

Appendix 2. Treatment recommendations extracted from the American Academy of Ophthalmology (AAO) Preferred Practice Pattern Guideline Statement (2015) for age-related macular degeneration (AMD)

		Section of PPP where recommendation appears			Systematic reviews cited	Randomized controlled trials cited	Other citations	
Management sections of PPP		Highlighted findings and recommendations for care (page 4)	Other sections of PPP					
Care process (pp 19-23)	Table 4. Treatment recommendations (pp 20-21)			Background (pp 7-16)	Appendix 3. Grading of recommendations (pp 30-35)			
1	"Patients who are currently smoking should be advised to stop." (page 19)	Not mentioned	"Smoking cessation is strongly recommended when advising patients who have AMD or are at risk for AMD."	"Smoking cessation is strongly recommended when advising patients" (page 7)	I++; Good; Strong	1 non-AMD intervention SR cited	None	2 NRSs; 1 CPG cited
2	Not mentioned	Not mentioned	"Patients who have been instructed to use aspirin by a physician should continue to use it as prescribed."	"In light of all the available information on the subject of aspirin use and AMD, the current preferred practice is for patients who have been instructed to use aspirin by a physician to continue their aspirin therapy as prescribed." (page 8)	II++; Good; Strong	1 non-AMD intervention SR cited	1 RCT cited	1 NRS cited
3	Not mentioned	Not mentioned	Not mentioned	"The routine use of genetic testing is not supported by the existing literature and is not recommended at this time." (page 8)	III; Insufficient; Discretionary	None	1 RCT cited	1 NRS cited
4	"Patients with early AMD and/or a family history of AMD should be encouraged to assess their own visual acuity using monocular vision testing (i.e., Amsler grid) and have scheduled dilated eye examinations for detecting the intermediate stage of AMD." (page 19)	"Monitoring of monocular near vision (reading/Amsler grid)"; "Fundus photos, fluorescein angiography, or OCT as appropriate"	Not mentioned	Not mentioned	III; Good; Strong	None	None	None
5	"Patients with a high-risk AMD phenotype are at increased risk of progression to advanced AMD and should be educated about methods of detecting new symptoms of CNV, including self-monitoring. They should also be educated about the need for promptly reporting new symptoms to an ophthalmologist who can confirm if the new symptoms are from CNV and who can begin any necessary treatment." (page 19)	Not mentioned	Not mentioned	Not mentioned	III; Good; Strong	None	None	None

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Management sections of PPP		Other sections of PPP						
Care process (pp 19-23)	Table 4. Treatment recommendations (pp 20-21)	Highlighted findings and recommendations for care (page 4)	Background (pp 7-16)	Appendix 3. Grading of recommendations (pp 30-35)				
6	"The risks, benefits, complications, and alternatives of the treatment should be discussed with the patient and informed consent obtained." (page 22)	Not mentioned	Not mentioned	Not mentioned	III; Good; Strong	None	None	1 AAO policy statement cited
7	"Treatment with antioxidants and minerals as described previously in the original AREDS and AREDS2 trials is recommended for patients who have progressed to intermediate or advanced AMD in at least one eye." (page 19)	"Antioxidant vitamin and mineral supplements as recommended in the original AREDS and AREDS2 reports"	"Antioxidant vitamin and mineral supplementation as per the original AREDS and AREDS2 trials should be considered in patients with intermediate or advanced age-related macular degeneration."	"The original AREDS results demonstrate a beneficial effect for the use of high-dose oral antioxidant vitamins (vitamins C, E, beta-carotene) and zinc supplementation in reducing progression of intermediate AMD or advanced AMD in the fellow eye to advanced AMD by 25%." (page 7)	I++; Good; Discretionary	None	2 RCTs cited	1 NRS; 1 textbook cited
8	Not mentioned	Early AMD not listed as diagnosis eligible for treatment	"There is no evidence to support the use of these supplements for patients who have less than intermediate AMD."	"There is no evidence to support the use of these supplements for patients who have less than intermediate AMD." (page 10)	I++; Good; Discretionary	None	None	None
9	Not mentioned	Not mentioned	Not mentioned	"Additional vitamin E supplementation above the AREDS levels should be avoided." (page 7)	Not mentioned	1 non-AMD intervention SR cited	None	None
10	Unclear	Not mentioned	Not mentioned	Unclear	"A lower zinc dose (25 mg) in the AREDS2 formulation could be considered"; I++; Good; Discretionary	None	None	None

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Management sections of PPP		Other sections of PPP						
Care process (pp 19-23)	Table 4. Treatment recommendations (pp 20-21)	Highlighted findings and recommendations for care (page 4)	Background (pp 7-16)	Appendix 3. Grading of recommendations (pp 30-35)				
11	Unclear	Not mentioned	"Replacement of the beta-carotene from the original AREDS formulation with lutein/zeaxanthin in the AREDS2 supplements may decrease the risk of lung cancer in smokers."	"Results of AREDS2 support the replacement of beta-carotene (from the original AREDS) with lutein/zeaxanthin in the new AREDS2 supplements." (page 7); "The final results of AREDS2 support the recommendation for substitution of beta-carotene with lutein (10 mg) and zeaxanthin (2 mg)." (page 11)	Not mentioned	None	4 RCTs cited	None
12	" Because of the potential adverse effects, such as increased rate of genitourinary conditions that may require hospitalizations, the high doses of antioxidant vitamins and minerals recommended by the original AREDS and AREDS2 should be reviewed by the patient's primary care physician." (page 23)	Not mentioned	Not mentioned	Not mentioned	III; Good; Strong	None	4 RCTs cited	None
13	Unclear	Unclear	"Intravitreal injection therapy using anti-vascular endothelial growth factor (VEGF) agents (e.g., aflibercept, bevacizumab, and ranibizumab) is the most effective way to manage neovascular AMD and represents the first line of treatment."	"Anti-VEGF therapies have become first-line therapy for treating and stabilizing most cases of neovascular AMD." (page 12)	I++; Good; Strong	1 reliable SR (Vedula 2008)	None	None

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Management sections of PPP		Other sections of PPP					
Care process (pp 19-23)	Table 4. Treatment recommendations (pp 20-21)	Highlighted findings and recommendations for care (page 4)	Background (pp 7-16)	Appendix 3. Grading of recommendations (pp 30-35)			
14	Unclear	“Less commonly used treatments for neovascular AMD” are PDT with verteporfin and thermal laser photocoagulation surgery	Not mentioned	“Current practice patterns support the use of anti-VEGF monotherapy for patients with newly diagnosed neovascular AMD, and suggest that these other therapies [verteporfin PDT and thermal laser photocoagulation surgery] are rarely needed yet may be used in unresponsive cases.” (page 13)	III; Good; Strong	None	None
15	“Assessment and treatment plans for non-neovascular and neovascular AMD are listed in Table 4.” (page 19)	“Aflibercept intravitreal injection 2.0 mg as described in published reports”	“Intravitreal injection therapy using anti-vascular endothelial growth factor (VEGF) agents (e.g., aflibercept, bevacizumab, and ranibizumab) is the most effective way to manage neovascular AMD and represents the first line of treatment.”	“Anti-VEGF therapies have become first-line therapy for treating and stabilizing most cases of neovascular AMD.” (page 12)	III; Good; Strong	None	2 RCTs cited
16	“Assessment and treatment plans for non-neovascular and neovascular AMD are listed in Table 4.” (page 19)	“Bevacizumab intravitreal injection 1.25 mg as described in published reports”	“Intravitreal injection therapy using anti-vascular endothelial growth factor (VEGF) agents (e.g., aflibercept, bevacizumab, and ranibizumab) is the most effective way to manage neovascular AMD and represents the first line of treatment.”	“Anti-VEGF therapies have become first-line therapy for treating and stabilizing most cases of neovascular AMD.” (page 12)	III; Good; Strong	None	6 RCTs cited 2 NRSs; 1 AAO policy statement cited
17	Not mentioned	“The ophthalmologist should provide appropriate informed consent with respect to the off-label status”	Not mentioned	Not mentioned	III; Good; Strong	None	1 insurance company document cited
18	“Caution should be used when dosing PRN bevacizumab, as it may be slightly less effective than other monthly anti-VEGF regimens.” (page 22)	Not mentioned	Not mentioned	Not mentioned	I++; Moderate; Discretionary	None	None

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Management sections of PPP		Other sections of PPP						
Care process (pp 19-23)	Table 4. Treatment recommendations (pp 20-21)	Highlighted findings and recommendations for care (page 4)	Background (pp 7-16)	Appendix 3. Grading of recommendations (pp 30-35)				
19	"Assessment and treatment plans for non-neovascular and neovascular AMD are listed in Table 4." (page 19)	"Ranibizumab intravitreal injection 0.5 mg as recommended in literature"	"Intravitreal injection therapy using anti-vascular endothelial growth factor (VEGF) agents (e.g., aflibercept, bevacizumab, and ranibizumab) is the most effective way to manage neovascular AMD and represents the first line of treatment."	"Anti-VEGF therapies have become first-line therapy for treating and stabilizing most cases of neovascular AMD." (page 12)	III; Good; Strong	None	4 RCTs cited	4 NRSs; 1 FDA document cited
20	"Small subretinal hemorrhages are a sign of active CNV or polypoidal choroidal vasculopathy and may be managed with anti-VEGF therapy." (page 22)	Not mentioned	Not mentioned	Not mentioned	Not mentioned	None	None	None
21	Unclear	Not mentioned	Not mentioned	"Most juxtafoveal lesions that may have been previously treated using laser photocoagulation are currently managed using the anti-VEGF agents." (page 14)	III; Good; Strong	None	1 RCT cited	None
22	Unclear	Not mentioned	Not mentioned	"The current trend is to use anti-VEGF agents in preference to laser photocoagulation" for extrafoveal lesions" (page 14)	III; Good; Strong	None	1 RCT cited	None
23	Not mentioned	"Patients should be instructed to promptly report symptoms suggestive of endophthalmitis"	"Symptoms suggestive of postinjection endophthalmitis or retinal detachment require prompt evaluation."	Not mentioned	III; Good; Strong	None	None	None
24	"Assessment and treatment plans for non-neovascular and neovascular AMD are listed in Table 4." (page 19) "Photosensitivity reaction (<3% of patients)...The stated, current recommendations are to avoid direct sunlight for the first 5 days after a treatment." (page 23)	"PDT with verteporfin as recommended in the TAP and VIP reports"	Not mentioned	Not mentioned	III; Good; Discretionary	None	2 RCTs cited	None
25		Not mentioned	Not mentioned	Not mentioned	Not mentioned	None	2 RCTs cited	None

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26	“Careful consideration should be given to patients with liver dysfunction and to patients who are pregnant, breast-feeding, or of pediatric age, because these patients were not studied in published reports.” (page 23)	Not mentioned	Not mentioned	Not mentioned	III; Good; Strong	None	None	None
27	“Assessment and treatment plans for non-neovascular and neovascular AMD are listed in Table 4.” (page 19)	“Juxtafoveal CNV is an off-label indication for PDT but may be considered in select cases”	Not mentioned	“Patients with juxtafoveal lesions may also be considered eligible for the off-label use of PDT with verteporfin.” (page 14) “There still remains a possible role for thermal laser surgery treatment in eyes with extrafoveal and peripapillary CNV lesions as defined by the MPS.” (page 14)	III; Good; Discretionary	None	1 RCT cited	None
28	“Assessment and treatment plans for non-neovascular and neovascular AMD are listed in Table 4.” (page 19)	“Thermal laser photocoagulation surgery as recommended in the MPS reports”	Not mentioned		III; Moderate; Strong	None	1 RCT cited	None
29	Thermal laser photocoagulation surgery: “These realities must be emphasized to the patient and family before treatment.” These realities = “Introduction or enlargement of pre-existing scotoma, with or without visual acuity loss, is not a complication of thermal laser photocoagulation; rather, it is an anticipated side effect of the treatment. Similarly, recurrence or persistence of CNV, or the development of new CNV and further visual deterioration after adequate thermal laser surgery, is usually a result of the disease process and is not a complication.” (page 23)	Not mentioned	Not mentioned	Not mentioned	III; Good; Strong	None	None	None
30	“Assessment and treatment plans for non-neovascular and neovascular AMD are listed in Table 4.” (page 19)	Macular CNV not listed as diagnosis eligible for treatment	Not mentioned	“Thermal laser photocoagulation surgery is no longer recommended for subfoveal CNV treatment.” (page 13)	None	None	1 RCT cited	None

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Care process (pp 19-23)	Table 4. Treatment recommendations (pp 20-21)	Highlighted findings and recommendations for care (page 4)	Background (pp 7-16)	Appendix 3. Grading of recommendations (pp 30-35)			
31 "Assessment and treatment plans for non-neovascular and neovascular AMD are listed in Table 4." (page 19)	Thermal laser photocoagulation surgery "may be considered for extrafoveal classic CNV, new or recurrent"	Not mentioned	"Laser surgery for extrafoveal lesions remains a less-commonly used, yet reasonable, therapy." (page 14)	III; Good; Strong	None	1 RCT cited	None
32 Not mentioned	Not mentioned	Not mentioned	"The data do not currently support the use of combination therapy [intravitreal corticosteroids and/or anti-VEGF agents in various drug combinations or with verteporfin PDT] at this time, especially with the long-term side effects of glaucoma and cataract that are associated with corticosteroid use." (page 13)	None	None	4 RCTs cited	2 NRSs cited
33 "Assessment and treatment plans for non-neovascular and neovascular AMD are listed in Table 4." (page 19)	"Observation with no medical or surgical therapies" recommended for early, non-neovascular AMD	Not mentioned	Not mentioned	III; Good; Strong	None	2 RCTs cited	1 NRS cited
34 Not mentioned	Not mentioned	Not mentioned	"Current therapies that have insufficient data to demonstrate clinical efficacy include radiation therapy, acupuncture, electrical stimulation, macular translocation surgery, and adjunctive use of intravitreal corticosteroids with verteporfin PDT. Therefore, at this time, these therapies are not recommended." (page 14)	III; Moderate; Strong	None	None	None
35 "The data on management of larger [submacular] hemorrhages are inadequate to make a recommendation at this time." (page 22)	Not mentioned	Not mentioned	Not mentioned	None	None	None	None