

## Commissioning guidance:

Commissioners may wish to bear the following in mind when considering ocular lubricants for the treatment of dry eye diseases:

- Treatments for dry or sore/tired eyes are included in the NHS England guidance on conditions for which over the counter (OTC) items should not be routinely prescribed in primary care.
- The NHS England guidance lists a number of general exceptions where patients should continue to have their treatments prescribed. These include (but are not limited to): the need to prescribe OTC products to treat an adverse effect or symptom of a more complex illness, use of OTC products in long-term chronic conditions, or to treat more complex forms of a minor illness, and situations where the prescriber believes that exceptional circumstances exist that warrant deviation from the recommendation to self-care.
- Self-care should form the mainstay of treatment in uncomplicated dry eye disease that does not require immediate referral to secondary care. All-Wales Medicines Strategy Group (AWMSG) guidance incorporating self-care measures is shown below.
- The systematic review evidence considered by MTRAC suggested that whilst ocular lubricants are efficacious in treating the symptoms of dry eye, there is insufficiently robust evidence to differentiate between products.
- Patients presenting with dry eyes, for whom non-pharmacological measures are insufficient, are advised to consult the local pharmacy or optometrist for assistance in selecting an appropriate OTC lubricant product. CCGs may wish to ensure that information and resources are available to surgeries to enable signposting to appropriate services.
- CCGs may wish to develop a local policy and implementation plan for the treatment of dry eyes, given the multiplicity of products available, the variations in costs of different products, and the potential population that may qualify for the exceptional circumstances quoted by NHS England.

*MTRAC was asked to review ocular lubricants as a potential commissioning issue in primary care.*

## Description of technology

This MTRAC guidance covers ocular lubricants or artificial tear replacements acting to supplement or augment the tear film. The products considered were those listed in the [Monthly Index of Medical Specialities \(MIMS\)](#)<sup>4</sup> in May 2018.

The products vary in terms of viscosity, electrolytes, pH, osmolarity and the presence or type of preservative used.<sup>1</sup> Constituents include: cellulose ethers, carbomers, polyvinyl alcohol (PVA), lipid-based formulations, sodium hyaluronate, N-acetylcysteine, silicone, soybean oil and liquid paraffin (for use mainly at night).<sup>2</sup>

Dosing advice from product information leaflets is consistently described as 1 or 2 drops, three or four times daily, or as often as required. Transient blurring of vision may occur after instillation of the drops.<sup>3</sup> The use of preservatives to avoid bacterial contamination and buffers to maintain pH can cause an issue in some patients. Repeated use of preservative-containing eye drops (especially benzalkonium chloride) is associated with ocular allergies and toxicities.<sup>2</sup> Preservative-free formulations of most products are available, especially where higher frequency dosing is needed, and there is existing corneal surface damage.<sup>4</sup>

## Background

Dry eye disease is a multifactorial condition that occurs where there is inadequate tear volume or function,

resulting in an unstable tear film and ocular surface disease<sup>5</sup>. It can arise as a result of systemic disease (e.g. Sjögren's syndrome) or as a result of, for example, contact lens wear, eye surgery, side effect from medication for another condition e.g. glaucoma treatment, or dry environment or computer use.<sup>6</sup>

The main types of dry eye syndromes are<sup>7</sup>:

- Aqueous insufficiency (due to reduced aqueous secretion from lacrimal [tear producing] glands)
- Evaporative dry eye is most commonly the result of dysfunctional mucin production.

Typical symptoms of dry eye syndromes are feelings of dryness, grittiness or soreness in both eyes, which worsens through the day, and watering of the eyes, particularly when exposed to wind.

The prevalence of dry eye disease ranges from 8 to 34%, depending on the criteria used. It becomes more common with increasing age, and affects more women than men.<sup>7</sup>

AWMSG<sup>8</sup> guidance advises that self-care forms the mainstay of treatment including:

- Good eyelid hygiene, including warm compresses and gentle massage where Meibomian glands are involved
- A limit on the use of contact lens wear if irritant
- Stopping smoking
- Use of a humidifier to moisten ambient air
- Avoidance of prolonged staring - at computer screens, for example, and taking frequent breaks
- Avoidance of makeup

If pharmacological treatment is required, hypromellose, carbomers or PVA are first-line treatment options<sup>8</sup>. If symptoms have not improved after 6 to 8 weeks, second-line treatment options are hydroxypropyl guar, carmellose sodium or sodium hyaluronate. Liquid paraffin lubricants should not be used with contact lenses, and are best used at night, because they can be uncomfortable and blur vision.<sup>8</sup> These measures are a small part of the overall diagnosis and treatment of this complex condition. Further details and algorithms for diagnosis and management can be found [here](#)<sup>5</sup>.

### **Clinical evidence for efficacy and safety**

MTRAC considered systematic reviews that evaluated ocular lubricants compared with placebo or another ocular lubricant. A 2016 Cochrane review of OTC treatments for dry eye included 43 randomised controlled trials (3,497 participants with dry eye) that compared OTC artificial tears with another class of OTC artificial tears, placebo, or no treatment.<sup>2</sup> There was considerable heterogeneity between the trials relating to types of diagnostic criteria, interventions, comparisons and outcomes, limiting the capacity to carry out meta-analyses of the data. In general, the review found that most OTC artificial tears may have similar efficacies, but that there was uncertainty due to the inconsistencies in study designs, and reporting of trial results. There was insufficient systematic review evidence available to draw conclusions about the effectiveness of individual formulations.

An earlier review in 2009<sup>9</sup>, focussed on changes in corneal surface damage, using Rose Bengal staining to assess differences in the efficacy of different classes of ocular lubricant. The review found no difference between the author-defined 'traditional artificial tears' (saline, hydroxyethylcellulose, hypromellose, hypromellose with dextran, PVA) and carbomer gels ( $p = 0.361$ ), but there was a difference between traditional artificial tears and hyaluronic acid-based products ( $p = 0.006$ ) in favour of hyaluronate.<sup>9</sup> There was a smaller but still just statistically significant difference between hyaluronic acid based products and carbomer gels ( $p = 0.037$ ). The authors also noted, however, the differences in patient populations included in the trials; studies assessing the effects of hyaluronic acid-based products had higher baseline scores suggesting use of patients with more severe dry eye scores and the potential to show greater improvement.<sup>9</sup> This suggests the results may be subject to selection bias.

A search for comparisons of individual products found two systematic reviews of sufficient quality evaluating 1) sodium hyaluronate-containing preparations vs. placebo or active comparators<sup>10</sup>, and 2) comparisons of carboxymethylcellulose (CMC) vs. sodium hyaluronate.<sup>11</sup>

The first systematic review identified 18 eligible clinical trials, of which 10 yielded data for meta-analysis. Overall, the review found no consistently nor clinically

significant superiority of one treatment over another. Slight differences between treatments were found for outcome measures such as tear-film break up time (TBUT) and the Schirmer tear volume test (SHI) but the differences between the treatments were small, within the expected variability for both outcome measures, and unlikely to be clinically significant.

The second systematic review involving CMC vs. sodium hyaluronate-containing preparations found five trials (total  $n = 251$ ) that all had TBUT as a common outcome measure. Meta-analysis of data from the trials found weak evidence that CMC had a significantly greater improvement in TBUT than hyaluronate, with a high degree of heterogeneity between the trials.

### **Adverse events**

Adverse events were reported as part of the Cochrane review, and included blurred vision, ocular discomfort, sticky eyes, grittiness or foreign body sensation; data were available from 30 of the 43 trials included.<sup>2</sup>

### **Potential cost impact**

According to manufacturer estimates adopted by [NICE](#), about 2.28% of the adult population have dry eye disease. In the West Midlands, this equates to 106,367 adults who may require treatment.

In the year April 2017 to March 2018, in four subscriber CCGs, the total cost of ocular lubricants was ca. £1.6 million. This is an increase of 8% on the spending for the previous year. The impact of the NHS England guidance (published March 2018) on OTC products will not yet be apparent in the data.

### **References**

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3. [Tear deficiency, ocular lubricants, and astringents. British National Formulary 2018](#)
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7. The management of dry eye. *BMJ* 2016 [www.bmj.com/content/353/bmj.i2333](http://www.bmj.com/content/353/bmj.i2333)
8. [Dry Eye Syndrome Guidance. All Wales Medicines Strategy Group 2016](#)
9. Doughty MJ, Glavin S. Efficacy of different dry eye treatments with artificial tears or ocular lubricants: a systematic review. *Ophthalmic Physiol Opt* 2009; 29(6):573-583.
10. Ang BCH et al. Sodium Hyaluronate in the Treatment of Dry Eye Syndrome: A Systematic Review and Meta-Analysis. *Sci Rep* 2017; 7(1):9013.
11. Song JK et al. Efficacy of Carboxymethylcellulose and Hyaluronate in Dry Eye Disease: A Systematic Review and Meta-Analysis. *Korean J Fam Med* 2017; 38(1):2-7.

**WARNING:** This sheet should be read in conjunction with the Summaries of Product Characteristics

This guidance is based upon the published information available in English at the time the drug was considered. It remains open to review in the event of significant new evidence emerging.

