NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Dexamethasone intravitreal implant and sirolimus for treating chronic non-infectious posterior segment uveitis

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of dexamethasone intravitreal implant and sirolimus within their marketing authorisations for treating chronic non-infectious posterior segment uveitis.

Background

Uveitis is an inflammation of the uveal tract of the eye, which consists of the iris, the ciliary body and the choroid. The majority of uveitis diagnoses are non-infectious and the disease is usually caused by an underlying autoimmune disorder or trauma to the eye. However, 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. Posterior uveitis affects the back of the eye, including the retina and the choroid.

Posterior segment uveitis encompasses intermediate and posterior uveitis. It is less common than anterior uveitis, accounting for around 1 in 4 uveitis diagnoses, but is more likely to cause vision loss. Complications of posterior segment uveitis include glaucoma, cataracts and cystoid macular oedema.

Between 1500 and 5000 people are diagnosed with non-infectious posterior segment uveitis each year in England (based on data from 2010). Uveitis is more common in people aged 20 to 59, but it can also occur in children, and affects men and women equally. The condition is defined as chronic when the duration is greater than three months, or a relapse occurs less than three months after discontinuing treatment.

Chronic non-infectious posterior segment uveitis is primarily managed with corticosteroids (such as prednisolone or dexamethasone). These can be administered systemically (oral/parenteral), through periocular or intravitreal injections, or using intravitreal implants. People with severe or chronic non-infectious posterior segment uveitis may also be given immunosuppressive drugs, which allow a reduction in the corticosteroid dose and associated complications (known as the steroid sparing effect). Currently, no immunosuppressive treatments have a marketing authorisation for uveitis in the UK.

The technologies

Dexamethasone intravitreal implant (Ozurdex, Actavis UK and Allergan) is a corticosteroid which suppresses inflammation by inhibiting the expression of vascular endothelial growth factor (VEGF). 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 (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.

Intervention(s)	Dexamethasone intravitreal implant Sirolimus
Population(s)	Adults with chronic non-infectious posterior segment uveitis
Comparators	• Periocular/intravitreal corticosteroid injections • Intravitreal corticosteroid implants • Systemic corticosteroids • Immunosuppressive therapies (not licensed in the UK for this indication) in combination with corticosteroids
Outcomes	The outcome measures to be considered include: • visual acuity (the affected eye) • visual acuity (the whole person) • complications associated with uveitis • 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.
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 (January 2014) Manual for prescribed specialised services 2013/14, chapter 12 (page 43)*:* Adult specialist ophthalmology services The committee for D12 Specialist Ophthalmology Services have published: D12/S/a NHS standard contract for specialised ophthalmology (adult). Schedule 2 – the services – A. service specifications **National Service Frameworks:** Older People **Department of Health:** Department of Health (November 2013) NHS Outcomes Framework 2014-2015. Domains 2, 4, 5. **Other policy:** UK Vision Strategy Advisory Group (2013) UK vision

	strategy: setting the direction for eye health and sight loss services 2013-2018.

Questions for consultation

Have all relevant comparators for dexamethasone intravitreal implant and sirolimus been included in the scope? Which treatments are considered to be established clinical practice in the NHS for chronic non-infectious posterior segment uveitis?

- Are immunosuppressive treatments routinely used for the treatment of chronic non-infectious intermediate or posterior uveitis?
    - If so, are there any specific immunosuppressive drugs which are more commonly used to treat this condition?
    - Are immunosuppressive treatments considered only when corticosteroids have failed (i.e. are they considered as second line treatment)? Or are they used earlier, for example at diagnosis?
- Are intravitreal corticosteroid implants routinely used in clinical practice in England for this condition? If so, which implants are used?
- Should best supportive care be included as a comparator?

What do you consider to be the relevant clinical outcomes and other potential health related benefits of dexamethasone intravitreal implant and sirolimus for treating chronic non-infectious posterior uveitis?

Are there any subgroups of people in whom dexamethasone intravitreal implant and sirolimus 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 and sirolimus 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 technologies;

- 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 and sirolimus to be innovative in their potential to make a significant and substantial impact on health-related benefits and how they might improve the way that current need is met (are they 'step-changes' in the management of the condition)?

Do you consider that the use of dexamethasone intravitreal implant and sirolimus 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 these technologies 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)