A recent flurry of new and rebranded ophthalmic steroids entering the market is sending optometrists into a tizzy. After years of a stagnant market for topical corticosteroids, new names have recently appeared (see Emerging and Reemerging Ophthalmic Steroids below). Many of these new products are entering the market because one highly effective medication, loteprednol etabonate, has come off patent.

As with the expiration of patent protection for any drug, there has been a burst of product development as other companies attempt to get their piece of a multimillion-dollar pie. US sales of loteprednol etabonate ophthalmic suspension 0.5% (Lotemax, Bausch + Lomb) were approximately $89 million for the 12 months ending in February. This does not include other formulations of the active ingredient loteprednol etabonate, including gels and ointments.

In my clinic, I prescribe loteprednol etabonate ophthalmic suspension 0.5% and fluorometholone acetate ophthalmic suspension 0.1% (Flarex, Alcon) frequently for the many patients we see every day with dry eye and ocular inflammation. It should be noted, however, that loteprednol etabonate is not labeled for use in the treatment of dry eye. The FDA labeling for loteprednol etabonate ophthalmic suspension 0.5% is “for the treatment of postoperative inflammation and pain following ocular surgery” and “for the treatment of steroid-responsive inflammatory conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe, such as allergic conjunctivitis, acne rosacea, superficial punctate keratitis, herpes zoster keratitis, iritis, cyclitis, and selected infective conjunctivitis, when the inherent hazard of steroid use is accepted to obtain an advisable diminution in edema and inflammation.”

EMERGING AND REEMERGING OPHTHALMIC STEROIDS

Generic Loteprednol Etabonate Ophthalmic Suspension, 0.5%

In April, Akorn, a manufacturer of specialty generic medications, announced that it had received abbreviated new drug application approval from the FDA for loteprednol etabonate ophthalmic suspension 0.5%. Akorn is now in final preparations for commercial launch of this new product. The medication will be in suspension form, as opposed to the gel form more commonly seen in the branded formulations of loteprednol etabonate. It is anticipated that patients will have to vigorously shake the bottle before use, and that the formulation will contain benzalkonium chloride (BAK) 0.01% as a preservative.

Loteprednol Etabonate Ophthalmic Gel 0.38% and Loteprednol Etabonate Ophthalmic Gel 0.5%

In February, Bausch + Lomb announced that it had received approval from the FDA for loteprednol etabonate ophthalmic gel 0.38% (Lotemax SM, Bausch + Lomb), and in April, the product was launched. This lower-dose ophthalmic gel form of loteprednol etabonate is formulated with submicron-sized particles (0.4 nm to 0.6 nm in diameter) of the active ingredient. Loteprednol etabonate ophthalmic gel 0.38% was found to provide two times greater penetration to the aqueous humor compared with loteprednol etabonate ophthalmic gel 0.5%, which is composed of micron-scale particles (3 nm in diameter). The submicron particle size in loteprednol etabonate ophthalmic gel 0.38% was found to provide two times greater penetration to the aqueous humor compared with loteprednol etabonate ophthalmic gel 0.5% (Lotemax Gel, Bausch + Lomb). It’s also been shown that loteprednol etabonate ophthalmic...
gel 0.38% had the same or improved concentration of active ingredients in the anterior segment following ocular instillation as loteprednol etabonate ophthalmic gel 0.5%, despite the 24% reduction in dose. The loteprednol etabonate ophthalmic gel 0.38% formulation retains many of the gel properties of loteprednol etabonate ophthalmic gel 0.5%; specifically, it transitions to a fluid upon topical ocular instillation while providing significant viscosity on the surface to prolong the drug’s exposure to the ocular surface.

I have had a great deal of success with the Lotemax family of medications because of its pH, which is very close to that of the tear film (pH 6.5) and its extremely low (0.003%) concentration of BAK. I have found that the neutral pH, comfortable moisturizing agents, and lowest BAK percentage in a loteprednol etabonate ophthalmic suspension 0.5% formulation made this drug an effective choice in my clinic.

Loteprednol Etabonate Ophthalmic Suspension 1%

In August 2018, the FDA approved loteprednol etabonate ophthalmic suspension 1% (Inveltys, Kala Pharmaceuticals) for the treatment of postoperative inflammation and pain following ocular surgery. This loteprednol etabonate ophthalmic suspension 1% is the only drop approved for twice-daily dosage and has the highest concentration of loteprednol etabonate available.

This formulation uses a proprietary mucus-penetrating particle drug delivery technology with submicron sized particles that are nearly half the size of the submicron particles in loteprednol etabonate ophthalmic gel 0.38%. These 0.2 nm to 0.4 nm particles have been shown to increase the delivery of loteprednol etabonate into ocular tissues by more than threefold compared with currently available loteprednol etabonate ophthalmic suspension 0.5% formulations. It is believed that the company’s selectively sized nanoparticles with coatings facilitate better penetration through the tear film mucins, allowing more effective dosing.

This formulation is a suspension, so it must be shaken for 1 to 2 seconds prior to instillation. The particles in this formulation are substantially smaller than those in other loteprednol etabonate suspension formulations, and therefore it is expected that significantly less shaking and agitation is required.

Due to the higher (1%) concentration compared with other formulations on the market combined with the small particle size, the recommended dosage schedule is twice per day, as opposed to the standard four times per day. This 1% formulation has a relatively high concentration of BAK (0.01%) and an unknown pH value, and it has been found to cause some burning upon instillation.

In our clinic, patients appreciate the simple dosage schedule and the easy accessibility of this medication through nationwide mail-order pharmacies.

Fluorometholone Acetate Ophthalmic Suspension 0.1%

A newly rebranded corticosteroid has emerged in the marketplace. Fluorometholone acetate ophthalmic suspension 0.1% was acquired by Eyevance Pharmaceuticals from Novartis in October 2018. It is a topical ophthalmic suspension containing fluorometholone acetate 0.1% and is without a generic equivalent. The active ingredient is fluorometholone acetate, whereas generic formulations of this steroid contain fluorometholone alcohol.

Fluorometholone acetate ophthalmic suspension 0.1% provides better penetration of the drug into ocular tissues compared with other ophthalmic steroids. This enhanced penetration delivers better drug potency. In a pivotal phase 3 study, fluorometholone acetate ophthalmic suspension 0.1% demonstrated superior efficacy over fluorometholone ophthalmic suspension 0.1% (FML, Allergan) in reducing inflammation of noninfectious external ocular inflammation. Additionally, this same phase 3 FDA approval study demonstrated that fluorometholone acetate ophthalmic suspension 0.1% was equivalent to prednisolone acetate 1.0% in reducing noninfectious external ocular inflammation.

Similar to loteprednol etabonate, fluorometholone acetate ophthalmic suspension 0.1% is indicated for the treatment of steroid responsive inflammatory conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the eye. The recommended dosing is one drop four times daily. During the first 24 to 48 hours, the dosage may be increased to two drops every 2 hours. Similar to other topical medications, it contains BAK 0.01% as the preservative. Fluorometholone acetate ophthalmic suspension 0.1% has found a home in my clinic for patients who generally tolerate the non-acetate suspension well but need a slightly stronger medication.

Dexamethasone Intraocular Suspension 9%

Dexamethasone intraocular suspension 9% (Dexycu, Eyepoint Pharmaceuticals), another ophthalmic steroid approved by the FDA last year, is a cohesive liquid that is inserted into the ciliary sulcus at the completion of cataract surgery. It is the first FDA approved intraocular steroid for postoperative inflammation and is designed to provide 30 days of sustained release. It is believed that with this treatment routine patients will not need topical steroids after uncomplicated phacoemulsification cataract surgery.

Dexamethasone Ophthalmic Insert 0.4 mg

Yet another new ophthalmic steroid, dexamethasone ophthalmic insert 0.4 mg (Dextenza, Ocular Therapeutix) was approved last year by the FDA. The corticosteroid intracanalicular insert is placed directly into the punctum and into the canaliculus immediately after cataract surgery. It is designed to deliver dexamethasone to the ocular surface for up to 30 days without preservatives. It is then reabsorbed by the body and exits via the nasolacrimal system.

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As 2019 shapes up to be the year of the 'roid wars with all the new and rebranded topical corticosteroids entering the market, it would be a mistake to ignore the entirely new subset of steroid delivery devices now emerging. Looking to the future, practitioners should closely monitor how these new treatments can improve patient compliance, comfort, and ocular health.

With the introductions of nanoparticles, intraocular injections, and punctal inserts, the future is bright and strong in the corticosteroid field.


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Financial disclosure: None