LEARNING DOMAINS

CLINICAL PRACTICE

SPECIALTY: CONTACT LENS OPTICIANS

PROFESSIONAL GROUPS

Dispensing opticians — CPD PROVIDER — General Optical Council

Optometrists — CPD PROVIDER — General Optical Council

Contact lens opticians — CPD PROVIDER — General Optical Council

CPD CODE: C-106629

MCQs AVAILABLE ONLINE: 1 November 2023

CLOSING DATE: 6 February 2024

ANSWERS PUBLISHED: March 2024

This CPD session is open to all FBDO members and associate member optometrists. Successful completion of this CPD session will provide you with a certificate of completion of one non-interactive CPD point. The multiple-choice questions (MCQs) are available online only from Wednesday 1 November 2023. Visit **www.abdo.org.uk** After member login, scroll down and you will find CPD Online within your personalised dashboard. Six questions will be presented in a random order. Please ensure that your email address and GOC number are up-to-date. The pass mark is 60 per cent.

CPD CODE: C-106625

What's in the bottle?

By Michelle Mehta BSc (Hons) FBDO CL FHEA

Dry eye disease (DED) is a common ocular condition affecting millions of people worldwide[1]. Characteristic symptoms of DED include ocular discomfort, foreign body sensation, ocular burning, redness, itching, excessive tearing, photophobia, blurred vision and intolerance to contact lenses. These symptoms can have a significant impact on the physical and psychosomatic wellbeing of patients, with a negative influence on quality of life. There have been reported cases of depression, anxiety, stress, sleep and mood disturbances in DED patients[2].

The Tear Film & Ocular Surface Society Dry Eye Workshop (TFOS DEWS) II definition for DED states that: "Dry eye 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 [**Figure 1**]. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface"[3].

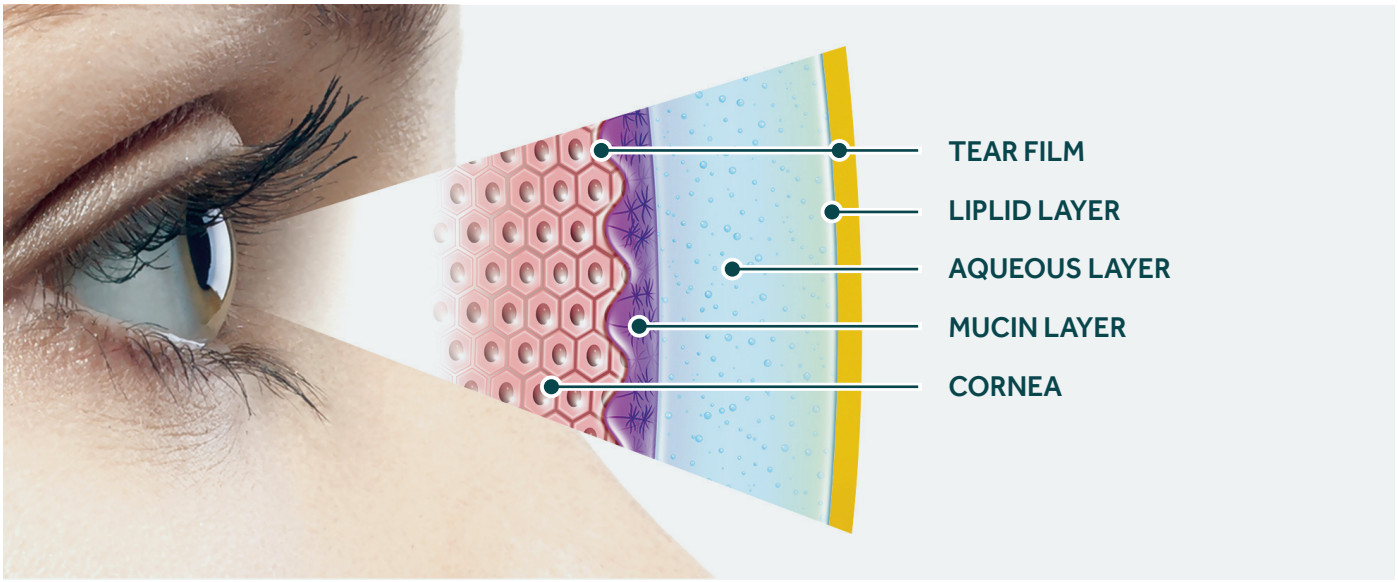
DED appears to be more prevalent in females than males[1], and in particular menopausal or post-menopausal women[4]. Other risk factors include long-term contact lens wear, the use of anti-depressants, humidity, pollution and some dietary habits[5]. Recent studies have also shown an increase in DED among younger patients thought to be linked to increased use of digital devices[6] particularly over the course of the COVID-19 pandemic.

DED can be divided into two major sub-types: aqueous deficient dry eye (ADDE), characterised by an inefficiency or inability of the lacrimal glands to produce tears; and evaporative dry eye (EDE), typically attributed to excessive evaporation of the tear fluid[7]. EDE appears to be the more common form of DED and is frequently associated with meibomian gland dysfunction (MGD) (**Figure 2**).

Many DED sufferers will experience both types of dry eye, otherwise known as mixed dry eye. Regardless of the aetiology, ocular surface instability promotes a vicious cycle of inflammation, exacerbating the signs and symptoms of the disease and damage to the ocular surface[8]. It is necessary to treat dry eye patients in a comprehensive way, taking into account their symptoms, meibomian gland physiology, tear film lipid quality and quantity and tear production, loss and run-off[8].

A healthy tear film contains a mixture of lipid, aqueous and mucin. The tear film is the eye's first line of defence with its various components working synergistically to fight pathogens on the ocular surface. A compromised tear film can lead to damage of the cornea and conjunctival epithelium (**Figure 3**), resulting in the discomfort symptoms associated with dry eye. The ultimate goal of DED management is the restoration of tear film homeostasis[6].

Tear replacement by way of artificial tears and lubricants is currently the most widely used therapy for dry eye, and a variety of components are used to formulate a considerable number of commercially available preparations[11]. The aim of these tear substitutes is to increase moisture at the ocular surface and to improve lubrication with subsequent secondary effects, such as smoothing of the corneal surface of dry eye patients which may, in turn, improve vision.



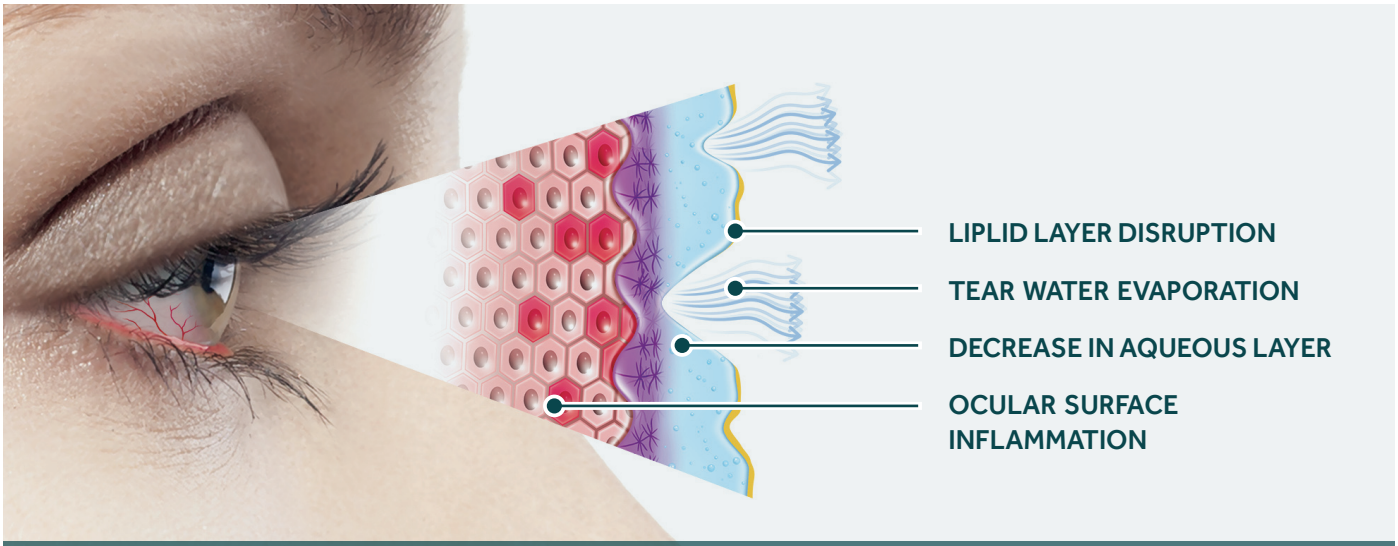


FIGURE 1: Comparison of a healthy tear film and a damaged tear film *(courtesy of Thea UK)*

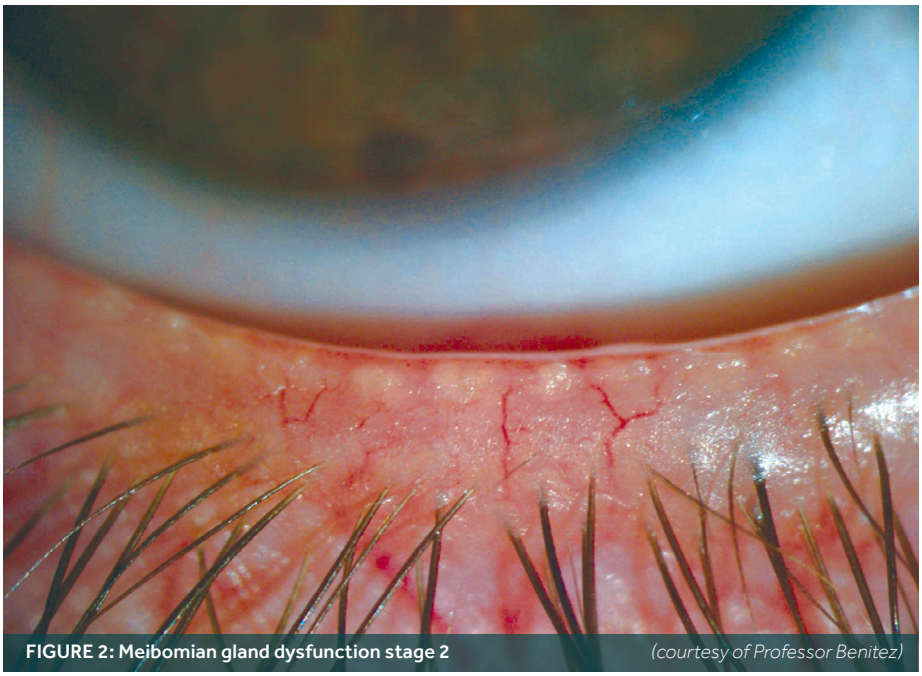


FIGURE 2: Meibomian gland dysfunction stage 2 *(courtesy of Professor Benitez)*

The use of artificial tears obviously has its limitations; natural tears have a complex composition of water, salts, mucins, proteins and lipids, which artificial tears cannot completely substitute. They are, nevertheless, used in all stages in DED, often alone in the case of mild to moderate disease, or in combination with other management in the case of moderate to severe cases[12].

With the wide array of commercially available drops, the choice of which to select can be difficult. As dispensing opticians and contact lens opticians, we will often be asked for advice by dry eye patients. This article describes the ingredients within the available formulations, so that clinicians may feel better equipped and more confident to offer advice.

FIGURE 3: Dry eye related conjunctival staining *(courtesy of Professor Benitez)*

The majority of artificial tears are aqueous based and contain viscosity enhancing agents, which aid lubrication and increase on-eye retention time. Other ingredients may include osmoprotectants, antioxidants, preservatives and inactives such as pH buffers, excipients and electrolytes[11].

PRESERVATIVES

Any drop delivered in a multidose format must have some mechanism for maintaining the sterility of the contents throughout its intended length of use. In multidose preparations, antimicrobial activity is most often achieved through the addition of preservatives, with the most commonly used preservative in topical eyedrops being benzalkonium chloride (BAK)[13]. Chronic exposure of the ocular surface to preservatives is now well recognised as inducing toxicity and adverse changes to the ocular surface.

There are many studies demonstrating that BAK can induce corneal and conjunctival epithelial cell apoptosis, damage to corneal nerves, delay corneal wound healing, interfere with tear film stability and cause loss of goblet cells[9]. In addition, patients using drops containing BAK report symptoms which include discomfort on instillation, burning or stinging sensations, dry eye, tearing and itchy eyelids[14]. If patients are experiencing these symptoms, these may impact on compliance with any recommended DED management.

Clinical signs of preservative toxicity may include superficial punctate keratitis, conjunctival hyperaemia, staining and follicles, blepharitis, increased osmolarity, reduced tear production and reduced tear break up time (TBUT)[13].

Although the concentration of preservatives in topical eyedrops is generally low, their prolonged presence on an already compromised cornea can lead to worsening of symptoms, especially as the application of drops may be required up to four times a day on an ongoing basis. For this reason, it is suggested that patients with severe DED who require frequent use of drops, or those who use lubricants in conjunction with other topical therapies, such as glaucoma medication, should avoid the use of drops containing BAK[8].

To avoid issues with long-term exposure to preservatives, newer preservatives which have a lower impact on the ocular surface are now more commonly used. These include sodium chlorite (Purite and OcuPure), polyquaternium (Polyquad) and SofZia. Products containing polyquad include the Systane range by Alcon and Soothe XP Emollient Eye Drops by Bausch + Lomb. Products containing Purite include the Refresh range by Allergan, and products containing OcuPure include Blink Tears, Blink Triple Care, Blink GelTears, which have recently been acquired by Bausch + Lomb.

OcuPure is a preservative used in some multidose topical eyedrops. It breaks down into sodium and chloride ions, oxygen and water on exposure to UV light after installation[9,13].

Polyquad has been used as a disinfectant in contact lens solutions since the mid-1980s, and then later as a preservative in both dry eye drops and glaucoma medication. It is thought to have minimised unwanted toxic effects on ocular surface calls in comparison to BAK[11].

SofZia is a branded ionic-buffered solution containing zinc chloride, borate, propylene glycol and sorbitol. It functions as an oxidising preservative and converts to non-toxic components on contact with the ocular surface[13]. There has been reduced conjunctival inflammation and corneal changes found in comparison with BAK[15]. Whilst it is available as a preservative in some glaucoma medication, it is not, as yet, used in dry eye drops.

Preservative-free drops may be a better choice for patients who have chronic allergies, sensitive skin, if they report mild to moderate stinging or irritation on insertion or if they need to use the drops more than four times a day[16]. It is also worth bearing in mind that preservative-free drops would be a better option for post-operative patients and contact lens wearers; however, if the drops are being applied when the lenses are not on the eye or about to be inserted then this may not be the case. Full discussions should take place with the patient and recorded on the patient records.

FIGURE 4: Thealoz Duo Gel Single-unit, preservative-free eye drops

(courtesy of Thea UK)

Delivery of preservative-free eyedrops can be enabled with the use of single-dose units (**Figure 4**); these have their obvious drawbacks by way of cost with such eyedrops sometimes costing as much as five to 10 times more than multidose preparations[7], which can in turn lead to a lack of compliance. They may also be difficult for some patients to handle. Additionally, there should be consideration given to the environmental costs of the packaging involved with unit-dose drops.

The creation of innovative dispensers with unidirectional valves now allows some multi-dose bottles to be preservative free. This includes products such as the Hycosan range from Scope Ophthalmic, Thealoz Duo and Hybak by Théa Pharmaceuticals[17] and HydraMed, which is distributed by Positive Impact in the UK. An example of a one-bottle design can be seen in **Figure 5**.

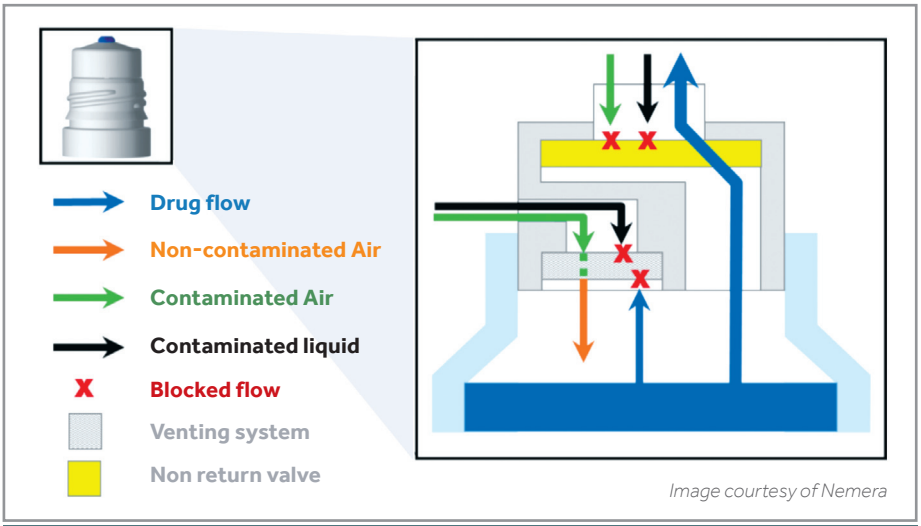


FIGURE 5: Diagrammatic representation of the Novelia multi-dose closing tip system, which avoids the need for preservatives in the drop and prevents bacterial contamination of the bottle

VISCOSITY ENHANCING AGENTS

Viscosity enhancing agents within topical eyedrops are considered to be beneficial to the ocular surface. They are known to increase tear film thickness, protect against desiccation, promote tear retention at the ocular surface, maintain physiological corneal thickness and relieve dry eye symptoms[9]. They act as water retention agents, which allows them to moisturise the ocular surface by preventing loss of water. Those used in artificial tears include carboxymethyl cellulose (CMC), hydroxypropyl methylcellulose (HPMC), hyaluronic acid (HA) and hydroxypropyl cellulose.

HA, also known as hyaluron, and sodium hyaluronate appear to be among the more commonly used viscosity enhancing agents which can be found in products such as Hybak by Théa Pharmaceuticals, Hycosan by Scope Ophthalmics, HydraMed distributed by Positive Impact, Lacrifresh moisture by Avizor, and Optrex Eye Drops by Optrex.

HA is naturally occurring and non-toxic and serves several crucial purposes in the human body including joint and tendon lubrication and cell-to-cell communication[18]. It is frequently used in skin care products and fillers for cosmetic and reconstructive purposes.

The viscosity of a HA-containing tear film will decrease during a blink and allow even distribution of the tear film. Once at rest, higher viscosity is restored, which in turn prolongs its residence time on the ocular surface[19]. HA is rich in hydroxyl groups that attract water molecules, which thicken and stabilise the tear film. It also reduces evaporation from the ocular surface, and it protects damaged surfaces during wound healing[18].

High viscosity agents can be known to cause visual blurring on instillation, and so lower viscosity agents are preferred for low to moderate DED. In more severe cases, higher viscosity ophthalmic gels and ointments may be needed to control symptoms. These can be associated with more blurring and are therefore used overnight. Examples of these include Hycosan Night by Scope Ophthalmics, Systane Gel Drops by Alcon, Artelac Nighttime Gel by Bausch + Lomb, and HydraMed Night Sensitive distributed by Positive Impact.

OSMOPROTECTANTS

Osmoprotectants are used in some topical eye drop formulations in order to prevent apoptosis (the process of programmed cell death) of the corneal and conjunctival epithelial cells, which can happen as a result of hyperosmolarity in DED. Examples of these include L-carnitine, erythritol, betaine, sorbitol, glycerin and trehalose[20]. A recent study also showed that, as well as decreasing cell apoptosis, osmoprotectants can reduce corneal staining and inflammatory cytokines.

BUFFERS

Buffers in topical eyedrops are included for the purpose of maintaining the pH of the natural tears as closely as possible when they are applied to the ocular surface. It has been reported that this is important as the pH of the tear film should be kept constant in order to maintain the normal function of the epithelial cells on the ocular surface[21]. Artificial tears contain a variety of buffers, which include citrate, phosphate and borate.

The concentration of these buffers is crucial as there have been reports of corneal calcification following extensive use of dry eye products containing high levels of calcium phosphate[9].

EXCIPIENTS

Excipients are used to bind the active ingredients together in topical eyedrops. However, due to the delicate nature of the ocular tissues, there are a limited number of acceptable excipients available for eye drops and these consist mainly of ionic and non-ionic isotonic agents[9].

ELECTROLYTES

The tear film is a complex structure that is rich in electrolytes including sodium, potassium, chlorine, magnesium and calcium, which maintain the osmotic balance of the ocular surface[9,20].

Electrolytes play a critical role in ocular surface homeostasis. Therefore, osmotic agents, such as electrolytes are used in artificial tears in order to reproduce the electrolytic profile of the tear film. Some of the more commonly used electrolyte salts include sodium chloride, potassium chloride, sodium borate, sodium phosphate and boric acid[9]. Some electrolytes, such as boric acid, can also act as buffering agents to stabilise the pH of formulations.

Electrolytes play a vital role in maintaining healthy osmolarity of the tear film by providing essential ions for the maintenance of the corneal epithelial cells, and by counterbalancing the hyperosmolarity of the tear film brought on by DED[20].

LIPID SUPPLEMENTS

The lipid layer of the tear film plays an important role in preventing tear evaporation. With EDE being one of the more common forms of DED, there is an increase in availability and demand for lipid-containing topical eyedrops. A variety of oils, such as mineral oils and phospholipids, have been included in formulations to assist in restoration of the lipid layer of the tear film[9].

Lipid containing drops are formulated as emulsions, defined as non-soluble liquids, which are finely dispersed within another liquid such oil and water[22]. Studies have shown that artificial tears formulated in this manner can increase tear film lipid layer thickness and patients' comfort when compared to drops that do not contain these oily agents[20]. In addition to this, they can help to provide a smooth optical surface for the cornea and help maintain good quality vision[23].

Drops containing lipids, phospholipids and mineral oils are not usually advised for use during contact lens wear, as the oily agents will leave a residue on the lenses, leading to blurred vision. The advice would be to instil the drops after lens removal and/or prior to lens insertion, allowing plenty of time for the drops to disperse before applying lenses. Examples of eyedrops that contain oily agents include Soothe by Bausch + Lomb, Systane Balance by Alcon, and Refresh Optive MEGA-3 by Allergan[21].

ANTIOXIDANTS

There has been some evidence that DED is also associated with oxidative stress, which causes tissue damage and increases inflammation[23]. This had led to the exploration of the potential use of antioxidants in formulations for the management of DED. Vitamin A, also known as retinol, has been shown to have significant effects in improving blurred vision, TBUT and Schirmer score in DED patients[9].

The use of retinol is well-known in many skin care products. However, it has also been found to be very unstable in liquid formulation and has been shown to increase MGD in animal models[9,20], and so its use is not recommended for patients where MGD has been diagnosed.

Lipoic acid as an antioxidant has also been trialled and this may improve tear film stability; epsilon aminocaproic acid, vitamins E, B6 and B12, and panthenol have been used in Japanese formulations of topical eyedrops[20]. It would appear, however, that more clinical studies are still required to fully assess the effects of antioxidants in artificial tears in order to fully understand their benefits and disadvantages for DED patients[20].

SUMMARY AND CONCLUSION

This article has provided examples of commercially available products but is by no means exhaustive. It is the role of the eyecare practitioner to be aware of what is available to them, and of the new products that are introduced onto the market.

When choosing artificial tears for patients with DED, clinicians should consider several factors to include the underlying cause of the disease, ease of installation, frequency of use, the presence of any other underlying ocular conditions and whether the patient wears contact lenses. As the integrity of the ocular surface for DED patients is already compromised, it is important not to further increase the risk of toxic reactions and any other adverse events.

A better understanding of the ingredients found in artificial tear formulations will help provide a better selection process for the most appropriate recommendation to target the signs and symptoms of DED patients that may enter the practice seeking advice. Not all artificial tears are equal, and there are many factors to take into consideration when providing advice.

In addition to the use of artificial tears for the management of DED, there may be other approaches included in a management plan to include avoidance of exacerbating factors such as environmental factors, digital device use and medications. There may also be a need for tear retention methods such as punctal plugs, tear stimulation, anti-inflammatory agents (such as topical corticosteroids) and other therapies such as nutritional supplements. Such approaches are beyond the scope of this article.

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LEARNING OUTCOMES FOR THIS CPD ARTICLE

DOMAIN: Clinical Practice

5.3: *Be aware of current good practice and research in relation to ocular lubricants to support the management of dry eye disease and consider how you may apply this to your clinical practice.*

7.5: *Provide effective advice on ocular lubricants to support the management of dry eye based on current good practice.*

DOMAIN: Contact Lens Speciality

Consider the individual needs and circumstances of your patients when making recommendations for ocular lubricants to support the management of dry eye.

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