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POLICY STATEMENT

The use of Biosimilars in Ophthalmic Practice- 2023

With regards to the off-label use of biosimilars in the eye, SAVRS strongly recommends against biosimilar substitution until there is robust clinical use data available for those indications. The ophthalmologist should assess any medico-legal risk associated with use of biosimilars lacking SAPHRA-approval for intravitreal use.

A biosimilar product has no clinically meaningful differences in terms of safety, purity, and potency to the reference product for its labelled indications, but have differences in inactive components, termed excipients. This is best demonstrated through human pharmacokinetic (exposure) and pharmacodynamic (response) studies, and an assessment of clinical immunogenicity. The excipients—including the stabilizer or buffer—may differ from what is used in the reference product. There should be studies demonstrating safety of those excipients for the approved indication and the target tissue (e.g. the eye). An example of an issue with excipients during intraocular use was the occurrence of cases of sterile inflammation when the first biosimilar of ranibizumab approved in India was introduced; this problem was addressed through a revised drug formulation.[1]

Step therapy is a widely used tool by insurers to reduce health care costs by requiring use of the least expensive treatment first, moving to a more expensive alternative if there is an inadequate response. SAVRS does not support step-therapy; the choice of treatment should be that of a patient and their ophthalmologist.

Bevacizumab (Avastin®) is not SAPHRA-approved for ocular use. It is repackaged by compounding pharmacies or the ophthalmologist as an off-label product. Bevacizumab has been widely studied for eye disease and is currently used in more than half of intravitreal injections in the South Africa. It has a favourable ten-year safety

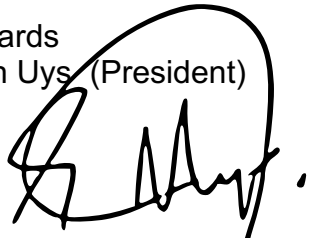
[1] Sharma A, Kumar N, Kuppermann BD et al. Ophthalmic biosimilars and biologics - role of endotoxins. *Eye* 2020; 34:674-615.

profile following the pivotal Comparison of Age-Related Macular Degeneration Treatment Trials (CATT) in 2011. [2]

In conclusion: By reducing cost, the South African Retinal Society recognizes the potential societal value of biosimilars for improving care of patients with eye disease. Biosimilars should have sufficient research demonstrating their safety and effectiveness for treatment of eye diseases before they are routinely recommended for ophthalmologic use. When used, the choice of biologic product—reference, biosimilar, or interchangeable—should be that of the treating ophthalmologist and their patient. The successful and cost effective off-label use of bevacizumab (Avastin®) for eye disease for over 15 years represents a unique history of a well-studied biologic agent injected into the eye, which has yet to be duplicated for bevacizumab biosimilars.

Before a biosimilar is required to be used for treatment or included in a step therapy regimen, it should be SAPHRA-approved for the ophthalmic indication. Such a pathway ensures there is evidence of safety—including for any excipients—and efficacy for its use in the eye. If that pathway is not possible, the treating ophthalmologist should review the published evidence of safety and effectiveness for any biosimilar proposed for treatment with each patient to determine if it is the best clinical option.

Kind regards
Dr Enslin Uys (President)



On behalf of SAVRS Exco
20 February 2023

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[2] CATT Research Group, Martin DF, Maguire MG et al. Ranibizumab and bevacizumab for neovascular age-related macular degeneration. *N Engl J Med* 2011; 364:1897-1908.

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