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Dexamethasone intravitreal implant (Ozurdex) for non-infectious intermediate or posterior segment uveitis

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Dexamethasone intravitreal implant (Ozurdex) for non-infectious intermediate or posterior segment uveitis

Target group

- Non-infectious intermediate or posterior segment uveitis; first line; adults.

Background

Uveitis is inflammation of the uveal tract of the eye, which consists of the iris, the ciliary body and the choroid. Uveitis may be classified by the anatomical location of the pathology into: anterior, intermediate (vitritis), posterior (retina and choroid) or panuveitis. The course of uveitis may be acute, recurrent or chronic[1]. Symptoms of uveitis can include: pain, redness, photophobia, headaches, floaters and decreased visual acuity. Non-infectious uveitis may be due to an underlying inflammatory condition, an autoimmune disorder or as a result of trauma to the eye. In many cases the cause remains uncertain[2,3].

Technology description

Dexamethasone intravitreal implant (Ozurdex, Dexamethasone intravitreal implant in applicator) is a system that delivers a sustained release formulation of dexamethasone to the posterior segment of the eye. Dexamethasone is a corticosteroid which has anti-inflammatory and anti-vascular endothelial growth factor (VEGF) properties[4]. Dexamethasone intravitreal implant is intended to replace current localised treatments and is administered by intravitreal injection every 6 months. One implant contains 700µg of dexamethasone[5].

Dexamethasone intravitreal implant is licensed in the EU for the treatment of adults with macular oedema following either branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO). Common adverse effects of dexamethasone intravitreal implant are increased intraocular pressure (25%)[5], conjunctival haemorrhage and cataract.

Innovation and/or advantages

Dexamethasone intravitreal implant is a new method of local delivery of corticosteroids for posterior uveitis which may reduce the need for systemic immunosuppressive therapies.

Developer

Allergan Ltd.

Availability, launch or marketing dates, and licensing plans

In phase III trials.

NHS or Government priority area

This topic is relevant to the National Service Framework for Long Term Conditions (2005).

Relevant guidance

- NICE technology appraisal in development. Dexamethasone intravitreal implant for the treatment of macular oedema caused by retinal vein occlusion (RVO). Expected June 2011[6.]
- The College of Optometrists. Clinical management guidelines. Uveitis (anterior, acute and recurrent) version 1. 2009[7].

Clinical need and burden of disease

Uveitis can affect people of any age, but most commonly affects people between the ages of 20 and 59 years. Uveitis is a leading cause of visual impairment with an incidence of impairment of 35%, mainly attributable to posterior uveitis; and almost half of people with posterior uveitis develop visual impairment with its attendant socioeconomic impact [8,9,10,11,12].

The incidence of uveitis is estimated to be between 17 and 52.4 per 100,000 population equating to between 9,318 and 28,720 new cases per year in England and Wales[13,14,15]. Posterior and intermediate uveitis are less common than anterior uveitis and tend to be more severe. The incidence of posterior and intermediate uveitis is 1.1 and 1.5 per 100,000 respectively, equating to around 600 and 800 new cases respectively per year[14].

Inappropriate management of uveitis can lead to significant complications including increased eye pressure, glaucoma, vascular occlusions, optic neuropathy, retinal detachment, neovascularisation of the retina, optic nerve or iris, cystoid macular oedema, macular ischaemia, cataracts and permanent loss of vision.

Existing comparators and treatments

Treatment is dependent on the type of uveitis, severity and cause. Systemic corticosteroids are the mainstay of treatment for sight threatening posterior uveitis, however they are associated with significant systemic and ocular complications (such as glaucoma or cataract) if used at high doses over the longer term. Consequently, other immunosuppressive 'corticosteroid sparing' therapies may be used in an effort to reduce the corticosteroid dose required. Current options include16:

- Cyclopegics eye drops – e.g. cyclopentolate or atropine sulphate.
- Corticosteroids:
    - Topical preparations – e.g. prednisolone or rimexolone eye drops (used mainly in anterior uveitis).
    - Intraocular therapy – triamcinolone injections (unlicensed for this indication) and flucinolone implants (unlicensed for this indication).
    - Systemic therapy – e.g. oral prednisolone or parenteral therapy (in more severe cases).
- Non-steroidal anti-inflammatory drugs (NSAIDs) – e.g. diclofenac eye drops (unlicensed for this indication).
- Other immunosuppressive drugs (unlicensed for this indication) – e.g. ciclosporin, tacrolimus, azathioprine, mycophenolate mofetil or mycophenolic acid, or methotrexate.
- Biologics (unlicensed for this indication) – e.g. infliximab or adalimumab.

Efficacy and safety

Trial	NCT00333814, 206207-014; dexamethasone intravitreal implant vs sham injection; phase II/III
Sponsor	Allergan Ltd.
Status	Complete but unpublished.
Source of information	Press release[17], abstract[18], trial registry[19].
Location	EU (inc UK), USA, Canada and other countries.
Design	Randomised.
Participants	n=229; adults; chronic intermediate or posterior uveitis in at least one eye; vitreous

and schedule	haze[a] ≥ +1.5; best corrected visual acuity (BCVA) 10 to 75; receiving topical corticosteroids, non-steroidal anti-inflammatory drugs, systemic immunosuppression, systemic corticosteroids, or topical cycloplegia. Randomised to dexamethasone 350µg or 700µg implant or sham injection at day 0.
Follow-up	26 weeks.
Primary outcome	Vitreous haze score 0 at week 8.
Secondary outcomes	Time to vitreous haze score 0; time to ≥ 1-unit improvement in vitreous haze score; BCVA; central retinal thickness; quality of life; intraocular pressure (IOP), safety.
Key results	For dexamethasone implant 350µg, 700µg and sham respectively: 15 letter gain in BCVA: 39.5%, 42.9% and 6.6% (p<0.001); vitreous haze score 0 at week 8: 35.5%, 46.8% and 11.8% (p<0.001); % with IOP ≥25mmHg: 8.7%, 7.1% and 4.2% (no statistically significant difference).
Expected reporting date	Publication expected Q1 2011.
AEs	For dexamethasone implant and sham respectively: cataracts: 14% and 10.6% (p=0.769).

Estimated cost and cost impact

The cost of one dexamethasone intravitreal implant is £870 excluding VAT. There will be associated costs of administration.

Claimed or potential impact – speculative

Patients

- ☐ Reduced mortality or increased length of survival
- ☑ Reduction in associated morbidity or Improved quality of life for patients and/or carers
- ☐ Quicker, earlier or more accurate diagnosis or identification of disease
- ☐ Other:
- ☐ None identified

Services

- ☑ Increased use: related to administration and monitoring.
- ☐ Service organisation
- ☐ Staff requirements
- ☑ Decreased use: potentially reduced complications if replaces high-dose steroids.
- ☐ Other:
- ☐ None identified

Costs

- ☐ Increased unit cost compared to alternative
- ☑ Increased costs: more patients coming for treatment
- ☐ Increased costs: capital investment needed
- ☑ New costs: additional treatment option.
- ☑ Savings: potentially reduced complication if reduces high-dose systemic steroids.
- ☐ Other:

Other issues

- ☑ Clinical uncertainty or other research question identified:
  There are no data on the need for repeat injection or the rate of development of cataracts in the longer term.
- ☐ None identified

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