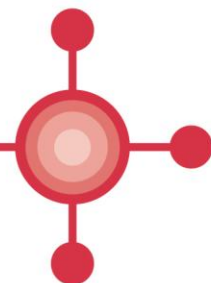


All Wales Medicines Strategy Group

Grŵp Strategaeth Meddyginiaethau Cymru Gyfan



Dry Eye Syndrome Guidance

December 2016

This document has been prepared by a multiprofessional collaborative group, with support from the All Wales Prescribing Advisory Group (AWPAG) and the All Wales Therapeutics and Toxicology Centre (AWTTC), and has subsequently been endorsed by the All Wales Medicines Strategy Group (AWMSG).

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CONTENTS

1.0 SUMMARY 2

2.0 DRY EYE SYNDROME 3

 2.1 Evaporative dry eye 3

 2.2 Aqueous tear-deficient dry eye 3

3.0 URGENT REFERRAL 4

4.0 MANAGEMENT OF DRY EYE SYNDROME 4

 4.1 Patient self-management 4

 4.1.1 Good eyelid hygiene..... 5

 4.1.2 Applying eye drops..... 5

 4.2 Pharmacological management: first-line and second-line treatment options 6

 4.2.1 Preservative toxicity from eye lubricants..... 7

 4.2.2 Eye drop dispensers..... 7

 4.3 Referral to an optometrist 8

 4.4 Pharmacological management: ophthalmologist-initiation only 8

5.0 FURTHER RESOURCES..... 9

REFERENCES.....10

1.0 SUMMARY

Dry eye syndrome is a chronic condition, loosely categorised as:

- Evaporative dry eye (EDE) – the most common form of dry eye syndrome, often associated with increased evaporation and an unstable tear film¹. Meibomian gland dysfunction (MGD) is thought to be the leading cause of EDE^{2,3}.
- Aqueous tear-deficient dry eye (ADDE) – refers chiefly to a failure of lacrimal tear secretion¹.

People with dry eye syndrome typically present with: feelings of dryness, grittiness, or soreness in both eyes, which worsen through the day; watering of the eyes, particularly when exposed to wind; no abnormalities on examination⁴.

By taking suitable precautions, patients can lessen the symptoms of dry eye syndrome and, in mild cases, this may be sufficient to avoid the need for treatment. Precautions include:

- maintaining good eyelid hygiene. Eyelids should be cleaned in a stepwise manner twice-daily initially, then once-daily as symptoms improve⁵:
 - apply a warm compress to closed eyelids for 5–10 minutes;
 - massage closed eyelids in a circular motion across the length of each lid;
 - to clean the eyelid, wet a cloth/cotton wool pad with cleaner and wipe along the eyelid margins;
- limiting contact lens use to shorter periods, especially if these cause irritation⁴;
- stopping smoking⁴;
- using a humidifier to moisten ambient air⁴, and avoiding prolonged periods in air-conditioned environments;
- if using a computer for long periods, placing the monitor at or below eye level, avoiding staring at the screen, and taking frequent breaks⁴;
- avoiding makeup⁵.

All dry eye syndrome treatments should be offered in conjunction with advice on appropriate self-management.

Table 1. Summary of prioritised treatment options for management of dry eye syndrome

First-line treatment*		
Hypromellose	Carbomers	Polyvinyl alcohol
<i>Insert health board choice(s):</i>	<i>Insert health board choice(s):</i>	<i>Insert health board choice(s):</i>
Appropriate for the majority with mild dry eye syndrome. May need to be instilled at 60-minute intervals until symptoms improve, then at a decreased frequency	Require less frequent administration but may be less well tolerated than hypromellose	
+/- liquid paraffin at night		
If failure to improve symptoms after 6 to 8 weeks, progress to second-line treatment options		
Second-line treatment*		
Hydroxypropyl guar	Carmellose sodium	Sodium hyaluronate
<i>Insert health board choice(s):</i>	<i>Insert health board choice(s):</i>	<i>Insert health board choice(s):</i>
		No evidence to support differences in efficacy between different strengths, although the different dropper systems may affect patient acceptability ⁶
+/- liquid paraffin at night		
If failure to improve symptoms after 6 to 8 weeks, refer for specialist input		

To insert health board choices, please request a Word version of this document from awttc@wales.nhs.uk.

* Combination treatment options are available; these should be considered on an individual patient basis.

2.0 DRY EYE SYNDROME

Dry eye syndrome is a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface¹.

Dry eye syndrome is a common condition, having an increasing prevalence with increasing age. It is about 50% more common in women than in men⁴. People with dry eye syndrome typically present with⁴:

- feelings of dryness, grittiness, or soreness in both eyes, which worsen through the day;
- watering of the eyes, particularly when exposed to wind;
- no abnormalities on examination.

Less commonly, people present with a complication of dry eye syndrome, for example conjunctivitis⁴.

Dry eye syndrome is loosely categorised as evaporative dry eye (EDE) or aqueous tear-deficient dry eye (ADDE). Both of these conditions may be seen in patients with dry eye syndrome⁷.

2.1 Evaporative dry eye

EDE is the most common form of dry eye syndrome and is often associated with deficiency of the lipid layer of the tear film, leading to increased evaporation and an unstable tear film¹. As it is an evaporative condition, symptoms get worse throughout the day.

Meibomian gland dysfunction (MGD) is thought to be the leading cause of EDE and may also have some association with ADDE³; it is important to note that the clinical symptoms of MGD overlap with those of other types of EDE, as well as those of ADDE^{8,9}. MGD is a chronic abnormality of the meibomian glands, commonly characterised by terminal duct obstruction and/or qualitative/quantitative changes in the glandular secretion. It may result in alteration of the tear film, symptoms of eye irritation, clinically apparent inflammation, and ocular surface disease⁸.

Posterior blepharitis is a term often used interchangeably with MGD, but they are not synonymous; posterior blepharitis affects the inner edge of the eyelid and is only one possible cause of MGD⁸.

When the lipid layer is poor, the tear film becomes particularly vulnerable to:

- environmental factors, such as windy conditions and low humidity, e.g. air conditioning¹⁰;
- low blink rate/wide eyelid aperture (e.g. prolonged reading/use of a computer)^{4,11}. Patients may complain of intermittent blurring of vision or discomfort after short periods of reading¹⁰.

2.2 Aqueous tear-deficient dry eye

ADDE refers chiefly to a failure of lacrimal tear secretion. However, a failure of water secretion by the conjunctiva could also contribute to ADDE¹. Patients often complain of a worsening of their symptoms towards the evening¹⁰.

ADDE can be associated with non-autoimmune causes, including some medications¹², lacrimal deficiency, lacrimal gland duct obstruction, and reflex block^{1,10}. ADDE can also be associated with autoimmune diseases, e.g. rheumatoid arthritis, Sjögren's syndrome and systemic lupus erythematosus¹⁰.

3.0 URGENT REFERRAL

In the majority of cases, dry eye syndrome can be managed with appropriate patient self-management and pharmacological treatment options, details of which can be found in section 4. However, symptoms such as moderate to severe eye pain or photophobia, marked redness in one eye and reduced visual acuity could be due to other potential severe eye conditions such as acute glaucoma, keratitis and iritis. The potential for sight-threatening complications from these is high and so same-day referral should be made⁴. In most circumstances, it is usually appropriate to advise people to see an optometrist before an ophthalmologist⁴. Those people who have an eye problem requiring urgent attention can be referred by a healthcare professional to an optometrist to have an eye examination at an [Eye Health Examination Wales \(EHEW\) accredited optometrist practice](#).

Associated diseases of dry eye syndrome require other specialist management⁴ (e.g. rheumatology for Sjögren's syndrome, or oculoplastics for eyelid deformities). Blepharokeratitis in children is a serious and potentially blinding disease. Urgent referral to an ophthalmologist is required for children with any corneal change (e.g. staining or vascularisation).

4.0 MANAGEMENT OF DRY EYE SYNDROME

Those people with an apparent eye-related problem can be referred by a healthcare professional to have a free eye health examination at an [EHEW accredited optometrist practice](#), details of which can be found in section 4.3.

Contact lens wearers presenting with dry eye syndrome should be encouraged to attend their prescribing optometrist¹⁰, as symptoms may be managed by changing the lens replacement frequency or material.

As MGD and posterior blepharitis are chronic conditions, it is important that patients are aware that they can be prone to exacerbations^{5,8}. As a result, these conditions require long-term management and likely treatment, which can lessen the impact of the condition but will not cure it. Ongoing active patient involvement and self-management are therefore essential.

Disease severity should not be based upon symptoms alone as they can be a relatively poor indicator. Currently, there is no gold standard test for determining dry eye syndrome severity².

4.1 Patient self-management

Advise patients that by taking suitable precautions, the symptoms of dry eye syndrome can be lessened and, in mild cases, this may be sufficient to avoid the need for treatment⁴. These precautions include:

- maintaining good eyelid hygiene to control posterior blepharitis or MGD⁸ (see section 4.1.1);
- limiting contact lens use to shorter periods, especially if these cause irritation⁴;
- being aware of the effect of cigarette smoke on dry eye syndrome, and stopping smoking⁴. Patients can be directed to call 'Stop Smoking Wales' free on 0800 085 2219;
- using a humidifier to moisten ambient air⁴, and avoiding prolonged periods in air-conditioned environments;
- if using a computer for long periods, placing their monitor at or below eye level, avoiding staring at the screen, and taking frequent breaks⁴.

There is some evidence to suggest that eating a healthy, balanced diet high in omega-3 fatty acids (e.g. oily fish, various nuts and seeds, vegetable oils, soya and soya products) can help improve dry eye syndrome¹¹. Some groups of people should be careful about the amount of oily fish in their diet, or omega-3 supplements (e.g. pregnant women), so the patient should check with their doctor or pharmacist¹³.

4.1.1 Good eyelid hygiene

- Some patients may find it difficult to perform eyelid hygiene properly; therefore, detailed instruction should be given to all patients (further patient information can be found in section 5.0). Advise the patient that their eyelids should be cleaned in a stepwise manner twice-daily initially, then once-daily as symptoms improve⁵:
 - Advise the patient to apply a warm compress to closed eyelids for 5–10 minutes. The compress can be a clean cloth warmed in hot water⁵. The compress should not be too hot, as it may burn the skin, although current research indicates that compression temperatures of less than 40°C applied for less than 5 minutes are ineffective¹⁴. A warm compress will not retain sufficient heat, so patients should be reminded to reheat frequently. Commercial devices are available and may be used instead¹⁵. Patients should be informed that these will need to be self-funded.
 - Following application of the compress, the patient should massage the closed eyelid in a circular motion across the length of each lid: this aids expression of meibomian gland secretions^{5,11}.
 - To clean the eyelid, the patient should wet a cloth or cotton wool pad with cleanser (for example, baby shampoo diluted 1:10 with warm water) and wipe along the eyelid margins. The overall aim is gentle mechanical washing, which clears the debris and therefore reduces inflammation of the eyelid margin. There are commercial eyelid cleansing solutions available⁵.
- Advise the patient to avoid eye make-up, especially eyeliner. If this is not possible, advise the patient to use one that washes off easily⁵ and to replace make-up products regularly.
- Contact lenses should not be worn during the eyelid hygiene procedure. Use should be limited in dry eye syndrome, especially if they cause irritation⁴.
- If there are signs of staphylococcal infection, eyelid scrubs/wipes can be used to wipe away the scales on the lashes[†].

4.1.2 Applying eye drops

Patients should be advised to:

- wash their hands before and after using eye drops¹⁶;
- administer eye drops on the side of the eye nearest the ear by pulling down the eyelid to form a sac¹⁶. To reduce contamination of the bottle, patients should avoid touching the ocular surface with the nozzle⁷.

If dry eye syndrome products are used in conjunction with other eye preparations, a time interval of around 5 minutes between applications should be advised, with the more viscous product being applied last⁷.

[†]Commercial devices are available which reduce scurf and bacterial debris and improve the overall health of the eyelid. Scurf and bacterial debris are the main causes of inflammatory eyelid disease.

4.2 Pharmacological management: first-line and second-line treatment options

Generic treatments, including lubricants, oily tear drops and eye ointments, selected in a prioritised manner may be prescribed to people with dry eye syndrome. These generic eye treatments do not however treat the root cause of MGD as they do not loosen blockages in the meibomian glands⁹. Therefore, eye drops should be used in conjunction with self-management methods.

A dry eye syndrome treatment should be tried for 4–6 weeks before assessing benefit¹⁰. Consider trying patients on treatments in a prioritised manner, as suggested within Table 2; this will allow selection and confirmation of the most appropriate dry eye syndrome treatment option for the patient. The patient should be encouraged to provide feedback on how their symptoms are progressing. This will facilitate a selection based upon their individual needs, thus satisfying the core elements of prudent healthcare, whilst optimising use of available resources.

Table 2. Prioritised treatment options for the management of dry eye syndrome[‡]

First-line treatment [§]		
Hypromellose	Carbomers	Polyvinyl alcohol
<i>Insert health board choice(s):</i>	<i>Insert health board choice(s):</i>	<i>Insert health board choice(s):</i>
If failure to improve symptoms after 6 to 8 weeks, progress to second-line treatment options		
Second-line treatment [§]		
Hydroxypropyl guar	Carmellose sodium	Sodium hyaluronate
<i>Insert health board choice(s):</i>	<i>Insert health board choice(s):</i>	<i>Insert health board choice(s):</i>
If failure to improve symptoms after 6 to 8 weeks, refer for specialist input		
Ophthalmologist-initiation only		
Acetylcysteine 5% eye drops		Ciclosporin 1 mg/ml eye drops

To insert health board choices, please request a Word version of this document from awttc@wales.nhs.

The majority of patients in primary care can be managed with first-line agents. Hypromellose is the traditional choice of treatment for tear deficiency and should be appropriate for the majority of patients presenting with mild dry eye syndrome. Hypromellose eye drops may need to be instilled frequently (at 60-minute intervals)¹⁷ initially until symptoms improve, then applied at a decreased frequency. Once symptoms are controlled, if the patient's maintenance regimen is greater than 4–6 times a day, a review of the dry eye syndrome treatment may be needed with consideration of alternative or additional options¹⁸.

Dry eye syndrome treatments containing carbomers or polyvinyl alcohol require less frequent administration but may be less well tolerated than hypromellose². A balance of longer retention time versus impact on vision should be addressed. Formulations containing wetting agents to retain moisture may be effective in managing symptoms. Within a first-line regimen, using both hypromellose and carbomers may be appropriate to try before progressing to second-line treatment options.

Patients who struggle to apply their eye drops (e.g. as a result of arthritis) may benefit from changing to a different type of product; some dispensers may be easier to use

[‡]With the exception of acetylcysteine and ciclosporin, most treatment options are available without a prescription.

[§]Combination treatment options are available; these should be considered on an individual patient basis.

than others⁷. A large range of tear replacement and ocular lubricant products for the treatment of dry eye syndrome are available (see the [British National Formulary](#)).

Consider adding the ocular lubricant liquid paraffin within first-line and second-line treatment regimens, if appropriate. Patients with ADDE often benefit from the use of a liquid paraffin ointment at night. However, eye ointments containing paraffin may be uncomfortable and blur vision, so they should not be used during the day and never with contact lenses⁴. Transient blurring can also be a problem with more viscous drops¹⁰.

Lubricants containing sodium hyaluronate, hydroxypropyl guar, or lipid-containing drops may be used for moderate to severe dry eye syndrome following a suitable trial of first-line agents. There is no evidence to support any differences in efficacy between the different strengths available for sodium hyaluronate, although the different delivery systems of the products may affect patient acceptability⁶. Some sodium hyaluronate delivery systems give longer in-use expiry dates⁶. If required, these should be considered on an individual patient basis.

Consider topical antibiotics (e.g. chloramphenicol ointment) if there are clear signs of staphylococcal infection. Antibiotics should usually be reserved for second-line use when eyelid hygiene alone has proved ineffective⁵.

If clinically appropriate, medications that exacerbate dry eye syndrome should be reviewed, e.g. topical and systemic antihistamines, tricyclic antidepressants, selective serotonin reuptake inhibitors¹², diuretics, beta-blockers, isotretinoin, and possibly anxiolytics and anti-psychotics¹⁹.

4.2.1 Preservative toxicity from eye lubricants

In a patient with mild dry eye syndrome, preserved drops are often well tolerated when used 4–6 times a day or less^{1,19}. However, for patients with moderate to severe dry eye syndrome, the absence of preservatives in the ocular lubricant is of more critical importance than the particular polymeric agent used¹. The ocular surface inflammation associated with dry eye syndrome is exacerbated by preserved lubricants and, if patients have more than one eye condition for which they are using eye treatments, their potential exposure to preservatives is increased¹⁹. The preservative that most often causes eye irritation is benzalkonium chloride (BAK)⁴.

Preservative-free formulations are appropriate for patients with:

- true preservative allergy¹⁹;
- evidence of epithelial toxicity from preservatives¹⁹;
- severe dry eye syndrome with ocular surface disease and impairment of lacrimal gland secretion¹;
- chronic eye disease who are on multiple, preserved topical medications¹;
- a prolonged daily frequency of administration greater than 6 times a day⁴;
- soft²⁰ or hybrid contact lens wearers.

Hypromellose, carbomers, polyvinyl alcohol, sodium chloride, carmellose sodium, hydroxyethylcellulose, and sodium hyaluronate are available without preservatives⁴.

4.2.2 Eye drop dispensers

It is important that patients are able to use their eye drops regularly. For those patients who encounter difficulties in administering their eye drops, consider recommending the use of a drop-aid device to aid self-instillation of their eye drops. These are particularly useful for the elderly, visually impaired, arthritic or otherwise physically limited patients. If dexterity is an issue, individual consultation with the patient about use should be considered.

4.3 Referral to an optometrist

Referral to an optometrist should be made, or advice from an optometrist should be obtained, if** :

- symptoms are not suitably controlled despite appropriate treatment for about 4 weeks;
- diagnosis requires specialist assessment (apply a lower threshold for obtaining specialist advice for younger people);
- vision deteriorates⁴.

The EHEW accredited optometrist scheme is available in most parts of Wales. An optometrist can assess people with dry eye syndrome and advise on treatment. A list of EHEW accredited optometrist practices, as well as details on how optometrists and ophthalmic medical practitioners can register for EHEW accreditation, is available [here](#). Some optometrist practices offer private specialist dry eye syndrome clinics of varying service levels⁷. Patients should be informed that it is likely that these clinics will need to be self-funded.

Referral to an optometrist and, where appropriate, an ophthalmologist is to be considered in patients with signs of corneal damage such as ulcers, or other secondary complications of dry eye syndrome (e.g. vascularisation, melt, infection).

4.4 Pharmacological management: ophthalmologist-initiation only

Ulcers or other signs of corneal damage⁴, or secondary complications (vascularisation, corneal scarring, melt, or infections)²¹ should be investigated by an ophthalmologist prior to prescribing the ophthalmologist-initiation only treatments stated in Table 2: acetylcysteine eye drops or ciclosporin eye drops⁶.

Acetylcysteine eye drops may be considered for people with visible strands of mucus. The patient should be informed that these may sting briefly when first administered⁴.

Ciclosporin ophthalmic emulsion is recommended by the National Institute for Health and Care Excellence (NICE) as an option, within its marketing authorisation, for treating severe keratitis in adult patients with dry eye disease that has not improved despite treatment with tear substitutes²². Response to treatment should be reassessed at least every 6 months²³. These reviews and any advice to discontinue therapy should be carried out by a corneal/external eye disease specialist in secondary care⁶.

** Consider referral to an optometrist if a preservative-free topical eye product is required for more than 4 weeks⁴.

5.0 FURTHER RESOURCES

Further information around the diagnosis and management of dry eye syndrome is available via:

- [Clinical Knowledge Summary \(CKS\) NICE – Dry eye syndrome](#)
- [Tear Film & Ocular Surface Society – MGD Report](#)
- [Tear Film & Ocular Surface Society – Report of the International Dry Eye Workshop \(DEWS\)](#)
- [The College of Optometrists – Dry Eye \(Keratoconjunctivitis Sicca, KCS\)](#)

Useful patient information is available at:

- [NHS Choices](#) – Information on dry eye syndrome and self-help techniques, including eyelid hygiene
- [Patient Dry eye information leaflet](#) (2014) – Information on how dry eye syndrome is diagnosed, complications of dry eye syndrome, and treatment with eye drops
- [Understanding Dry Eye](#) (2015) – Produced by The Royal College of Ophthalmologists and Royal National Institute of Blind People. Contains information on diagnosis, treatment, living with dry eye syndrome, and useful contacts.

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