

Dry eye therapy attempts to fill unmet needs in artificial tears

A look at the history of artificial tears traces progression of products, dry eye market

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ANDOVER, MA ::

DRY EYE—one of the most common ophthalmic diseases affecting 1 in 3 patients who seek treatment from an ophthalmologist—can drastically impact the quality of life of those plagued by the disease.¹

Unfortunately, dry eye is also one of the most difficult diseases to study and consequently, the number of truly effective therapies is limited. What sounds simple in therapy is not so simple in practice, and that is creating an artificial tear to target the signs and symptoms of dry eye while restoring the ocular surface.

THE PROGRESSION OF ARTIFICIAL TEARS

The artificial tear market has changed drastically over the years, and ophthalmology is now into the fourth generation of artificial tears.

FIRST GENERATION. The first generation of tear substitutes is saline-based artificial tears, composed of isotonic sodium chloride. Generally speaking, these artificial tears spread poorly across the ocular surface and their short retention time leads to transient symptoms relief and very high frequency of instillations. While these products can provide hydration without blurring, they do not protect against evaporation or allow for optimal spreading on the ocular surface.

SECOND GENERATION. The transition from first- to second-generation products brought along the concept of preservative-free and multi-dose formulations with softer, gentler preservatives. This shift in the dry eye artificial tear market—from the overwhelming use of strong preservatives to the use of preservative-free, “disappearing” and other, more gentle preservatives for those patients who are hypersensitive to preservatives—was a critical point in the over-the-counter, artificial tear landscape. Polymers are the second-generation of products, existing of two groups: natural polymers (e.g., methycellulose derivatives) and synthetic

polymers (e.g., polyethylene glycol, polyvinyl alcohol, povidone, carbopol, polyguar, and HP guar). Nowadays, this group represents the widest class of marketed products. Polymers have hygroscopic and high-viscosity properties, offering a better retention time than saline products. These products also provide good lubrication of the ocular surface and can compensate for inadequate tear production. Unfortunately, the challenge with this group of products is to find a compromise between high viscosity and low blurring at instillation. Examples of this group of tears include Systane Ultra (Alcon Laboratories) and Refresh Classic (Allergan).

THIRD GENERATION. The inclusion of hyaluronic acid in artificial tears is considered to be the third generation of dry eye therapy. Hyaluronic acid is long-chain mucopolysaccharide with high-molecular weight. Products with hyaluronic acid have both hygroscopic and osmocorrective properties. Additionally, they support the regeneration of the corneal epithelium and improve the ocular surface structure as a result of mucoadhesive properties, which prolong the retention time on the ocular surface. This allows for a more convenient dosing regimen without impeding blinking or causing the marked visual blurring associated with earlier-generation artificial tears. These first three generations of artificial tears have found some performance in certain patient populations, but are not effective in all types of dry eye patients.

FOURTH GENERATION. The unmet need for an all-encompassing artificial tear was met with the development of the fourth-generation lipid emulsions. Lipid emulsions reduce tear evaporation without impairing vision while also providing hydration and osmocorrection. These nanoemulsions were developed to improve ocular bioavailability of lipophilic or poorly water-soluble drugs and are quite effective ocular drug delivery vehicles. To date, all emulsions marketed with the exception of one are anionic, including Systane Balance (Alcon) and Optive

Plus (Allergan), and due to electrostatic repulsion, have a poor retention time on the ocular surface. Cationic oil-in-water emulsions extend the benefits of negatively charged oil-in-water emulsions. Retaine MGD (OCuSOFT) is the only preservative-free, cationic emulsion currently available. Its composition is designed to target all three layers of the tear film and improves spreading and residence time on the ocular surface, enhancing the protection and restoration of a healthy tear film and corneal epithelium.

NEED FOR COMPLETE OTC ARTIFICIAL TEAR

Through the generations of artificial tears, there have been a number of advanced therapeutic options, but none that come fully equipped to tackle dry eye. In eye drop formulations of any kind, one of the most significant challenges is that the product is rapidly eliminated from the ocular surface following instillation due to a variety of ocular barriers.² An artificial tear with an improvised residence time can combat the barriers to drug delivery and provide a more complete system for dry eye symptom relief.

Retaine MGD is a unique preservative-free artificial tear option that serves to address the unmet needs of the artificial tear industry. The drug contains a proprietary cationic oil-in-water nanoemulsion technology with novel bioadhesive properties (Novasorb). The principle of the technology is based on electrostatic interactions between the positively charged oil nanodroplets and the negatively charged ocular surface. This electrostatic attraction increases the residence time on the ocular surface and enhances the ocular drug bioavailability.^{3,5} By acting against the vicious cyclical nature of dry eye to relieve symptoms and restore the ocular surface, fourth-generation products, like Retaine MGD, exemplify the optimal tear substitute for dry eye disease. ■

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take-home

► Through the generations of artificial tears, ophthalmology has seen a number of advanced therapeutic options.

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MR. OUSLER is the vice president of dry eye at Ora, inc. He has no conflicts of interest with the subject matter