



### Ophthalmic Antibiotic-Steroid Combination Agents

**Month/Year of Review:** November 2012

**Date of Last Review:** March 2010

**PDL Class:** Ophthalmic Antibiotics-steroids combination

**Source Document:** Provider Synergies (PS)

Current Preferred Agents	Current Non-Preferred Agents
Neo/polymyx B sulf/dexamethasone drops	Fluometholone/sulfacetamide (FML-S Liquifilm®) drops
Neomy sulf/bacitrac/poly/HC ointment	Gentamicin/prednisolone (Pred-G®) 0.3%/1% drops and 0.3%/0.6% ointment
Sulfacetm NA/prednisol AC (Belphamide S. O. P®) ointment	Loprednol/tobromycin (Zylert®) drops
Sulfacetm NA/prednisol AC (Blephamide®) drops	
Tobramycin sulf/dexamethasone drops	
Tobramycin sulf/dexamethasone (Tobradex®) Ointment	

**Previous Recommendations:**

1. There is no difference in efficacy/effectiveness or in safety between agents. (Strength of recommendation: C)
2. There is insufficient evidence to make a specific recommendation.

**PA Criteria/QL:** None

**Recommendations:**

No further research or review needed at this time.

**Background:**

The use of a combination drug with anti-infective component is indicated where the risk of superficial ocular infection is high or where there is an expectation that potentially dangerous numbers of bacteria will present in the eye.

**Methods:**

A MEDLINE OVID search was conducted using all ophthalmic antibiotics-steroid combination agents limited to randomized controlled trials and meta-analysis, English language, and conducted in humans since the literature search conducted for the previous PS review. The Agency for Healthcare Research and Quality (AHRQ), Cochrane Collection, and the Canadian Agency for Drugs and Technologies in Health (CADTH) resources were searched for high quality systematic reviews. The FDA website was searched for new drugs, indications, and safety alerts, and the AHRQ National Guideline Clearinghouse (NGC) was searched for updated and recent evidence-based guidelines.

**New Trials:**

A total of 36 citations resulted and after review for inclusions, two potentially relevant clinical trials were identified (Appendix 1). These trials are briefly described in Table 1.

Table 1: Potential Relevant New Trials

Study	Comparison	Population	Primary Outcome	Results
Blair J <sup>1</sup> , 2011 RCT	Dexamethasone + gatifloxacin compared with gatifloxacin + Placebo	Over the age of 12 years with bacterial corneal ulcer confirmed by culture.	Residual ulcer size at 10 weeks based on digital photographs.	All subjects (n = 30) demonstrated a reduction in ulcer size over the study period. There was no significant difference between the 2 groups in terms of the primary outcome.
Torkildsen GL <sup>2</sup> , 2011 RCT, MC, investigator- masked	Tobramycin/dexamethasone (ST) compared to azithromycin	Patients with moderate to severe blepharitis/ blepharoconjunctivitis.	Seven-item global score defined as the total score of lid margin redness, bulbar conjunctival redness, palpebral conjunctival redness, ocular discharge (0-3 scale), and lid swelling, itchy eyelids, and gritty eyes (0-4 scale).	A statistically significant lower mean globa score (p = 0.0002) was observed in subjects treated with ST compared to subjects treated with azithromycin at Day 8. No serious adverse events were reported during the course of the study in either group.

RCT = Randomized control trial; MC = multi-center

**New drugs:**

None identified.

**New FDA Indications:**

None identified.

**New FDA safety alerts:**

None identified.

**New Systematic Reviews:**

None identified.

**Guidelines:**

None identified.

## **References:**

1. Blair J, Hodge W, Al-Ghamdi S, et al. Comparison of antibiotic-only and antibiotic-steroid combination treatment in corneal ulcer patients: double-blinded randomized clinical trial. *Can. J. Ophthalmol.* 2011;46(1):40–45.
2. Torkildsen GL, Cockrum P, Meier E, et al. Evaluation of clinical efficacy and safety of tobramycin/dexamethasone ophthalmic suspension 0.3%/0.05% compared to azithromycin ophthalmic solution 1% in the treatment of moderate to severe acute blepharitis/blepharoconjunctivitis. *Curr Med Res Opin.* 2011;27(1):171–178.

## Appendix 1

1. Blair J, Hodge W, Al-Ghamdi S, et al. Comparison of antibiotic-only and antibiotic-steroid combination treatment in corneal ulcer patients: double-blinded randomized clinical trial. *Can. J. Ophthalmol.* 2011;46(1):40–45.

Objective: To determine the benefit of early addition of corticosteroids to antibiotics in the treatment of corneal ulcers.

Participants: Thirty eyes of 30 patients, over the age of 12 years, with bacterial corneal ulcer confirmed by culture.

Methods: Patients were randomized before enrollment; 15 were treated with gatifloxacin (Zymar) and a masked placebo and the other 15 were treated with gatifloxacin and masked dexamethasone 0.1% (Maxidex). Primary outcome was residual ulcer size at 10 weeks based on digital photographs. Secondary outcomes included residual ulcer area by clinician estimate, visual acuity, VF-14 score, and time to healing.

Results: All subjects (n = 30) demonstrated a reduction in ulcer size over the study period. There was no significant difference between the 2 groups in terms of the primary outcome. There was a significant difference between the 2 groups in 1 of the secondary outcomes. The mean residual ulcer size compared with the baseline by clinician estimate (slit-lamp) was -0.789 mm<sup>2</sup> for the antibiotic-only group and -4.206 mm<sup>2</sup> for the antibiotic-steroid group (p = 0.05). Among the other secondary outcomes there were no significant differences between the 2 groups.

Conclusions: No benefit was demonstrated in our primary outcome for using steroids in combination with antibiotic therapy in treatment of corneal ulcers. This study suggests that the early addition of steroids to the antibiotic treatment of corneal ulcers does not seem to be harmful when employed in a closely monitored clinical setting.

2. Torkildsen GL, Cockrum P, Meier E, et al. Evaluation of clinical efficacy and safety of tobramycin/dexamethasone ophthalmic suspension 0.3%/0.05% compared to azithromycin ophthalmic solution 1% in the treatment of moderate to severe acute blepharitis/blepharoconjunctivitis. *Curr Med Res Opin.* 2011;27(1):171–178.

Objective: To evaluate the clinical efficacy and safety of tobramycin/dexamethasone (TobraDex ST ; 'ST') ophthalmic suspension 0.3%/0.05% compared to azithromycin (Azasite®) ophthalmic solution (1%) in the treatment of moderate to severe blepharitis/blepharoconjunctivitis.

Research design and methods: The study was a multicenter, randomized, investigator-masked, and active-controlled, 15-day study. Enrolled in the study were 122 adult subjects (at least 18 years of age) diagnosed with moderate to severe blepharitis/blepharoconjunctivitis, defined by a minimum score of at least '1' for one of the lid signs, one of the conjunctival signs, and one of the symptoms in at least one eye and a minimum global score (total signs and symptoms score) of '5' in the same eye. One group of 61 subjects received ST with instructions to dose 1 drop four times daily (QID) for 14 days. The other group of 61 subjects received azithromycin and dosed with 1 drop twice daily (BID) for 2 days followed by once daily (QD) dosing for 12 days. Visits were conducted at Day 1 (baseline), Day 8 and Day 15. The a priori primary outcome parameter of the study was the seven-item global score defined as the total score of lid margin redness, bulbar conjunctival redness, palpebral conjunctival redness, ocular discharge (0-3 scale), and lid swelling, itchy eyelids, and gritty eyes (0-4 scale). The study utilized standardized, validated photograph control scales developed by Ora, Inc. (Andover, MA). Clinical trial registration: The study was registered at ClinicalTrials.gov under the registry number NCT01102244.

Results: A statistically significant lower mean global score (p = 0.0002) was observed in subjects treated with ST compared to subjects treated with azithromycin at Day 8. No serious adverse events were reported during the course of the study in either group.

Conclusion: ST provides a fast and effective treatment of acute blepharitis compared to azithromycin. Initial therapy with the combination of tobramycin/dexamethasone provides faster inflammation relief than azithromycin for moderate to severe blepharitis/blepharoconjunctivitis.