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Position statement on the use of dexamethasone (Ozurdex®) implant for Non-Infectious Uveitis

Background on Uveitis Treatment

Non-infectious uveitis represents a heterogeneous group of inflammatory ocular conditions, and establishing the diagnosis requires a careful exclusion of infectious etiologies. The diagnostic work-up typically includes targeted investigations to rule out common infectious causes. These may involve serologic testing such as rapid plasma reagin (RPR), Treponema pallidum hemagglutination assay (TPHA), and fluorescent treponemal antibody absorption (FTA-ABS) for syphilis; Toxoplasma IgG and IgM for ocular toxoplasmosis; and interferon-gamma release assays (IGRA), chest radiography, and the Mantoux skin test for tuberculosis. Only after infectious causes have been reasonably excluded can a diagnosis of non-infectious uveitis be confidently established, guiding the clinician toward appropriate immunosuppressive or corticosteroid-based therapy.

Non-infectious uveitis is primarily treated using corticosteroids, as they are highly effective in controlling inflammation within the eye. However, the administration of systemic corticosteroids can be associated with side effects such as hypertension, weight gain, and immune suppression, which complicate long-term management (Valdes & Sobrin, 2023)¹. These side effects are particularly concerning for uveitis patients, as they may require prolonged therapy or repeated doses.

For patients with intermediate, posterior, or panuveitis, topical and systemic corticosteroids may not adequately control inflammation. Intravitreal corticosteroid implants, such as Ozurdex®, are advantageous in these cases because they deliver the drug directly to the site of inflammation, minimising the systemic exposure and reducing side effects (Mikhail et al., 2024)². Research by José-Vieira et al. (2022)³ further supports the role of intravitreal corticosteroids, demonstrating their efficacy in improving visual outcomes and reducing inflammation in non-infectious uveitis.

¹ Valdes, L. M., & Sobrin, L. (2023). *Uveitis Therapy: The Corticosteroid Options*. Journal of Ophthalmology.

² Mikhail, M., Sallam, A., & collaborators. (2024). *Novel Intraocular Therapy in Non-infectious Uveitis of the Posterior Segment of the Eye*. Ophthalmology Review.

³ José-Vieira, R., Ferreira, A., Menéres, P., Sousa-Pinto, B., & Figueira, L. (2022). *Efficacy and Safety of Intravitreal and Periocular Injection of Corticosteroids in Noninfectious Uveitis: A Systematic Review*. Journal of Ocular Pharmacology and Therapeutics, 38(6), 456-463.

Pathophysiology of Ocular Inflammation

The pathophysiology of uveitis is characterised by immune system dysfunction, where the body's own immune cells, such as T-lymphocytes and macrophages, target the eye's structures. This leads to the release of inflammatory mediators, such as cytokines, chemokines, and prostaglandins, that increase vascular permeability, resulting in oedema and the recruitment of more inflammatory cells to the site of damage (Mikhail et al., 2024). In non-infectious uveitis, this immune response can cause damage to the ocular tissues, leading to complications such as macular oedema, retinal damage, and potential vision loss if left untreated.

Macular oedema is one of the most significant manifestations of ocular inflammation, caused by the breakdown of the blood-retinal barrier and leakage of fluid into the retina. The use of corticosteroids like dexamethasone helps restore the integrity of this barrier by suppressing the inflammatory response, thus reducing oedema and preventing further damage to the retina (Valdes & Sobrin, 2023). This treatment approach has shown to improve both visual acuity and the long-term preservation of sight.

Clinical Evidence and Efficacy

The Ozurdex® implant, which releases dexamethasone in a controlled manner over several months, has shown significant benefits for patients with non-infectious uveitis. By providing localised delivery of corticosteroids, it reduces systemic exposure and associated side effects.

The POINT trial, which examined the effectiveness of intravitreal dexamethasone implants, demonstrated that Ozurdex® improves visual outcomes and reduces macular oedema in patients with uveitic macular oedema (MUST Research Group et al., 2020)⁴. In particular, the POINT trial found that intravitreal therapies—including dexamethasone implants—were significantly more effective at reducing central retinal thickness and improving vision than periocular injections, with a faster and more substantial reduction in oedema seen at the 8-week mark.

In addition, the MERIT trial⁵ (Intravitreal Therapy for Uveitic Macular Oedema—Ranibizumab versus Methotrexate versus the Dexamethasone Implant) further supports the use of Ozurdex®. The trial compared three intravitreal treatments and found that the dexamethasone implant was associated with greater short-term improvements in best-corrected visual acuity (BCVA) and central macular thickness compared to intravitreal methotrexate and ranibizumab. While all three agents were found to be beneficial, dexamethasone had the most rapid and pronounced anatomical and functional effects, suggesting it may be particularly suitable for patients requiring a swift therapeutic response.

The sustained release of dexamethasone offers therapeutic benefits that extend beyond a single injection, reducing the need for frequent treatments and improving patient adherence.

⁴ The Multicenter Uveitis Steroid Treatment Trial (MUST) Research Group, Thorne, J. E., Sugar, E. A., Holbrook, J. T., Burke, A. E., Altaweel, M. M., Vitale, A. T., Acharya, N. R., Kempen, J. H., & Jabs, D. A. (2020). *Periocular Triamcinolone Versus Intravitreal Triamcinolone Versus Intravitreal Dexamethasone Implant for the Treatment of Uveitic Macular Oedema: The PeriOcular versus INTravitreal Corticosteroids for Uveitic Macular Oedema (POINT) Trial*. *Ophthalmology*, 127(10), 1377-1386.

⁵ Ehlers JP, Thorne JE, Wallis J, Jabs DA, Van Gelder RN, Dunn JP, et al. Intravitreal Therapy for Uveitic Macular Oedema: The MERIT Trial. *Ophthalmology*. 2022;129(6):637–648.

Mechanism-Based Rationale for Corticosteroid Use in Uveitis

Unlike diabetic macular oedema or neovascular age-related macular degeneration, where vascular endothelial growth factor (VEGF) plays a primary pathogenic role, uveitic macular oedema arises primarily from immune-mediated inflammation. This distinction is critical when selecting treatment.

The MERIT trial directly compared the efficacy of three intravitreal therapies: methotrexate (an immunosuppressant), ranibizumab (an anti-VEGF agent), and the dexamethasone implant (a corticosteroid).

Although ranibizumab did demonstrate some anatomical and visual improvements, the dexamethasone implant outperformed it in both visual acuity gains and reduction of macular thickness, particularly in the early treatment window. This highlights the importance of targeting inflammatory pathways over VEGF-driven mechanisms in non-infectious uveitis.

These findings reinforce that uveitic macular oedema should primarily be treated with anti-inflammatory agents like corticosteroids, as they directly address the underlying immune dysregulation that drives the disease.

Novel Therapies for Non-Infectious Uveitis

Recent advancements in the management of uveitis highlight the growing preference for treatments that deliver medication directly to the site of inflammation⁶. Ozurdex®, as a sustained-release implant, is a prime example of how intraocular drug delivery can address the challenges of long-term uveitis management. As discussed in *Novel Intraocular Therapy in Non-infectious Uveitis of the Posterior Segment of the Eye* by Mikhail and Sallam (2024), the use of intraocular implants has revolutionised the treatment of posterior uveitis, providing patients with a more targeted and effective solution.

This approach helps avoid the systemic complications associated with oral corticosteroids and offers improved outcomes for patients who need ongoing control over inflammation. Furthermore, studies such as the one by Valenzuela et al. (2023)⁷ on pharmacological strategies for uveitis treatment confirm that sustained-release corticosteroid implants like Ozurdex® are becoming a cornerstone of therapy for non-infectious uveitis, especially for patients with recurrent or chronic disease.

Patient-Centric Benefits

Ozurdex® provides a significant advantage in terms of patient convenience and comfort. With its long-lasting effects, the implant reduces the need for frequent injections, which can improve adherence and lessen the burden on patients. Additionally, because the implant delivers a sustained anti-inflammatory effect, it decreases the risk of flare-ups and vision-threatening complications, leading to better overall disease control.

The targeted nature of the Ozurdex® implant also reduces the systemic side effects often seen with oral corticosteroids, such as increased intraocular pressure, cataracts, and metabolic disturbances

⁶ National Institute for Health and Care Excellence (NICE). (2018). *Final Scope for the Appraisal of Flucinolone Acetonide Ocular Implant for Treating Recurrent Non-Infectious Uveitis*. Retrieved from www.nice.org.uk.

⁷ Valenzuela, R. A., Flores, I., Urrutia, B., Fuentes, F., Sabat, P. E., Llanos, C., Cuitino, L., & Urzua, C. A. (2023). *New Pharmacological Strategies for the Treatment of Non-Infectious Uveitis: A Minireview*. *Journal of Therapeutic Advances in Ophthalmology*, 15, 204-211.

(Valdes & Sobrin, 2023). As a result, patients are able to manage their condition with fewer side effects, which is critical in preserving their long-term eye health and quality of life.

Cost-Effectiveness

Although the initial cost of the Ozurdex® implant may be higher compared to traditional therapies, it is important to assess the overall cost-effectiveness. The sustained-release formulation of Ozurdex® reduces the frequency of injections, which may lower the overall cost of care in the long term. Furthermore, by reducing inflammation and preventing complications such as macular oedema and cataracts, Ozurdex® helps avoid more expensive interventions down the line, including surgery and rehabilitation due to vision loss (Mikhail et al., 2024).

The improved visual outcomes achieved with Ozurdex® are associated with higher productivity and reduced disability, which has economic benefits both for patients and the healthcare system. Effective treatment⁸ that prevents long-term damage to vision can also reduce the need for disability benefits and rehabilitation services.

Risks of intravitreal corticosteroid use

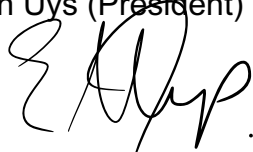
Although the dexamethasone (Ozurdex®) implant is associated with notable therapeutic benefits, its use may be accompanied by certain well-recognised adverse effects, most commonly the development or acceleration of cataract formation in phakic eyes and elevations in intraocular pressure (IOP). These complications are well-documented in the literature and are routinely anticipated and managed within standard ophthalmic clinical practice. Patients receiving intravitreal corticosteroids are monitored at regular intervals to facilitate the early detection of IOP elevation, which is typically managed with topical agents. In the majority of cases, such pressure increases are transient and do not necessitate surgical intervention. Cataract progression, when it occurs, can be effectively treated with cataract extraction, which is a safe and commonly performed procedure. Importantly, these potential complications are generally outweighed by the clinical benefits of sustained intraocular inflammation control, particularly in patients at risk of vision loss due to chronic or recurrent uveitis.

Conclusion

In conclusion, the dexamethasone (Ozurdex®) implant provides an innovative, effective, and patient-friendly option for the management of non-infectious uveitis. Supported by robust clinical evidence from the POINT and MERIT trial and its ability to deliver sustained anti-inflammatory effects with fewer side effects, Ozurdex® is a valuable addition to the therapeutic armamentarium for uveitis.

Kind regards

Enslin Uys (President)



On behalf of SAVRS

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⁸ Reekie, I. R., Gordon, I., Safi, S., Lingham, G., Ghadiri, N., Evans, J. R., & Keel, S. (2022). *Systematic Review of Clinical Practice Guidelines for Uveitis*. British Journal of Ophthalmology, 106(9), 1257-1264.