.6	77.6	84.6	84.6	80.6	80.6	69.6
Veterans Affairs	I-Vite Protect Tablets	69.6	80.6	72.6	74.6	74.6	80.6	77.6	84.6	84.6	80.6	80.6	69.6
	I-Vite Tablets	80	91	83	85	85	91	88	95	95	91	91	80

Table 4. Amounts of vitamin A in ocular vitamins, daily multivitamins, and combined levels. Amounts of vitamin A were taken from the product label and are displayed as International Units (IU) of retinol. Product labelling with units of beta-carotene were converted to units of retinol. Numbers highlighted in red represent the combined amounts of vitamin A that are above the daily total upper intake limit of 10000 IU of retinol established by the Institutes of Medicine.

		Vitamin A (IU)	Centrum									Veterans Affairs	
			Adults under 50		Flavor Burst		Ultra		Silver			Specialist	
			Tablet	Liquid	Grape	Mixed Fruit	Men's	Women's	Men's	Women's	Adults 50+	Energy	Multivitamin
Preservision	Eye Vitamin with Lutein Formula, Soft Gels	0	3500	1300	2000	2000	3500	3500	3500	3500	2500	3500	2500
	Soft Gel	28640	32140	29940	30640	30640	32140	32140	28640	28640	28640	28640	28640
	Tablet	28640	32140	29940	30640	30640	32140	32140	28640	28640	28640	28640	28640
	AREDS 2, Soft Gels	0	3500	1300	2000	2000	3500	3500	3500	3500	2500	3500	2500
Ocuvite	Adult 50+, Soft Gel	0	3500	1300	2000	2000	3500	3500	3500	3500	2500	3500	2500
	Eye Vitamin with Lutein, Tablet	1000	4500	2300	3000	3000	4500	4500	4500	4500	3500	4500	3500
iCaps	Tablet	0	3500	1300	2000	2000	3500	3500	3500	3500	2500	3500	2500
	Eye Vitamin with Lutein and Zeaxanthin Tablet	6600	10100	7900	8600	8600	10100	10100	10100	10100	9100	10100	9100
	Eye Vitamin with Lutein and Omega-3, Tablet	4000	7500	5300	6000	6000	7500	7500	7500	7500	6500	7500	6500
	AREDS Formula Coated Tablets	28640	32140	29940	30640	30640	32140	32140	28640	28640	28640	28640	28640
	AREDS Formula Soft Gels	28640	32140	29940	30640	30640	32140	32140	28640	28640	28640	28640	28640
Veterans Affairs	I-Vite Protect Tablets	28640	32140	29940	30640	30640	32140	32140	28640	28640	28640	28640	28640
	I-Vite Tablets	2000	5500	3300	4000	4000	5500	5500	5500	5500	4500	5500	4500

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