NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Fluocinolone acetonide micro-insert for treating recurrent non-infectious uveitis

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of fluocinolone acetonide micro-insert within its marketing authorisation for treating recurrent non-infectious uveitis.

Background

Uveitis is inflammation of the uveal tract of the eye, which consists of the iris, the ciliary body and the choroid. Uveitis can be caused by a bacterial, viral or fungal infection or trauma to the eye, but it is more commonly associated with an underlying autoimmune disorder. The autoimmune disorder may be associated with systemic disease, such as ankylosing spondylitis, or it may affect only the eyes. One or both eyes may be affected. Symptoms of uveitis include eye pain and redness of the eye, blurred vision, sensitivity to light, temporary loss of peripheral vision and headaches. Uveitis may be acute (where the symptoms come in short episodes of about 6 weeks and may recur) or chronic (where the inflammation persists for more than 3 months possibly flaring up at times). Consequences of uveitis can include glaucoma (increased pressure inside the eye), cataracts (cloudiness of the lens), cystoid macular oedema (swelling of the retina) and permanent loss of peripheral or central vision.

Uveitis is classified according to the location of the 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 choroid at the back of the eye, and often involves the retina. Posterior segment uveitis includes both intermediate and posterior uveitis. Pan uveitis is inflammation of the whole of the uveal tract (front and back). Intermediate, posterior and pan uveitis are less common than anterior uveitis (they account for around 1 in 4 uveitis diagnoses[1]).

It is estimated that non-infectious uveitis affects less than 4.8 people per 10,000 in the European Union[2]. It is estimated that up to 26,300 people are affected by non-infectious uveitis in England each year. Uveitis affects people of any age, but most commonly affects people between the ages of 20 and 59 years[3].

There is no nationally agreed treatment pathway for recurrent non-infectious uveitis. Localised non-infectious uveitis (that is, uveitis affecting one or both eyes, whether or not it is associated with an underlying systemic autoimmune

disorder) is initially treated with corticosteroids. Corticosteroids may be administered systemically (orally or parenterally), by periocular or intravitreal injection, 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 responded adequately to corticosteroid treatment over 4 weeks, or for whom corticosteroids are not appropriate, may be offered systemic immunosuppressive drugs such as methotrexate, ciclosporin, mycophenolate mofetil and azathioprine. Methotrexate may also be given by intravitreal injection. This may allow a reduction in the corticosteroid dose and associated complications (known as the steroid-sparing effect). Immunosuppressive drugs may also be given when corticosteroids are contraindicated or not tolerated. If there is an inadequate response to immunosuppressive treatments over 3 months, or if they are not tolerated, biological tumour necrosis factor (TNF)-alpha inhibitors may be used. In rare cases, surgery (vitrectomy) may be needed to treat complications associated with recurrent or severe uveitis.

The technology

Fluocinolone acetonide micro-insert (Iluvien, Alimera Sciences) is an injectable, sustained-release non-bioerodible drug delivery system that is loaded with the corticosteroid fluocinolone acetonide. It is implanted intravitreally into the posterior segment of the eye.

Fluocinolone acetonide micro-insert does not currently have a marketing authorisation in the UK for treating uveitis. It has been compared with sham injection in clinical trials in adults with chronic (at least 1 year since diagnosis) recurrent (evidence of 2 recurrences in the 12 months preceding study entry) non-infectious posterior segment uveitis in one or both eyes with or without anterior uveitis, and with or without systemic corticosteroids or immunosuppressant at the time of study entry.

Intervention(s)	Fluocinolone acetonide micro-insert
Population(s)	Adults with recurrent non-infectious uveitis

Comparators	• Periocular or intravitreal corticosteroid injections • Intravitreal corticosteroid implants including dexamethasone intravitreal implant (in line with NICE technology appraisal 460) • Systemic corticosteroids • Systemic immunosuppressive therapies including azathioprine, methotrexate, cyclophosphamide, ciclosporin, chlorambucil, tacrolimus, mycophenolate mofetil (and mycophenolic acid) (with the exception of ciclosporin, none of the listed immunosuppressive therapies currently have a marketing authorisation in the UK for this indication) • TNF-alpha inhibitors including adalimumab (in line with NICE technology appraisal 460) • Intravitreal methotrexate • Best supportive care (when all other treatment options have been tried)
Outcomes	The outcome measures to be considered include: • recurrence of uveitis (the affected eyes) • visual acuity (the affected eyes) • visual acuity (both eyes) • need for further corticosteroid treatment • mortality • 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. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost-comparison may be carried out. 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 of any patient access schemes for the intervention or comparator technologies will be taken into account. The availability and cost of biosimilars should be taken into consideration.
Other considerations	If evidence allows, consideration will be given to subgroups according to: • Type of uveitis (acute or chronic; single incident or recurrent; posterior segment, posterior, intermediate or pan uveitis) • Baseline visual acuity • Previous treatment history 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	Related technology appraisals: Adalimumab and dexamethasone for treating non-infectious uveitis (2017) NICE technology appraisals guidance TA460. Review date July 2020. Related NICE Pathways:

	Eye conditions (2018) NICE Pathway.
Related National Policy	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 (September 2017) Manual for prescribed specialised services 2017/18, chapter 12 (page 44): Adult specialist ophthalmology services NHS England (2013) NHS standard contract for specialised ophthalmology (adult). Schedule 2 – The services – A. Service specifications. D12/S/a NHS England (2013) NHS standard contract for ophthalmic pathology service (all ages). D12/S(HSS)/b Department of Health (April 2016) NHS Outcomes Framework 2016-2017. Domains 2, 4, 5. Other policy: UK Vision Strategy Advisory Group (2013) UK Vision Strategy 2013-2018: Setting the direction for eye health and sight loss services

Questions for consultation

Have all relevant comparators for the fluocinolone acetonide micro-implant been included in the scope? Which treatments are considered to be established clinical practice in the NHS for recurrent non-infectious uveitis? How should best supportive care be defined?

Are the outcomes listed appropriate?

Are the subgroups suggested in 'other considerations' appropriate? Are there any other subgroups of people in whom the fluocinolone acetonide micro-implant is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider the fluocinolone acetonide micro-implant will fit into the existing NICE pathway, Eye conditions?

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 the fluocinolone acetonide micro-implant 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 the fluocinolone acetonide micro-implant 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 the fluocinolone acetonide micro-implant 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.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) 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).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?

- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?

- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?

- Is there any substantial new evidence for the comparator technologies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1. NHS Choices website. Uveitis – overview. Accessed July 2018.

2. European Medicines Agency (2010) Public summary of opinion on orphan designation: Fluocinolone acetonide for the treatment of non-infectious uveitis.

3. RNIB. Uveitis. Accessed July 2018.

