NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Fluocinolone acetonide intravitreal implant for treating chronic diabetic macular oedema in phakic eyes after an inadequate response to previous therapy (review of TA613)

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of fluocinolone acetonide intravitreal implant within its marketing authorisation for treating chronic diabetic macular oedema in phakic eyes after an inadequate response to previous therapy.

Background

Diabetic macular oedema (DMO) is a common complication associated with diabetic retinopathy, and is the most common cause of visual impairment in diabetes mellitus. It occurs as a result of changes in retinal blood vessels in people with diabetes. Disruption of the blood–retinal barrier allows fluid to leak from blood vessels in the central part of the retina (the macula), leading to fluid accumulation and thickening of the macula. This can lead to severe visual impairment in the affected eye.

DMO can be classed as focal, diffuse or ischaemic (although no universal definition has been agreed). The majority of vision loss occurs when DMO involves the centre of the macula. This is known as clinically significant macular oedema (CSMO), and is regarded as the threshold for treatment. DMO can be categorised as either phakic or pseudophakic. These are terms used to describe the status of a person's lens. Phakic refers to an eye with an intact natural lens, while pseudophakic refers to eyes that have had the lens extracted and replaced with an artificial (intraocular) lens.

More than 3.7 million people have been diagnosed with diabetes in England (2023),[1] and the condition is more common in people of African–Caribbean and South Asian family origin than in those of European family origin. Approximately 7% of people with diabetes may have DMO in England, of whom 39% have CSMO.[2] The prevalence of DMO is related to the duration and severity of diabetes, and to numerous risk factors including age, pregnancy, smoking, hypertension, nephropathy, obesity and high cholesterol.

Good management of diabetes and other risk factors may delay the onset and progression of DMO. This includes diet and lifestyle modification, blood pressure control and pharmacological treatments. For DMO specifically, NICE technology appraisals TA274, TA346, TA799 and TA820 recommend anti vascular endothelial growth factors (anti-VEGF) ranibizumab, aflibercept, faricimab and brolucizumab as options for treating visual impairment due to DMO if the eye has a central retinal thickness (CRT) of 400 micrometres or more at the start of treatment. For eyes with a CRT of less than 400 micrometres, laser photocoagulation may be a treatment option. In addition, bevacizumab is used outside its marketing authorisation in some NHS centres.

NICE technology appraisal TA824 recommends dexamethasone intravitreal implant as an option for DMO in adults, only if their condition has not responded well enough

to, or if they cannot have non-corticosteroid therapy. NICE technology appraisal TA301 recommends fluocinolone acetonide intravitreal implants as an option for treating chronic DMO that is insufficiently responsive to available therapies if the implant is to be used in an eye with an intraocular (pseudophakic) lens. In cases where there is no suitable treatment available, a watch-and-wait strategy may be adopted until the point where treatment with anti-VEGFs becomes suitable, or surgical intervention is required.

NICE technology appraisal TA613, a part-review of TA301, did not recommend fluocinolone acetonide intravitreal implant for treating chronic diabetic macular oedema in phakic eyes. There is new evidence that indicates that a review of TA613 will resolve a significant unmet need and supports the clinical effectiveness of fluocinolone acetonide for the full population in the marketing authorisation, including people with phakic lenses. Therefore, the decision was taken to review TA613.

The technology

Fluocinolone acetonide intravitreal implant (Iluvien, Alimera Sciences) has a marketing authorisation in the UK for treating vision impairment associated with chronic diabetic macular oedema, considered insufficiently responsive to available therapies.

Intervention(s)	Fluocinolone acetonide intravitreal implant
Population(s)	People with chronic diabetic macular oedema that is insufficiently responsive to available therapies who have phakic lenses.
Comparators	• Laser photocoagulation alone • Watch-and-wait (for people who are unsuitable for treatment with both anti-VEGFs and laser photocoagulation) The following technologies alone or in combination with laser photocoagulation: • Dexamethasone intravitreal implant • Aflibercept (only if the eye has a central retinal thickness of 400 micrometres or more) • Brolucizumab (only if the eye has a central retinal thickness of 400 micrometres or more) • Ranibizumab (only if the eye has a central retinal thickness of 400 micrometres or more) • Faricimab (only if the eye has a central retinal thickness of 400 micrometres or more) • Bevacizumab (does not currently have a marketing authorisation in the UK for this indication)

Outcomes	The outcome measures to be considered include: • best corrected visual acuity (the affected eye) • best corrected visual acuity (both eyes) • central foveal subfield thickness • central retinal thickness • contrast sensitivity • mortality • need for cataract surgery • adverse effects of treatment (including cataract formation and glaucoma) • health-related quality of life, including the effects of changes in visual acuity.
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. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The 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	**Related technology appraisals:** Dexamethasone intravitreal implant for treating diabetic macular oedema (2022) NICE technology appraisal 824.

	Brolucizumab for treating diabetic macular oedema (2022) NICE technology appraisal 820. Faricimab for treating diabetic macular oedema (2022) NICE technology appraisal 799. Fluocinolone acetonide intravitreal implant for treating chronic diabetic macular oedema in phakic eyes after an inadequate response to previous therapy (2019) NICE technology appraisal 613. Aflibercept for treating diabetic macular oedema (2015) NICE technology appraisal 346. Fluocinolone acetonide intravitreal implant for treating chronic diabetic macular oedema after an inadequate response to prior therapy (2013) NICE technology appraisal 301. Ranibizumab for treating diabetic macular oedema (2013) NICE technology appraisal 274. **Related NICE guidelines:** Type 1 diabetes in adults: diagnosis and management (2015) NICE guideline NG17. Type 2 diabetes in adults: management (2015) NICE guideline NG28. **Related NICE guidelines in development:** Diabetic retinopathy. NICE guideline. Publication expected January 2024. **Related quality standards:** Diabetes in adults (2011) NICE quality standard 6.
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2018) NHS manual for prescribed specialist services (2018/2019) Chapter 12 Adult specialist ophthalmology services

Questions for consultation

Where do you consider fluocinolone acetonide intravitreal implant will fit into the existing care pathway for treating chronic diabetic macular oedema in phakic eyes after an inadequate response to previous therapy?

Is laser photocoagulation a relevant comparator for treating chronic diabetic macular oedema in phakic eyes after an inadequate response to previous therapy?

Would fluocinolone acetonide intravitreal implant be a candidate for managed access?

Do you consider that the use of fluocinolone acetonide intravitreal implant can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

The full marketing authorisation for fluocinolone acetonide intravitreal implant is “for the treatment of vision impairment associated with chronic diabetic macular oedema,

considered insufficiently responsive to available therapies". Does this mean that fluocinolone acetonide intravitreal implant should only be used after anti-VEGFs and dexamethasone intravitreal implant, or would fluocinolone be given after anti-VEGFs only (at the same point in the treatment pathway as dexamethasone intravitreal implant)?

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

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 fluocinolone acetonide intravitreal implant is 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.

NICE is considering evaluating this technology through its cost comparison evaluation process.
Please provide comments on the appropriateness of appraising this topic through this process.
(Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

Technologies can be evaluated through the cost-comparison process if they are expected to provide similar or greater health benefits, at a similar or lower cost, compared with technologies that have been previously recommended (as an option) in published NICE guidance for the same indication. Companies can propose cost-comparison topics to NICE at any stage during topic selection and scoping. NICE will route technologies for evaluation through the cost-comparison process if it is agreed during scoping that the process is an appropriate route to establish the clinical and cost effectiveness of the technology.

NICE's health technology evaluations: the manual states the methods to be used where a cost comparison case is made.

- Is the technology likely to be similar in its clinical effectiveness and resource use to dexamethasone intravitreal implant? Or in what way is it different to dexamethasone intravitreal implant?

- Will the intervention be used in the same place in the treatment pathway as the dexamethasone intravitreal implant? Have there been any major changes to the treatment pathway recently? If so, please describe.
- Will the intervention be used to treat the same population as the dexamethasone intravitreal implant?
- Overall is the technology likely to offer similar or improved health benefits compared with dexamethasone intravitreal implant?
- Is this technology suitable for a cost-comparison with dexamethasone intravitreal implant?

References

1. National Diabetes Audit (NDA) 2022-23 quarterly report for England, Integrated Care Board (ICB), Primary Care Network (PCN) and GP practice. (2023) NHS Digital. Accessed July 2023.

2. Minassian DC, Owens DR, Reidy A. Prevalence of diabetic macular oedema and related health and social care resource use in England. British Journal of Ophthalmology 2012; 96:345-349.