NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Dexamethasone intravitreal implant, sirolimus intravitreal injection and adalimumab for treating non-infectious uveitis

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of dexamethasone intravitreal implant, sirolimus intravitreal injection and adalimumab 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 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 diagnoses[1]) 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. People with pan uveitis may also be offered topical corticosteroids, to treat the front of the eye, and dilating eye drops to relieve pain. People with severe or chronic non-infectious uveitis, whose disease has not responded to corticosteroid treatment, may also be given immunosuppressive drugs such as methotrexate, ciclosporin, mycophenolate mofetil and azathioprine (either systemically or with an intravitreal injection), which 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, biological tumour necrosis factor (TNF)-alpha inhibitors may be used.

The technologies

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.

Sirolimus intravitreal injection (Opsiria, Santen) suppresses cytokine-driven T-cell proliferation and inhibits the production, signalling, and activity of many cytokines and growth factors relevant to uveitis. It is administered by intravitreal injection. Sirolimus does not currently have a marketing authorisation in the UK for the treatment of uveitis. It has been studied in a clinical trial comparing different doses of sirolimus in adults with active non-infectious posterior segment uveitis.

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).

Intervention(s)	Dexamethasone intravitreal implant Sirolimus intravitreal injection Adalimumab subcutaneous injection
Population(s)	Adults with non-infectious, intermediate, posterior or pan uveitis
Comparators	The interventions listed above compared with each other, and: • Periocular or intravitreal corticosteroid injections • Intravitreal corticosteroid implants • Systemic corticosteroids • Systemic immunosuppressive therapies including azathioprine, methotrexate, cyclophosphamide, ciclosporin, chlorambucil, tacrolimus, mycophenolate mofetil and infliximab • Intravitreal methotrexate

Outcomes	The outcome measures to be considered include: • visual acuity (the affected eye) • visual acuity (both eyes) • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. 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. Costs will be considered from an NHS and Personal Social Services perspective. Cost effectiveness analysis should include consideration of the benefit in the best and worst seeing eye. The availability and cost of biosimilars should be taken into consideration.
Other considerations	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.
Related NICE recommendations and NICE Pathways	None
Related National Policy	**NHS England:** NHS England Clinical Commissioning Policy (July 2015) Infliximab (Remicade) and Adalimumab (Humira) as Anti-TNF Treatment Options for Adult Patients with Severe Refractory Uveitis NHS England (January 2014) Manual for prescribed specialised services 2013/14, chapter 12 (page 43): Adult specialist ophthalmology services **National Service Frameworks:** Older People

	Department of Health: Department of Health (November 2014) NHS Outcomes Framework 2015-2016. Domains 2, 4, 5.

Questions for consultation

Have all relevant comparators for dexamethasone intravitreal implant, sirolimus intravitreal injection and adalimumab been included in the scope? Which treatments are considered to be established clinical practice in the NHS for treating non-infectious intermediate, posterior or pan uveitis?

- Are corticosteroids always considered as the first treatment option?
- Are there people for whom corticosteroids would not be a treatment option?
- Is infliximab routinely used to treat non-infectious intermediate, posterior or pan uveitis?
- Is triamcinolone acetonide routinely used to treat non-infectious intermediate, posterior or pan uveitis? If so, which formulation is used?

What is the expected place in the treatment pathway for adalimumab?

- Would adalimumab be used for previously untreated people?
- Would adalimumab be used instead of local treatments (such as periocular or intravitreal corticosteroid injections)? Or would it be used instead of systemic treatment?
- Would adalimumab be used on its own? Or in addition to the existing treatment options?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom dexamethasone intravitreal implant, sirolimus intravitreal injection or adalimumab are expected to be more clinically effective and cost effective or other groups that should be examined separately?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which dexamethasone

intravitreal implant, sirolimus intravitreal injection and adalimumab will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider dexamethasone intravitreal implant, sirolimus intravitreal injection and adalimumab to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of dexamethasone intravitreal implant, sirolimus intravitreal injection and adalimumab can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

NICE intends to appraise this technology through its Multiple Technology Appraisal (MTA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction)

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]