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[SAVRS guidelines for the Management of neovascular Age-Related Macular Degeneration](#)

The Academic Advisory Committee (AAC) of the SA Vitreoretinal Society (SAVRS) would like to update the guidelines for the management and treatment of exudative/neovascular Age-related Macular Degeneration (AMD). The committee would like to record the following points:

1. Age-related Macular Degeneration is the leading cause of irreversible visual loss in patients over 65 years of age. It is a chronic condition that requires life-long management. AMD is a PMB condition (ICD-10 H35.3). (904B in the CMS PMB coded list 2013).
2. The Council for Medical Schemes (COMS) updated PMB ICD 10 codes list for 2013 for the treatment of neovascular AMD refers to a schedule of diagnosis and treatment pairs dated 1998. In the PMB list, the treatment options listed are therefore outdated and no longer valid and are no longer the current level of care. The treatment options listed are no longer valid viz. vitrectomy surgery, laser surgery, other surgery. In 2016 different and new treatment options are required by qualified ophthalmologists registered with the HPCSA. In fact, not to treat appropriately for 2016 would make the ophthalmologist medico-legally liable for outdated care of their patients. Therefore this SAVRS guideline is a brief attempt to guide current ophthalmologists and funders with the current state of treatment. It would therefore be indefensible in terms of the Medical Schemes Act and HPCSA regulations to refer to COMS 1998 treatments.
3. Anti-VEGF monotherapy is the standard of care for the management of choroidal neovascularisation secondary to AMD, as demonstrated by multiple international, multi-centre peer-reviewed, randomised controlled trials (RCT). Guidelines for treatment are detailed in Appendix 1. Up until recently Ranibizumab (Lucentis®) has been the only anti-VEGF registered internationally and locally for the treatment of AMD. Now Aflibercept (Eylea) also has international and local registration.
4. Bevacizumab (Avastin®) carries international registration and MCC registration for the treatment of carcinoma of the colon but is NOT registered for use in the eye. The use of Bevacizumab (Avastin®) for the management of AMD is therefore in an "off-label" capacity. This is despite evidence that it is efficacious for the treatment of neovascular AMD and that there is sufficient evidence to equate its efficacy and safety profile to Ranibizumab. The SAVRS would like to emphasize that although the use of Bevacizumab (Avastin®) for the treatment of AMD is used widely in practice due to price, the decision to use Bevacizumab (Avastin®) is often dictated by funding/funders and may not be the first choice of the treating surgeon.
5. Bevacizumab (Avastin®) is packaged in a single, sterile vial for use as an intravenous agent. The fluid content of each vial is commonly compounded into smaller quantities in order to make the unit cost more affordable. In other countries where Bevacizumab (Avastin®) is used, compounding pharmacies undertake the process of preparing the units under strict aseptic conditions. Where no such pharmacies exist locally in South Africa, the pharmacist or surgeon needs to perform the compounding process themselves. In the absence of a compounding pharmacy, the SAVRS recommends that the compounding is performed under

sterile conditions in the operating theatre or under a laminar flow hood suitable for preparation of sterile intravenous medication. This compounding should be performed by an experienced operator. Compounding costs are expected to vary amongst centres with the different usage patterns, facility costs and other economic determinants.

6. Certain sub-types of neovascular AMD require special consideration. These sub-types require additional treatment modalities besides anti-VEGF monotherapy. The use of Visudyne Photodynamic Therapy (PDT), with anti-VEGF therapy may be indicated for neovascular AMD secondary to Idiopathic Polypoidal Choroidal Vasculopathy (PCV), Retinal angiomatous proliferation or neovascularisation resistant to monotherapy with an anti-VEGF agent. Studies have documented significantly improved success rates over anti-VEGF monotherapy. Because these conditions are rarer there will not be level 1 evidence from RCTs.
7. Where funders have not consulted the appropriate South African specialist opinion (SAVRS), funders have used guidelines from other countries. Most commonly the comprehensive Royal College of Ophthalmologists guideline has been used. This excellent guideline has not, in many instances, been applied appropriately by funders to the South African situation. This is because funders are not aware that NICE (National Institute for Health and Care Excellence, United Kingdom), which oversees the use of treatments in the British National Health System (NHS) does not authorise the use of Avastin for intraocular use in the UK in the NHS.

APPENDIX 1: Recommended treatment for subfoveal exudative/neovascular AMD

1. Patients should be referred to a suitably trained ophthalmologist for treatment.
2. The diagnosis of exudative AMD should be confirmed by the ophthalmologist and baseline visual acuity should be recorded. There are no visual acuity exclusions for treatment and treatment should be discussed and offered, unless contra-indicated, for all levels of vision.
3. Current standard of care recommendations include the performing of a fluorescein angiogram of the eye at baseline to confirm the diagnosis. The fluorescein angiogram is performed either in a hospital or at the doctor's rooms depending on the doctor's discretion and the emergency resuscitation facilities available. Indications for repeating the fluorescein angiogram include failure to respond to treatment and worsening of visual acuity. Indocyanin green angiography is indicated for investigation of non-responders to standard treatment or suspected atypical neovascularisation such as PCV.
4. The Optical Coherence Tomography (OCT) scan is a pivotal investigation for the diagnosis and follow-up of the therapy. OCT scan should be performed at least at baseline, month 3 after initiation of therapy and repeated when clinical history or examination suggests disease activity.
5. The standard of care dictates treatment with a single intravitreal injection of an anti VEGF agent, either 0.5mg Ranibizumab (Lucentis®), Aflibercept (Eylea) or 1.25mg Bevacizumab (Avastin®) monthly for the first 3 months as a loading dose. The response to treatment and disease activity is then reassessed, initially monthly, and further therapy is applied if there is persistent activity until there is no further activity or no reasonable prognosis for vision stabilisation or improvement.
6. The place where the injection is performed is in a suitable aseptic environment which may either be in a hospital setting or in the doctor's rooms depending on the treating doctor's discretion.
7. Current evidence from RCTs conducted for two years shows that the best visual outcome is achieved with monthly intravitreal injections. Alternative treatment regimens to monthly anti-VEGF injections would include the "treat-and-extend" regimen and the PRN dosing schedule. Whilst both of these schedules aim to reduce the burden of monthly injections, regular re-assessments with an ophthalmic examination and OCT are still required and repeat treatments are performed with any decrease in vision or evidence of disease activity eg exudation, haemorrhage, intra- or subretinal fluid.

8. As not all subfoveal neovascular AMD lesions respond to the first anti VEGF agent used, this group of non-responders will require alternative treatment regimes. This would include changing to a different antiVEGF agent or using combination strategies eg combination of an anti-VEGF with PDT.
9. Note that for the purposes of this guideline, Aflibercept (Eylea) has been called an anti-VEGF agent, although its mechanism of action (VEGF trap) differs slightly from the other two anti-VEGF agents mentioned.

References:

1. Abraham P, et al. Randomized, Double-Masked, Sham-Controlled Trial of Ranibizumab for Neovascular Age-Related Macular Degeneration: PIER Study Year 2. *Am J Ophthalmol*. 2010; 150: 315-324.
2. Abell et al. Intravitreal injections: is there benefit for a theatre setting? *Br J Ophthalmol* 2012; 96: 1474-1478.
3. Amoaku WM et al. Defining response to anti-VEGF therapies in neovascular AMD. *Eye* 2015; 29: 721-731
4. Allen C, et al. Twenty-four-Month Efficacy and Safety of 0.5 mg or 2.0 mg Ranibizumab in Patients with Subfoveal Neovascular Age-Related Macular Degeneration. *Ophthalmology* 2014; 121: 2181-2192.
5. Arnold JJ, et al. Two-Year Outcomes of “Treat and Extend” Intravitreal Therapy for Neovascular Age-Related Macular Degeneration. *Ophthalmology* 2015; 122:1212-1219.
6. Berg K, et al. Comparison of Ranibizumab and Bevacizumab for Neovascular Age-Related Macular Degeneration According to LUCAS Treat-and-Extend Protocol. *Ophthalmology* 2015; 122: 146-152.
7. Brown DM, et al. Ranibizumab versus Verteporfin Photodynamic Therapy for Neovascular Age-Related Macular Degeneration: Two-Year Results of the ANCHOR Study. *Ophthalmology* 2009 116:57-65.
8. Chakravarthy U, et al. Alternative treatments to inhibit VEGF in age-related choroidal neovascularisation: 2-year findings of the IVAN randomised controlled trial. *Lancet* 2013;12;382:1258-1267.
9. Gupta OP, et al. A Treat and Extend Regimen Using Ranibizumab for Neovascular Age-Related Macular Degeneration. *Ophthalmology* 2010;117:2134-2140.
10. Holz FG, et al. Safety and Efficacy of a Flexible Dosing Regimen of Ranibizumab in Neovascular Age-Related Macular Degeneration: The SUSTAIN Study. *Ophthalmology* 2011; 118:663-671.
11. Lalwani GA, et al. A Variable-dosing Regimen with Intravitreal Ranibizumab for Neovascular Age-related Macular Degeneration: Year 2 of the PrONTO Study. *Am J Ophthalmol* 2009; 148:43-58
12. Lally DR et al. Preferred therapies for neovascular age-related macular degeneration. *Curr Opin Ophthalmol* 2012; 23: 182-188

13. Maguire MG, et al. Five-Year Outcomes with Anti-Vascular Endothelial Growth Factor Treatment of Neovascular Age-Related Macular Degeneration. *Ophthalmology* 2016;123:1751-61.
14. Martin DF, et al. Ranibizumab and Bevacizumab for Treatment of Neovascular Age-Related Macular Degeneration: 2-Year Results: Comparison of Age-related Macular Degeneration Treatments Trials. *Ophthalmology* 2012; 119(7):1388-98.
15. Oubraham H, et al. Inject and extend dosing versus dosing as needed. *Retina* 2011; 31:26-30.
16. Royal College of Ophthalmologists. Age related Macular Degeneration: Guidelines for Management. September 2013.
17. Schmidt-Erfurth U et al. Guidelines for the Management of Neovascular Age-Related Macular Degeneration by TH European Society of Retina Specialists (EURETINA). *Br J Ophthalmol* 2014; 98: 1144-1167.
18. Silva R et al. The SECURE Study: Long-Term Safety of Ranibizumab 0.5 mg in Neovascular Age-related Macular Degeneration. *Ophthalmology* 2013; 120:130-139.
19. Toalster N, et al. A 12-month prospective trial of inject and extend regimen for ranibizumab treatment of age-related macular degeneration. *Retina* 2013; 33:1351-1358.
20. Wykoff CC, et al. Prospective Trial of Treat-and-Extend versus Monthly Dosing for Neovascular Age-Related Macular Degeneration. *Ophthalmology* 2015; 122: 2514-22.

2017

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