Optometric Physicians of Washington

EMERGING OCULAR PHARMACEUTICALS
Immunomodulators

- Aldara (imiquimod [3M Pharma])
- Acular (ketorolac tromethamine [Allergan])
- Voltaren (diclofenac [CIBA])
- Alomide (lodoxamide tromethamine [Alcon])
- Crolom (cromolyn sodium [B&L])
- Patanol (olpatadine HCl [Alcon])
- Zaditor (ketotifen fumarate [Ciba])
- Optivar (azelastine HCl [B&L])
- Alamast (pemirolast potassium [Santen])
- Alocril (nedocromil sodium [Allergan])
- Pentyde (pentygetyde)
- Livostin (levocabastine HCl [Ciba])
- Emadine (emedastine difumarate [Alcon])
- Lotemax (loteprednol etabonate .5% [Pharmos/Bausch & Lomb])
- Alrex (loteprednol etabonate .2% [Pharmos/Bausch & Lomb])
- Profenal (suprofen [Alcon])
- Ocufen (flurbiprofen [Allergan])
- Feldene (piroxicam [Akorn])
- Oruvail (ketoprofen [Wyeth-Ayerst])
- Toradol (ketorolac [Syntex])
- Indocin (indomethacin [Merck])
- Indocin Ophthalmic Solution (indomethacin [Merck])
- Vexol (rimexolone [Alcon])

- Flairex (flurometholone acetate [Alcon])
- eFlone (flurometholone acetate [Ciba])
- interferon
- Enbrel (etanercept [Immunex])
- Neosar (cyclophosphamide [Pharmacia])
- Leukeran (chlorambucil [GlaxoWellcome])
- Surodex (dexamethosone implant [Oculex])
- Envision TD (fluocinolone acetonide implant [B&L)]

Immunomodulators are potent modifiers of the inflammatory process. Most would also be considered non-steroidal anti-inflammatory agents. Interferon in various forms is a potent immunomodulator which is gradually finding many applications including the treatment of Hepatitis C, Rheumatoid Arthritis, and Multiple Sclerosis. Aldara is a topical immunomodulator being used to treat warts. A number of the listed medications are cyclo-oxygenase inhibitors that inhibit the enzyme cyclo-oxygenase markedly reducing the synthesis of prostaglandins.

Alomide and Crolom are mast cell stabilizers. Pentyde (pentygetyde) also acts at the level of the mast cells, but competes with antibodies for binding sites on the mast cells. Patanol is an inhibitor of the release of histamine from the mast cells and it is a relatively, selective histamine H1 antagonist that inhibits type 1 immediate hypersensitivity reaction. It is now the most prescribed ophthalmic medication. Zaditor is a relatively selective, non-competitive histamine antagonist (H1 receptors) and mast cell stabilizer. Ketotifin inhibits the release of mediators from cells involved in hypersensitivity reactions. Decreased chemotaxis and activation of eosinophils has also been demonstrated with Zaditor. The action of ketotifin occurs rapidly with an effect seen within minutes after administration. Optivar has activity similar to Patanol and Zaditor. It is indicated for the treatment of the itching present with allergic conjunctivitis. Alamast, and Alocril are mast cell stabilizers. Alocril is a second-generation mast cell stabilizer and has a more rapid onset of action than other mast cell stabilizers (15 minutes).

Livostin is a potent H1 histamine blocker. Emedastine is also a potent H1 blocker; it is effective after histamine is already present.

The immunomodulators are valuable for the treatment of giant papillary conjunctivitis and vernal conjunctivitis (Ocufen, Profenal, Feldene, and Lotemax). Several of the oral medications are valuable for the treatment of cystoid macular edema (Oruvail, Toradal, and Indocin); Indocin ophthalmic solution is also being investigated for the treatment of cystoid macular edema. The NSAIDs are valuable for modulating the healing and reducing the pain of corneal abrasions and corneal erosions. The use of Acular and Voltaren and other immunomodulators in combination with ocular steroids is becoming more common with photorefractive keratectomy and their use has helped to reduce complications as well as reducing the mild to moderate pain associated with corneal procedures.

Vexol is a new "soft" steroidal immunomodulator ("soft" medications have more rapid systemic metabolism and excretion via decreased half-lives resulting in reduced side effects). It is less likely than other steroids to increase ocular tensions in steroid responders. Vexol is approved for the treatment of anterior uveitis and for post-operative inflammation control. Vexol also is valuable for longer term treatment of GPC.

Loteprednol etabonate (Lotemax .5% and Alrex .2%) are "soft" steroids, that are effective for uveitis

and ocular allergies. Loteprednol etabonate is effective in the prophylaxis of seasonal allergic conjunctivitis and has an acceptable safety profile. As "soft" steroids any loteprednol etabonate absorbed systemically, after topical administration, is rapidly transformed into inactive metabolites, and eliminated from the body mainly through the bile and urine. Loteprednol etabonate has less propensity to cause clinically significant elevations in IOP than prednisolone acetate (1% incidence and 6.7% incidence respectively). Extended use of loteprednol etabonate at a concentration and frequency equal to or greater than the intended therapeutic dose does not result in detectable systemic levels or hypothalamic pituitary axis suppression. In dose response studies the 0.2% concentration of loteprednol etabonate (Alrex) has been shown as effective in the reduction of mean redness and itching for patients with environmental seasonal allergic conjunctivitis. The rapid therapeutic response, combined with the low incidence, late development, and transient nature of any IOP elevation indicates Alrex as an appropriate treatment for giant papillary conjunctivitis including contact lens-associated GPC. Loteprednol etabonate 0.5%
(Lotemax) is indicated for uveitis.

Flairex and eFlone are fluorometholone acetate preparations that are equal in effect to prednisolone acetate but are also less likely to increase ocular tensions.

Enbrel, Neosar, and Leukeran are currently available systemic immunomodulators that are being researched to treat ocular autoimmune disorders.

Surodex is in clinical trials for the reduction of inflammation following cataract surgery. It is a biodegradable implant that releases a therapeutic dose of dexamethasone (60 micrograms per day). The implant is placed directly in the anterior chamber during surgery. The anti-inflammatory effects last for up to two weeks following placement. The fluocinolone acetonide implant is placed intravitreal for the treatment of noninfectious posterior uveits. It releases steroid for up to 3 years and should benefit patients who would otherwise require systemic steroids or Tenon’s steroid injections.