



**RANZCO**

The Royal Australian  
and New Zealand  
College of Ophthalmologists

# Clinical Practice Guidelines for the Use of Intravitreal Triamcinolone Acetonide

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**Approved by:**

Board

**Next review:**

29 June 2017

**Approval date:**

29 June 2014

## 1. Purpose and scope

The aim of this policy is to provide a guideline for ophthalmologists in the appropriate patient selection and clinical indication for the use of intravitreal triamcinolone acetonide (IVTA). Included are specific guidelines for the appropriate preparation of the medication, prevention and management of the possible complications of IVTA, the manner in which to obtain informed consent for the use of IVTA as well as appropriate documentation of its use.

## 2. What is Triamcinolone Acetonide?

Corticosteroids include both glucocorticoids and mineralocorticoids. Triamcinolone acetonide is a synthetic glucocorticoid agonist. Glucocorticoids and the glucocorticoid receptor play a role in several regulatory networks that inhibit a number of inflammatory pathways. The glucocorticoids inhibit the transcription of inflammatory and immune genes, and these actions include blocking the release of arachadonic acid and its subsequent eicosanoids (ie prostaglandins, thromboxanes, prostacyclins and leukotrienes).<sup>1</sup>

With an intravitreal triamcinolone injection there is a natural dissolution of insoluble triamcinolone crystals into soluble triamcinolone within the vitreous. This creates a diffusional drug gradient from depot to macula with minimal systemic exposure. While a portion of the drug targets the macula, a larger portion will either diffuse through the retina and be cleared or diffuse anteriorly to the crystalline lens or iris and outflow pathways. Exposure of glucocorticoid to the lens may cause posterior subcapsular cataract. Exposure of glucocorticoid to the outflow tissues alters the extracellular matrix. This increases outflow resistance and may increase intraocular pressure (IOP).<sup>2</sup>

## 3. Use of Intravitreal Triamcinolone Acetonide

Intravitreal steroid therapy has been used for many years for the management of a number of ocular conditions including macular oedema of varied aetiology (diabetic, retinal vein occlusion, post-operative and inflammatory) and intraocular inflammation. Ophthalmologists consider IVTA for patients in an aim to limit systemic steroid complications and to maximize local steroid dosage by bypassing the blood-retinal-barrier. IVTA has also been used by vitreoretinal and anterior segment surgeons to help visualize the vitreous intra-operatively.

### **Diabetic macular oedema**

Diabetic macular oedema (DMO) is a common cause of vision loss in diabetic patients. For many years this was treated with argon laser photocoagulation according to findings from the Early Treatment Diabetic Retinopathy Study.<sup>3</sup> More recently intravitreal steroid and intravitreal anti-vascular endothelial growth factor (anti-VEGF) agents have been used. In patients with DMO that persisted or recurred after laser treatment, IVTA (Kenacort A-40) has been shown to improve vision and reduce macular thickness. With repeated treatment, this effect was seen for up to 2 years.<sup>4</sup> The Diabetic Retinopathy Clinical Research Network reported on a randomized trial evaluating intravitreal 0.5 mg

ranibizumab or 4 mg triamcinolone (Trivaris, not available in Australia) combined with focal/grid laser compared with focal/grid laser alone for treatment of DMO. Their 2 year results for all patients showed the mean change in the visual acuity letter score from baseline was 3.7 letters improvement in the ranibizumab and prompt laser group, 5.8 letters improvement in the ranibizumab and deferred laser group and 1.5 letters worse in the triamcinolone and prompt laser group.<sup>5</sup> For pseudophakic patients, however, the combination of ranibizumab and laser had equivalent outcomes for vision compared with IVTA and laser. This has led many ophthalmologists toward anti-VEGF therapy as a first line treatment for phakic patients with DMO, however not all patients respond, and in this instance, IVTA may be a reasonable second line treatment. For pseudophakic patients with DMO, IVTA may be considered as first line treatment.

### **Macular oedema secondary to retinal vein occlusion**

The Central Vein Occlusion Study looked at the effect of macular grid laser for cystoid macular oedema (CMO) in both non-ischaemic and ischaemic occlusions. While CMO decreased, there was no difference in vision between the treated and non-treated groups throughout the study.<sup>6</sup> The Branch Vein Occlusion Study showed that patients with vision of 6/12 or worse at 3 months from CMO were more likely to improve vision by 2 lines or more with laser treatment compared with controls.<sup>7</sup> The SCORE study looked at IVTA for macular oedema in CRVO (v observation) and BRVO (v laser). The IVTA was shown to be superior to observation in treating CMO in CRVO at month 12, with attenuation of result at month 24.<sup>8</sup> Visual acuity outcomes were no different in BRVO patients between laser and IVTA groups.<sup>9</sup> More recent trials have shown greater benefit for intravitreal anti-VEGF therapy on CMO secondary to CRVO (CRUISE<sup>10</sup>, COPERNICUS<sup>11</sup>) and BRVO (BRAVO<sup>12</sup>). While these remain first line treatment, there is some evidence to consider the use of IVTA for CMO secondary to CRVO that persists despite multiple intravitreal bevacizumab injections.<sup>13</sup>

### **Uveitic macular oedema**

Cystoid macular oedema is a common cause of vision loss in patients with uveitis.<sup>14</sup> For patients with posterior segment inflammation and macular oedema, topical steroid therapy is often inadequate. These patients have the option of local (orbital floor, posterior subtenon or intravitreal) or systemic steroid. In an attempt to minimize systemic steroid side effects (such as Cushingoid state, osteoporosis and increased difficulty controlling diabetes) local steroid is often considered, especially for unilateral inflammation. Uveitic CMO has been shown to be effectively reduced with IVTA.<sup>15</sup> Visual acuity improvements were demonstrated and were more significant if the CMO was present for 12 months or less or the patients were aged 60 years or younger. The IOP increased by greater than 10mmHg in 43.1% patients and 54.5% patients were able to cease or reduce systemic immunosuppressive therapy. Cystoid macular oedema that persists in eyes with quiescent, non-infectious uveitis has also been shown to resolve with IVTA with corresponding significant improvements in visual acuity.<sup>16</sup> As a single IVTA injection lasts approximately 3 to 6 months, repeat IVTA injections may be required. Repeat IVTA injections for uveitic CMO in 41 eyes of 35 patients have been demonstrated to provide significant vision improvements after each injection with no evidence of reducing efficacy.<sup>17</sup> An IOP increase of 10mmHg or more from baseline was

seen in 46% eyes, and an IOP increase to greater than 30mmHg in 25% of eyes. After five IVTA injections, all phakic eyes had undergone cataract surgery. One eye developed sterile endophthalmitis.

### **Post-operative macular oedema**

Cystoid macular oedema is a well known complication of cataract surgery. If it fails to adequately clear with topical non-steroidal and steroidal therapy, then local steroid injections become an option. Intravitreal triamcinolone acetonide has been shown to reduce CMO and improve vision in cases of long-standing pseudophakic CMO<sup>18</sup>, and the effect may be sustained for more than 6 months.<sup>19</sup>

### **Other uses for intravitreal triamcinolone acetonide**

Injections of IVTA have been used for a variety of other causes of CMO including retinitis pigmentosa<sup>20</sup>, radiation retinopathy<sup>21</sup>, parafoveal telangiectasia<sup>22</sup> and idiopathic CMO.<sup>23</sup> It is also used for intraoperative visualisation of vitreous. As the vitreous is usually optically transparent, small amounts of triamcinolone may be injected into the anterior chamber or posterior segment to assist with visualisation, and hence more complete removal, of the vitreous. The triamcinolone is generally removed at the completion of the procedure unless it is required for therapeutic reasons.

### **Intravitreal Triamcinolone Preparations**

Kenacort is a triamcinolone acetonide suspension formulated for intra-articular and intramuscular injections. Triesence is a preservative-free triamcinolone acetonide suspension formulated for intravitreal injection. Preservatives have been postulated to play a role in sterile endophthalmitis following IVTA and in one study, the incidence of severe sterile endophthalmitis fell from 13.0% to 4.3% after switching to preservative free triamcinolone acetonide.<sup>24</sup> Kenacort has a duration of effect of up to 6 months.<sup>25</sup> Triesence continues to have an effect for approximately 4 months. Animal studies have shown that different triamcinolone acetonide preparations have different pharmacokinetics and pharmacodynamics.<sup>26</sup> The longest vitreous durability appeared to correlate with the largest particle size (these were 47µm for Kenacort, 26µm for Triesence and 22µm for Trivaris).

### **Intravitreal Triamcinolone Dosage**

There are different doses of intravitreal triamcinolone acetonide used in the various aetiologies of CMO described above (ranging from 1mg to 25mg). Overall, a number of reviews and articles have suggested a dose of 4mg in 0.1mL for intravitreal use as this dose appears to strike a balance between maximising effect and minimising ocular complications. The recommended dose for Triesence is 1 to 4mg in the product information provided by Alcon.<sup>27</sup>

## 4. Guidelines for the Use of Intravitreal Triamcinolone Acetonide

### 4.1. Patient and treatment selection

- The treating ophthalmologist must always consider which treatment option is in the best interest of their patient
- If other treatments have been previously attempted, their use and outcome (successful or otherwise) should be documented
- All investigation results pertaining to the patient's condition (such as OCT and fluorescein angiography) should be documented
- The decision-making process that led to the decision for IVTA use should be documented

### 4.2. Preparation of the medication

- Appropriate aseptic technique should be used to prepare and administer the IVTA. For further information on the appropriate procedure of an intravitreal injection please refer to the RANZCO Intravitreal Injection Guidelines.<sup>28</sup>

### 4.3. Preventing and managing complications from intravitreal injections of triamcinolone acetonide

- Complications of IVTA include:
  - Infection (endophthalmitis)
  - Non-infectious inflammation (sterile endophthalmitis)
  - Raised IOP
  - Cataract (traumatic and steroid-induced)
  - Retinal detachment
- Appropriate sterile technique should be used to reduce the risk of endophthalmitis (as above)
- Patients should be monitored after the injection for possible complications and appropriate follow-up arranged
- Patients should be informed of the symptoms of possible complications and how to seek timely treatment should these occur, and this discussion should be documented
- If complications occur that do not respond to treatment or are outside the area of expertise of the treating ophthalmologist, then the patient should be referred in a timely manner to an appropriate sub-specialist ophthalmologist
- When complications are being treated the ophthalmologist should remain in contact with the patient, even if this treatment is being given by a sub-specialist ophthalmologist

### 4.4. Informed consent discussion and documentation

- Each patient should be informed of their diagnosis, all treatment options and the reason for choosing IVTA for their specific condition. This discussion should be documented
- The known risks and complications of the procedure and medication should be explained and documented. Consider providing the patient with written information on these risks.

- Each patient should be guided through a consent form and then freely sign the consent form prior to the administration of IVTA
- If patients have specific risks pertaining to their individual situation, then these should be explained and documented (such as increased risk of infection in diabetic patients, increased risk of an IOP rise in glaucoma patients)
- An IVTA-specific consent form should be signed by the patient
- Prior to any repeat injections the patient's clinical condition needs to be reassessed and the need for further IVTA needs to be established and documented
- If the patient's condition changes at a future point where the risk/benefit ratio is no longer in favour of IVTA treatment, then this treatment should be reassessed
- If the patient refuses an IVTA injection at any point in their management where the ophthalmologist feels it is the most appropriate treatment, then the ophthalmologist needs to determine and address the reason for this decision and document this discussion as well as any other treatment options offered

#### 4.5. Documentation of care

- Document the clinical findings and investigation results that enabled a diagnosis to be made
- Document the decision-making process that led to IVTA being considered
- Document any previously attempted treatments and their outcomes
- Document the patient discussion on reasons for IVTA treatment and possible risks
- Document any refusal of IVTA, including the reasons the patient refused care
- Document the details of the IVTA dose, vial lot number and procedure
- Document any reaction to the IVTA
- Provide follow-up instructions, and document that these have been given
- Document efforts to monitor for and treat complications
- Document referrals to sub-specialists and keep a copy of the consultation letter in the patient's file
- Document all communication to and from the patient, including phone calls

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## 6. Record of amendments to this document

Page	Details of amendment	Date approved
Entire document	Created	29/06/2014 (Board)