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SAVRS guidelines for the Management of Diabetic Macular Oedema

The Academic Advisory Committee of the SA Vitreoretinal Society (SAVRS) would like to review the guideline for the management of Diabetic Macular Oedema (DMO). The purpose of these guidelines is to advise ophthalmologists and funders. The committee would like to record the following points:

1. Diabetic macular oedema is the leading cause of irreversible visual loss in those under 65 years of age. It is a chronic condition that requires life-long management. Diabetic maculopathy is a PMB condition (904B in the CMS PMB Coded List 2013.) ICD10 codes H35.0; H35.2; H35.3; H36.0, E11.3; E10.3.
2. The Council for Medical Schemes (COMS) updated PMB ICD 10 Coded list for 2013 for the treatment of 904B conditions under which Diabetic Macular Oedema is grouped with other unrelated conditions refers to a schedule of diagnosis and treatment pairs dated 1998. In the PMB list, the treatment options listed are therefore outdated and are no longer the current level of care. The treatment options listed for the whole group of 904B conditions is "vitrectomy surgery, laser surgery, other surgery". In 2016 different and new treatment options are required to be used 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 In fact, not to treat appropriately for 2016 would make the ophthalmologist medico-legally liable for outdated care of their patients.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 for an ophthalmologist in terms of the Medical Schemes Act and HPCSA regulations to refer to COMS 1998 treatments and this likewise applies to funders.
3. Anti-VEGF monotherapy with Ranibizumab (Lucentis®) intra-vitreal injections is the current standard of care for the management of Diabetic maculopathy causing Diabetic macular oedema (DMO) resulting in vision loss due to centre involvement, as demonstrated by multiple international, multi-centre , randomised controlled trials in peer reviewed journals (Level 1 evidence)[1,2,3,4]. Guidelines for treatment are detailed in Appendix 1. Additional anti-VEGF monotherapy agents await approval shortly by the MCC but are already registered by the FDA and in Europe. Ranibizumab (Lucentis®) is registered internationally and locally in South Africa by the MCC for the treatment of DMO.
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 in South Africa. The use of Bevacizumab (Avastin®) for the management of DMO is therefore in an "off-label" capacity when used intravitreally in SA. This is despite evidence that it is efficacious for this indication and substantiated in the literature (Level 1 evidence)[5,10,11]. The decision to use Bevacizumab (Avastin®) is in most cases dictated by 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 contents of each vial are 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 such a pharmacy is not available

locally in South Africa, the local pharmacists or surgeon will need 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. Compounding costs are expected to vary amongst treatment centres with differing usage patterns, facility costs and other economic determinants.

6. 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[7]. 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 NHS.
7. Note that DME (Edema - American English) and DMO are used interchangeably in the literature.

APPENDIX 1: Recommended treatment for diabetic macular oedema (DMO).

1. Patients should be referred to a suitably trained ophthalmologist for treatment.
2. Diagnosis of DMO should be confirmed by the ophthalmologist and baseline visual acuity should be recorded[7]. Where there is vision loss, 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 and assess the degree of capillary non-perfusion. The fluorescein angiogram is performed either in a hospital or at the doctor's rooms depending on the doctor's discretion. Repeat angiography may be required to assess response to treatment or unexplained visual loss.
4. The Optical Coherence Tomography (OCT) scan is an essential investigation for the diagnosis and follow-up of the therapy[7].
5. For DMO with centre involvement causing vision loss, the current guideline (Level 1 evidence) dictates treatment with anti-VEGF monotherapy[1,2,7]. During this phase re-assessment with visual acuity (VA) and OCT is required and this may be required at least monthly. Once the vision has stabilised for at least two consecutive monthly visits, the treatment is stopped but monitoring should be continued on a monthly basis. If the VA deteriorates due to DMO, then monthly injections should be restarted until a stable VA is again attained. Alternative strategies that are similar to treat and extend protocols used in Age-related Macular Degeneration, are emerging as options in DME treatment as well. This approach allows for a reduced number of visits and injections in the long-term while maintaining visual outcomes.[12,13]
6. The place where the injection is performed is in a suitable sterile environment which may either be in a hospital setting or in the doctor's rooms depending on the treating doctor's discretion[6].
7. The role of adjunctive laser (focal or grid) is currently unclear in the short term though long-term data have shown a reduction in the number of intravitreal treatments when combined with laser[1,9]. As VA improvement following laser treatment occurs slowly, this effect may still be seen in the long term and the outcome of current trials is awaited[9].
8. Because funders are interpreting the NICE and Royal College of Ophthalmologists guidelines themselves, the following needs to be clarified:
    - Reference is made in the Royal College of Ophthalmologists guidelines to the NICE use of 400 microns as the central retinal thickness (CRT) at which to initiate the induction of Lucentis intravitreal treatment. This is a NICE recommendation for the use of Lucentis and does not have level 1 evidence. It refers to a subset of patients in the original RCT of Lucentis who had better visual outcomes but the RCT were not powered to make this analysis[1].

9. Where there is DMO with centre involvement of the macula but no vision loss, the patient requires observation and treatment according to ETDRS guidelines - see below (Level A recommendation).
10. Where there is DME with no centre involvement, the patient requires treatment according to ETDRS guidelines (Level A recommendation)[1,8].
    - Summary of ETDRS guidelines: Focal photocoagulation : treatment of individual micro aneurysms that fill with fluorescein and/or leak
    - Grid laser: treatment of areas of thickened retina showing diffuse fluorescein leakage and / or capillary dropout.
11. Systemic management of the patient is critical to achieving optimum visual outcome and improvement of the DMO and therefore must be optimised by monitoring systemic factors under the guidance of a Diabetic clinic or Diabetologist on a regular basis.
12. This guideline covers DMO and not proliferative diabetic retinopathy. However, caution is advised when proliferation is present as accelerated fibrosis may be precipitated by injection of anti-VEGF agents and this may lead to vision loss.
13. Non-responders to the primary anti-VEGF monotherapy should be considered for alternative treatment options. This would include changing to another anti-VEGF agent, retinal laser or intravitreal steroids[7]. Ozurdex® (dexamethasone 700 µg intravitreal implant) is registered in SA for the treatment of adult patients with macular oedema following either Branch Retinal Vein Occlusion (BRVO) or Central Retinal Vein Occlusion (CRVO); its registration for DMO is imminent.
14. Because DME is the complication of a systemic condition, it is expected that the rate of bilateral cases requiring treatment will be higher.
15. Cataract surgery on patients with previous/present DMO may exacerbate the oedema. Consideration should be given to the use of anti-VEGF agents at the time of cataract surgery in selected patients.

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