Appendix B

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Lifitegrast for treating dry eye disease

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of lifitegrast within its marketing authorisation for treating dry eye disease.

Background

Dry eye disease (keratoconjunctivitis sicca) is chronic inflammation of the eyes caused by reduced tear production or excessive tear evaporation. It can affect one or both eyes. Dry eye disease can be attributed to a variety of factors, including dry or air-conditioned environments, auto-immune diseases (such as Sjogren's syndrome, rheumatoid arthritis and lupus), and the adverse effects of some medications. Symptoms include discomfort, irritation and redness in the eyes, blurred vision, and a sensation of grittiness or a foreign body in the eye. In severe cases, it can cause damage to the surface of the eye, irreversible loss of visual acuity and corneal perforation. Dry eye disease can be painful and can have serious effects on quality of life and vision-based activities such as driving and reading.

Dry eye disease may be classified as aqueous-deficient (in which the lacrimal glands fail to produce enough of the watery component of tears to maintain a healthy eye surface) or evaporative (in which the Meibomian glands in the eyelids do not produce enough of the lipid or oily part of tears that slows evaporation). The severity of dry eye disease can be measured using the Dry Eye Workshop (DEWS) classification system, which describes 4 levels of disease severity, ranging from 1 (least severe) to 4 (most severe).

The prevalence of dry eye disease is difficult to estimate because there is no defined diagnostic test. Although it can affect people of any age, it is more prevalent in women and in older people. It is reported that 15 to 33% of people aged 65 years or over have dry eye disease[1]. This is likely to be an underestimate of the true prevalence because people with mild symptoms may not report the condition to their doctor.

There is no cure for dry eye disease. Management aims to relieve discomfort and prevent damage to the cornea at the front of the eye. Current treatment options for dry eye disease depend on the cause and severity of the symptoms. Lubrication treatments such as artificial tears and eye ointments may be used for the treatment of mild to moderate dry eye disease along with advice on lessening the impact of environmental factors that exacerbate dry eyes, for example, by using room humidifiers and re-assessing the use of some medications. In moderate cases, additional treatment options include anti-inflammatory agents (including acute use of topical corticosteroids such

as betamethasone, dexamethasone, fluorometholone or prednisolone) and specialised eyewear. In severe cases, NICE's technology appraisal guidance on ciclosporin for dry eye disease recommends topical ciclosporin as an option for treating severe keratitis in adult patients with dry eye disease that has not improved despite treatment with tear substitutes. In people with severe, aqueous-deficient dry eye disease, punctal plugging (in which tear ducts are blocked with dissolvable collagen) can be undertaken. In very severe cases, autologous serum tears or surgery may be considered.

The technology

Lifitegrast (brand name unknown, Shire) is a lymphocyte function-associated antigen-1 (LFA-1) antagonist. It reduces the inflammation associated with dry eye disease. It is administered as an eye drop.

Lifitegrast does not currently have a marketing authorisation in the UK for treating dry eye disease. It has been studied in clinical trials compared with placebo in adults with self-reported dry eye disease, who have used over-the-counter artificial tears within the past 30 days.

Intervention(s)	Lifitegrast
Population(s)	People with dry eye disease
Comparators	Established clinical management without lifitegrast including: • artificial tears, eye ointments, acute use of topical corticosteroids • topical ciclosporin for severe keratitis, in line with NICE guidance on ciclosporin for dry eye disease.
Outcomes	The outcome measures to be considered include: • eye pain and discomfort • symptoms of dry eye disease (including photosensitivity, ability to open eyes, visual acuity and ability to concentrate) • adverse effects of treatment • health-related quality of life.

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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.
Other considerations	If the evidence allows, consideration will be given to subgroups according to: • **T**he severity of the dry eye disease (mild, moderate or severe) • Sjogren's syndrome 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: Ciclosporin for treating dry eye disease that has not improved despite treatment with artificial tears (2015). NICE Technology Appraisal 369. Review date December 2018. Related NICE Pathways: Eye conditions (2017) NICE pathway
Related National Policy	NHS England: NHS England (2013) 2013/14 NHS standard contract human T-cell lymphotropic virus type 1 and 2 (all ages). B07/S/d, appendix 1, section 6 (page 25) NHS England (2016) Clinical commissioning policy: rituximab for the treatment of primary Sjogren's

	Syndrome (PSS) in adults. Reference 05527s, (page 5) Department of Health: Department of Health (2016) NHS outcomes framework 2016 to 2017: Domains 2, 4, 5. National Service Frameworks: Older People - archived

Questions for consultation

Is the population defined appropriately in the scope?

- Would lifitegrast be used to treat mild, moderate and/or severe dry eye disease?
- Would lifitegrast be used to treat dry eye disease associated with Sjogren's syndrome?

Where do you consider lifitegrast will fit into the current treatment pathway for dry eye disease?

- Would lifitegrast be used for untreated dry eye disease?
- Would lifitegrast be used on its own or in addition to the existing treatment options?

Have all relevant comparators for lifitegrast been included in the scope?

- Which treatments are considered to be established clinical practice in the NHS for dry eye disease?
- Should autologous serum tears or surgery be included as comparators?
- Are there other comparators that should be included?

Are the outcomes listed appropriate?

- Should damage to the eye that leads to visual impairment or the need for surgery be included as outcomes?

Are the subgroups suggested in 'other considerations' appropriate?

- Are there any other subgroups of people in whom lifitegrast is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider lifitegrast 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 lifitegrast 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 lifitegrast 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 lifitegrast 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. We welcome comments on the appropriateness and suitability of the cost comparison methodology to 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 technology that has not been considered? Are there any important ongoing trials reporting in the next year?

References

[1] The epidemiology of dry eye disease: Report of the Epidemiology Subcommittee of the International Dry Eye Workshop (2007). The Ocular Surface 5: 93-107