

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Adalimumab and dexamethasone for treating non-infectious uveitis

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of adalimumab and dexamethasone intravitreal implant within their marketing authorisations for treating non-infectious, intermediate, posterior or pan uveitis.

Background

Uveitis is an inflammation of the uveal tract of the eye, which consists of the iris, the ciliary body and the choroid. It is usually caused by an underlying autoimmune disorder or trauma to the eye. In some people the cause is unknown. Uveitis is classified according to the main location of inflammation. Anterior uveitis is inflammation of the iris. Intermediate uveitis affects the posterior part of the ciliary body and the vitreous humour. Posterior uveitis affects the back of the eye, including the retina and the choroid. Pan uveitis is inflammation of the whole of the uveal tract (front and back of the eye). Symptoms include pain and redness in the eye, blurred vision, sensitivity to light, loss of peripheral vision and headaches. One or both eyes may be affected.

Intermediate, posterior and pan uveitis are less common than anterior uveitis (they account for around 1 in 4 uveitis diagnoses¹) but are more severe and more likely to cause vision loss. Consequences of uveitis include glaucoma (increased pressure inside the eye), cataracts (cloudiness of the lens) and cystoid macular oedema (swelling of the retina). Between 1500 and 5000 people are diagnosed with non-infectious intermediate or posterior uveitis each year in England^{2,3}. There are no data on the incidence of pan uveitis in England.

Non-infectious intermediate, posterior and pan uveitis are initially treated with corticosteroids. Corticosteroids may be administered systemically (oral or parenteral), through periocular or intravitreal injections, or using intravitreal implants. Additionally, if the front of the eye is also affected, topical corticosteroids and dilating eye drops may be offered. People with severe or chronic non-infectious uveitis whose disease has not adequately responded to corticosteroid treatment, or for whom corticosteroids are not appropriate, may also be given immunosuppressive drugs such as methotrexate, ciclosporin, mycophenolate mofetil and azathioprine (either systemically or as an intravitreal injection). Immunosuppressive drugs can allow a reduction in the corticosteroid dose and associated complications. Immunosuppressive drugs may also be given when corticosteroids are contraindicated or not tolerated. If

the disease does not respond to these treatments, or if they are not tolerated, biological tumour necrosis factor (TNF)-alpha inhibitors may be used.

The technologies

Adalimumab (Humira, AbbVie) is a monoclonal antibody that inhibits the pro-inflammatory cytokine, TNF-alpha. It is administered by subcutaneous injection. Adalimumab does not currently have a marketing authorisation in the UK for treating uveitis. It has been compared with placebo in clinical trials in adults with active, non-infectious intermediate, posterior, or pan uveitis despite conventional therapy (that is, corticosteroids with or without immunosuppressives).

Dexamethasone intravitreal implant (Ozurdex, Actavis UK and Allergan) is a corticosteroid which suppresses inflammation by inhibiting the expression of pro-inflammatory mediators. It is a biodegradable implant which is administered by intravitreal injection. Dexamethasone has a marketing authorisation in the UK for treating inflammation of the posterior segment of the eye presenting as non-infectious uveitis.

Intervention(s)	Adalimumab subcutaneous injection Dexamethasone intravitreal implant
Population(s)	People with non-infectious, intermediate, posterior or pan uveitis
Comparators	The interventions listed above compared with each other where appropriate, and with: <ul style="list-style-type: none"> • Periocular or intravitreal corticosteroid injections • Intravitreal corticosteroid implants • Systemic corticosteroids • Systemic immunosuppressive therapies including azathioprine, methotrexate, cyclophosphamide, ciclosporin, chlorambucil, tacrolimus, mycophenolate mofetil and TNF-alpha inhibitors • Intravitreal methotrexate • Best supportive care (when all other treatment options have been tried).

Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • visual acuity (the affected eye) • visual acuity (both eyes) • mortality • adverse effects of treatment • health-related quality of life.
Economic analysis	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>Cost effectiveness analysis should include consideration of the benefit in the best and worst seeing eye.</p> <p>The availability and cost of biosimilars should be taken into consideration.</p>
Other considerations	<p>Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.</p>
Related NICE recommendations and NICE Pathways	None
Related National Policy	<p>NHS England:</p> <p>NHS England Clinical Commissioning Policy (July 2015) Infliximab (Remicade) and Adalimumab (Humira) as Anti-TNF Treatment Options for Adult Patients with Severe Refractory Uveitis</p> <p>NHS England (January 2014) Manual for prescribed specialised services 2013/14, chapter 12 (page 43): Adult specialist ophthalmology services</p> <p>National Service Frameworks:</p>

	<p>Older People</p> <p>Department of Health:</p> <p>Department of Health (November 2014) NHS Outcomes Framework 2015-2016. Domains 2, 4, 5.</p>
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References

- 1 NHS Choices website. [Uveitis - overview](#) [accessed November 2015]
- 2 North East Treatment Advisory Group (NETAG) 2012 [Ozurdex® dexamethasone ocular implant for uveitis](#) [accessed November 2015]
- 3 Committee for Orphan Medicinal Products 2010 [Public summary of opinion on orphan designation: Dexamethasone \(intravitreal implant\) for the treatment of non-infectious uveitis affecting the posterior segment of the eye](#) [accessed November 2015]