Glaucoma Management and Ocular Surface Disease
COPE 40918-GL

Michael Chaglasian, OD
Objectives

1. Understand the prevalence, severity and impact of OSD and glaucoma in the population.
2. Understand the clinical signs of OSD and glaucoma.
3. Understand the histological effects of BAK on the ocular surface.
4. Be familiar with recent studies examining the effects of topical glaucoma agents on patients.
5. Be familiar with all options for treating glaucoma patient with medications that do not include BAK.

OSD is Just Like Glaucoma

- A chronic disease that increases with age
- Definitions of the disease vary
- Signs of the disease rarely match the symptoms and vice versa
- Diagnostic tests are variable, not repeatable, and often inconclusive
- Treatment regimens are variable and often not effective
- Majority of patients are non-compliant

Why should we care?

Glaucoma Management and Ocular Surface Disease

A Very Current Topic

Glaucoma and Dry Eye: A Tough Combo

How chronic glaucoma treatment can give rise to ocular surface disease, and how you can treat them both.

This article has no commercial sponsorship.
Will there be something to replace topical therapy in glaucoma in the near future?

Glorcoma Care for the Future

- New Ophthalmic Drug Delivery Systems are Coming for Glaucoma.
  - The future therapy for glaucoma remains pharmacologically based (vs. laser/surgery).
  - Some new therapeutic agents will arrive.
  - But more importantly new drug delivery systems will significantly alter how we start therapy for our glaucoma patients.

New Delivery Systems

- Three types of drug delivery systems
  - biodegradable or non-biodegradable implants,
  - implantable pump systems
  - atypical implantable systems

- No implantable pump systems for ocular drug delivery have been developed to date because of the inability to simultaneously miniaturize them and achieve low power operation.

QLT’s punctal plug drug delivery technology

Iluvien (Alimera)

- Iluvien
  - extended release intravitreal
  - delivers fluocinolone acetonide, to the retina for up to three years for treatment of DME
  - Completed Phase III Clinical Trial
  - Medidur™ Technology is a miniaturized, injectable, sustained-release drug delivery system
**Subconjunctival Injection**

- **Anecortave acetate**
  - Angiostatic, initially for wet AMD
  - Posterior juxtascleral injection
  - Initial success of 3 month IOP reduction, then failure in large scale studies

- **Latanoprost**
  - Encapsulated in poly-glycolide micro particles
  - Animal studies showed up to 30 days IOP reduction post injection

**Mini Drug Pump**

- **MEMS**
  - Pump that is refillable, enables long-term use, and possesses broad drug compatibility
  - The pumping mechanism is based on electrolysis and the pump includes a drug refill port as well as a check valve to control drug delivery

  - *Current Eye Research, 35(5), 192–201, 2010*

**Replenish MicroPump**

- Replenish, Inc. is developing a small, refillable, implantable ocular drug pump.

  - The pump can be programmed to dispense precise nanoliter-sized doses (a drug flow sensor gives closed-feedback) of drugs every hour, day or month as needed over six to nine months before the next refill.

  - Not Available In US  http://www.replenishinc.com/

**Iontophoresis**

- Iontophoresis uses an electrical current to drive drugs in the form of ions through a tissue or membrane.

  - http://www.drugdeliverytech.com/ME2

**A nanomedicine approach for ocular neuroprotection in glaucoma.**

- A new medical/topical option for glaucoma is coming.....

  - CAI?  PGA?
  - Combination?
  - New Class??
Look and sound familiar?

• 75y/o female with primary open angle glaucoma
• Controlled IOP, moderate field loss but \textit{STABLE}.
• On Xalatan, Cosopt and Brimonidine
• You pat yourself on the back, ready to conquer the next challenging patient but wait… “that’s nice that my glaucoma is doing well, but doctor, my eyes are tearing”

We Are Treating the Whole Patient

• Goals of Glaucoma Management
  – Treatment
    • Lower IOP to Target
    • Preserve Vision
  – Quality of Life Considerations
    • Long Term Impact of Medications
    • Balance of Efficacy and Side Effects
    • Do No Harm
      – Primum non nocere

Glaucoma and Ocular Surface Disease (OSD)

Overview

Age and Glaucoma

OSD in the Elderly

• 2,520 residents of Salisbury, MD.
• 65 years or older as of 1993.
• Standardized questionnaire (6 questions).
• Exam:
  – Schirmer
  – Rose bengal
  – Assessment of meibomian glands

**OSD in the Elderly**

14.6% reported one or more dry eye symptom “often” or “all the time.”


**OSD and Glaucoma**

- Review of Literature:
  1. Moderate OSD in 20-60%
  2. Severe OSD in 14-66%

**Cornea 2006**

Incidence and Prevalence of Glaucoma in Sever Ocular Surface Disease

**Quality of Life**

**How do we study/measure and quantify this?**

Important for documenting any claims of improvement in response to treatment options.
Ocular Surface Disease Index “OSDI”

- Developed by Outcomes Research Group at Allergan, Inc.
- 12 item questionnaire.
- Provide rapid assessment of symptoms of ocular irritation consistent with dry eye disease.
- Designed as endpoint in clinical trial testing of treatment for dry eye disease.

**OSDI Severity Grading**

<table>
<thead>
<tr>
<th>Score</th>
<th>Normal</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-12</td>
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<td>23-32</td>
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<tr>
<td>33-100</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Total OSDI Score = (Sum of Score for All Questions Answered) X (25)

*Total # of Questions Answered*

Ocular Surface Disease Index (OSDI)

OSDI Results: 630 Glc Patients

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Normal</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>51.6%</td>
<td>21.3%</td>
<td>13.3%</td>
<td>13.8%</td>
<td></td>
</tr>
</tbody>
</table>

OSDI Severity


Impact of Multiple Medications

Impact of Multiple Medications

- Number of Medications
  - 1 N=253
  - 2 N=227
  - 3 N=114

OSDI Score

12.9
16.7
19.4

* p=0.007 (1 Med vs. 2 Meds) † p=0.001 (1 Med vs. 3 Meds)

Leung: Key Learnings

“A large proportion of patients with open-angle glaucoma or ocular hypertension had signs and/or symptoms of OSD in at least 1 eye.

The co-existence of OSD and the use of BAK-containing medications may impact vision-related quality of life in this patient population.”

OSD in Glaucoma Prevalence: Summary

- Ocular Surface Disease is a Significant Problem For Many Glaucoma Patients.
- Prevalence is High, ranging from 48.4% to 60%.1,2
- Previously Reported in a Population Based Study of Elderly (~15%).3
- OSD Severity Increases With The Number of Medications Used.2,4


OSD (Glaucoma Today ’08)

- Any condition that adversely affects the stability and function of the tear film.
- Common causes → dry eye syndrome, blepharitis, meibomian gland dysfunction, and preservative toxicity.
- Pathology involves corneal epithelial cell changes, decreased goblet cell density, and increased inflammatory mediators.

Global Features of Dry Eye

- Tear film instability.
- Tear hyperosmolarity.
- Ocular surface inflammation.
- Epithelial cell damage.
- Discomfort and visual degradation.

Dry Eye Cascade

- Aging
- Dry Environment
- Hormonal Changes
- Contact Lenses
- Blepharitis
- LASIK
- Autoimmune Disease
- Alcohol Use
- Pollution
- Computer Use
- Anti-depressants
- Quaternary Ammoniums (i.e. BAK)

Aqueous Deficient Dry Eye

Evaporative Dry Eye
OSD Affects Quality of Life

- Impact on patients’ day-to-day lives comparable to that of moderate-to-severe angina.\(^1\)
- \% of Patients reporting interference with daily life functions:\(^2\)
  - Night time driving: 32.3\%
  - Reading: 27.5\%
  - Computer work: 25.7\%
  - Watching TV: 17.9\% 

OSD Affects Quality of Vision

Unfortunately, Just Can’t Feel Vision

Detecting OSD

- **Signs do not always match symptoms.**
  - Multiple approaches possible.
  - Should be validated.
  - Need a better system!

Signs and Symptoms

“The lack of concordance between signs and symptoms presents a problem to the diagnosis of the disease and assessment of severity.”

-M. Lemp, MD

Diagnostic Tools

- Tear Film Break-Up Time
- Injection
- Rose Bengal Staining
- Lissamine Green Staining
- Fluorescein Staining
- Blink Rate
- Schirmer Testing
- Osmolarity

DTS Study Group Most Commonly Used Diagnostic Tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Percent Regular Use (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluorescein</td>
<td>100%</td>
</tr>
<tr>
<td>TBUT</td>
<td>94%</td>
</tr>
<tr>
<td>Schirmer</td>
<td>94%</td>
</tr>
<tr>
<td>Rose Bengal Staining</td>
<td>94%</td>
</tr>
<tr>
<td>Lissamine Green Staining</td>
<td>94%</td>
</tr>
<tr>
<td>Corneal Topography</td>
<td>94%</td>
</tr>
<tr>
<td>Osmolarity</td>
<td>94%</td>
</tr>
<tr>
<td>Impression Cytology</td>
<td>94%</td>
</tr>
<tr>
<td>Tear Fluorescein Clr</td>
<td>94%</td>
</tr>
<tr>
<td>NEIVFQ-25</td>
<td>94%</td>
</tr>
<tr>
<td>OSDI</td>
<td>94%</td>
</tr>
<tr>
<td>Tear Osmolarity</td>
<td>94%</td>
</tr>
<tr>
<td>Conjunctival Biopsy</td>
<td>94%</td>
</tr>
<tr>
<td>TEST</td>
<td>100%</td>
</tr>
</tbody>
</table>
 Clinician Ratings for Diagnostic Tests

- Highest
  - History
  - TBUT
- Lowest
  - Schirmer test
  - Cotton thread test

Lissamine Green Staining

Lissamine green is a dye, used for staining cells which are devitalized or have lost their normal mucin surface.

Written 25 filter:
The lissamine green staining appears black.

Sequence of Testing

- Clinical history
- Symptom questionnaire
- TBUT (fluorescein)
- Ocular surface staining (fluorescein/rose-bengal filter)
- Schirmer I (w/ or w/o anesthetic)
- Schirmer II (nasal abolition)
- Lid evaluation
- Meibomian expression

The Effects of Benzylalkonium Chloride (BAK)

Preservative Systems

<table>
<thead>
<tr>
<th>Preservative</th>
<th>Example</th>
<th>Detergents</th>
<th>Oxidative Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzalkonium chloride (BAK)</td>
<td>Timoptic, Lumigan</td>
<td>Xalatan, Timoptic, Lumigan</td>
<td>Travatan Z</td>
</tr>
<tr>
<td>Benozidecium bromide (BD)</td>
<td>Timoptic XE</td>
<td>Xalatan, Timoptic, Lumigan</td>
<td>Travatan Z</td>
</tr>
<tr>
<td>Chlorobutanol</td>
<td>Travatan Z</td>
<td>Timoptic XE</td>
<td>Travatan Z</td>
</tr>
<tr>
<td>Polyoquaternium-1 (Polyquad)</td>
<td>Travatan Z</td>
<td>Timoptic XE</td>
<td>Travatan Z</td>
</tr>
<tr>
<td>Sodium perborate (GenAqua)</td>
<td>Travatan Z</td>
<td>Timoptic XE</td>
<td>Travatan Z</td>
</tr>
<tr>
<td>Sustained oxychloro complex (SOC)</td>
<td>Travatan Z</td>
<td>Timoptic XE</td>
<td>Travatan Z</td>
</tr>
</tbody>
</table>
**BAK is a Common Preservative**

- Quaternary ammonium compound.
- Cationic surfactant properties (a detergent).
- In majority of ophthalmic medications (72%), ranging in concentrations from 0.004-0.02%.
- Preserves multi-dose containers from microbial contamination.
- Enhances corneal penetration of some drugs by causing epithelial separation.
- Efficacy impact on some drugs.

**Preservative Affect on Cornea**

- **Directly:**
  - Modifying anatomical and physiological the epithelium which affects optical properties and epithelial barrier function.

- **Indirectly:**
  - Modifying tear film leading to ocular non-wetting tear disorders

**Percent of Eye Drops Preserved with BAK**

- 28% BAK Preserved
- 72% Non BAK Preserved

**Preservatives in IOP-Lowering Medications**

<table>
<thead>
<tr>
<th>Generic (Trade Name)</th>
<th>Concentration/Preservative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brimonidine (Alphagan)</td>
<td>0.005% BAK</td>
</tr>
<tr>
<td>Brimonidine with Purse (Alphagan P)</td>
<td>0.005% SOC</td>
</tr>
<tr>
<td>Brinzolamide (Azopt)</td>
<td>0.01% BAK</td>
</tr>
<tr>
<td>Levobunolol (Belgan)</td>
<td>0.005% BAK</td>
</tr>
<tr>
<td>Betaxolol (Betoptic S Suspension)</td>
<td>0.01% BAK</td>
</tr>
<tr>
<td>Dorzolamide/Timolol (Cosopt)</td>
<td>0.0075% BAK</td>
</tr>
<tr>
<td>Bimatoprost (Lumigan)</td>
<td>0.005% BAK</td>
</tr>
<tr>
<td>Dose (Niscalu)</td>
<td>0.015% BAK</td>
</tr>
<tr>
<td>Timolol (Timoptic)</td>
<td>0.01% BAK</td>
</tr>
<tr>
<td>Timolol (Timoptic-XE)</td>
<td>0.012% BDD</td>
</tr>
<tr>
<td>Travoprost (Travatan)</td>
<td>0.015% BAK</td>
</tr>
<tr>
<td>Dorzolamide (Trusopt)</td>
<td>0.0035% BAK</td>
</tr>
<tr>
<td>Latanoprost (Xalatan)</td>
<td>0.02% BAK</td>
</tr>
</tbody>
</table>

**Preservatives in PGA's: 2011**

- **XALATAN** 0.02% BAK
- **LUMIGAN 0.01%** 0.02% BAK
- **LUMIGAN 0.03%** 0.005% BAK
- **TRAVATAN Z®** BAK Free soZia™

**When is BAK Use Most Problematic?**

- **High BAK Concentration:**
  - Cell Death is Dose-Dependent
  
  - High Concentration in a Single Drop or Due to The Accumulation of Dose With Multiple Drops.

  - Treatment of Chronic Ophthalmic Diseases, such as Glaucoma, with BAK Containing Medications.
    - Longer Duration of BAK Exposure → Increased Corneal Epithelial Cell Lysis.

  - **XALATAN®** package insert
  - **LUMIGAN®** package insert
  - **TRAVATAN Z®** package insert
  - Trademarks are the property of their respective owners.
BAK Impact on Ocular Surface Health

- Decreases Epithelial Cell Integrity.¹
  - Epithelial Barrier is Compromised.
  - Healing is Impaired.
- Increases Conjunctival Inflammatory Cells.¹
- Loss of Goblet Cells.¹
- Reduction in Tear Function.²
- Decreases Tear Film Break-up Time (TBUT).²


BAK Effect on Cornea

- BAK on Corneal Epithelial Surface
- Tear Film Instability
- Epithelial Damage
- Epithelial Cell Apoptosis
- Decrease MUC5A (gel forming mucin secreted by the goblet cells of the ocular surface)
- Increase ICAM (intracellular adhesion molecule for cell to cell adhesion: a marker for inflammation)

Dry Eye Work Shop 2007

"The single most critical advance in the treatment of dry eye came from the elimination of preservatives, such as benzalkonium chloride, from OTC lubricants."

BAK Adversely Affects TBUT in 30 Healthy Volunteers

- TBUT Pre/Post Single Drop
- Decrease from Baseline

 chronic Effect of Preservatives

- Patients treated >1 year with preserved latanoprost (21), preserved timolol (15) or unpreserved timolol (17) were compared to normals.
- Unpreserved timolol was similar to controls.
- Preserved latanoprost and preserved timolol with 0.02% BAK showed pro-inflammatory and pro-apoptotic effects but less than 0.02% BAK alone.
Is Chronic Exposure to BAK a Big Deal?

“The Single Most Critical Advance in the Treatment of Dry Eye Came with The Elimination of Preservatives, such as BAK from OTC Lubricants.”

Stephen Pflugfelder, MD

“BAK is Largely Responsible for the Ocular Toxicities and Inflammation Associated with the Chronic Use of Many Ophthalmic Solutions.”

Christoph Baudouin, MD, PhD

Factors Contributing to Preservative Toxicity

- Concentration.
- Frequency and duration of use.
- Tear production and clearance (blink rate and corneal sensitivity).
- Contact lens use.
- Number and type of concurrent medications.
- Type of preservative.

Implications for Glaucoma Therapy

- Chronic therapy with BAK preserved medications may:
  - Promote development of dry eye and OSD
  - Increase risk of:
    - Corneal complications: haze, infiltrates, ulcers.
    - Irritation symptoms.
    - Decreased functional vision.

Other Clinical Effects on Chronic Glaucoma Medications

- Decreased mucus layer of the tear film.
- Reduced tear secretion, basal Schirmer’s and TBUT.
- Increased Rose-Bengal staining of cornea.
- Foreshortening of the inferior conjunctival fornix.
- Inflammatory cell infiltration in trabecular meshwork.

Summary

- Do preserved glaucoma medications have a deleterious effect on superficial eye tissues? Yes
- Are preservatives like BAK deleterious? Yes
- Are the changes dose/time dependent? Yes
- Are the changes reversible? Probably
- Is it clinically important? In many patients

Experience with BAK-Free Glaucoma Medications

Human Clinical Data
Human Clinical Data

- **Purpose:** Examine the safety, tolerability, and efficacy of travoprost BAK-free compared to latanoprost or bimatoprost.
- **Methods:**
  - 694 POAG or OH patients treated with latanoprost or bimatoprost monotherapy who demonstrated a need for greater tolerability, and judged by the physician to be a good candidate, were changed to travoprost BAK-free ophthalmic solution and returned for a second visit 3 months later.
  - Prospective, multi-center, open-label, 3-month study with 2 visits (baseline and month 3).
  - Variables measured:
    - IOP
    - Ocular hyperemia grading
    - Global OSDI score
    - Visual acuity
    - Patient global preference
    - Slit-lamp biomicroscopy
    - Adverse events


OSDI Severity Grading

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<thead>
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<tr>
<td>33-100</td>
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<td></td>
<td></td>
<td>✓</td>
</tr>
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</table>

Total OSDI Score: (Sum of scores for all questions answered) x (25) 
(100) 

Mild

Normal

Severe


Compliance Component

- “A major cause of intolerance or poor tolerance to glaucoma medication is the ocular surface changes created by treatment.”

Non BAK PGA Options

- **Travatan Z**
  - SofZia Preservative

When TRAVATAN® Z solution comes in contact with the positively charged ions in the tear film, the ionic buffered preservative system becomes inactive, providing a solution that is safe and gentle on the eye.

**Bitmatoprost**

- Lumigan
  - 0.01
  - 0.02% BAK
  - 0.03%
  - 0.005% BAK

[Lumigan.com](http://www.lumigan.com)

**Latanoprost Generic**

- Latanoprost ophthalmic solution is supplied as a sterile, isotonic, buffered aqueous solution of latanoprost with a pH of approximately 6.7 and an osmolality of approximately 287 mOsm/kg.
- Each mL of latanoprost contains 50 micrograms of latanoprost. Benzalkonium chloride, 0.02%, is added as a preservative.
- The inactive ingredients are: sodium chloride, sodium dihydrogen phosphate monohydrate, disodium hydrogen phosphate anhydrous, and water for injection.

**Other Non-BAK Options for Glaucoma Patients with OSD**

- Alphagan P
  - Brimonidine PURITE® 0.1%
- PURITE® (stabilized oxychloro complex) is a preservative that is effective at low concentrations.


**PURITE® Is a Gentle Preservative**

- SEM of rabbit corneal epithelium (800X)
  - Untreated
  - PURITE® Qd 7 days
  - BAK Qd 7 days
  - The clinical significance of these data is unknown.

**New to USA (March 2012)**

Preservative Free PGA

- Zioptan
- Tafluprost 0.015%
- Merck
Zioptan: Efficacy

- **Clinical Trial:**
  - IOP reduced by 6.4 – 7.5 mmHg at 12 weeks
    - Baseline 23-26 mmHg
    - n=618
  - AJO June 2012

Multiple Clinical Trials

<table>
<thead>
<tr>
<th>Country</th>
<th>Patients</th>
<th>Prescription</th>
<th>Treatment</th>
<th>IOP reduction</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Japan</td>
<td>69 patients with POAG and CHG</td>
<td>Tafluprost 0.001%</td>
<td>1 drop a day</td>
<td>6.4 ± 3.0 mmHg</td>
<td>20</td>
</tr>
<tr>
<td>Japan</td>
<td>53 patients with POAG (converting POAG and CHG)</td>
<td>Tafluprost 0.001%</td>
<td>3 drops a day</td>
<td>5.1 ± 5.7 mmHg</td>
<td>See product overview - <a href="http://www.santen.com/download/pdf/tafluprost_PositionPaper.pdf">http://www.santen.com/download/pdf/tafluprost_PositionPaper.pdf</a></td>
</tr>
<tr>
<td>Japan</td>
<td>44 patients with HKG</td>
<td>Tafluprost 0.001%</td>
<td>1 drop a day</td>
<td>2.5 ± 4.6 mmHg</td>
<td>24</td>
</tr>
<tr>
<td>Europe</td>
<td>573 patients with POAG and CHG</td>
<td>Tafluprost 0.001%</td>
<td>1 drop a day</td>
<td>7.1 ± 7.2 mmHg</td>
<td>24</td>
</tr>
<tr>
<td>Italy</td>
<td>108 patients with POAG or CHG, reassessed by visual examination</td>
<td>Tafluprost 0.001%</td>
<td>1 drop a day</td>
<td>4.3 ± 2.7 mmHg</td>
<td>15</td>
</tr>
<tr>
<td>US, Spain</td>
<td>100 patients with POAG or CHG</td>
<td>Tafluprost 0.001%</td>
<td>1 drop a day</td>
<td>6.6 ± 2.7 mmHg</td>
<td>15</td>
</tr>
</tbody>
</table>

Zioptan Non-Clinical Data

- Tafluprost: less toxic than travoprost, latanoprost, or unoprostone.
  - Application of PF tafluprost at 5-minute intervals on 15 occasions had no toxic effects on the rabbit corneoconjunctival surface.

Zioptan vs. Latanoprost

- “Both treatments had a substantial IOP-lowering effect which persisted throughout the study.”
  - 7.1 mmHg for tafluprost
  - 7.7 mmHg for latanoprost
  - at 24 months

Multicenter Study

Conclusion

- Preservative-free tafluprost is a well tolerated hypotensive agent that can be used in eyes with surface problems and in naive eyes.
  - Br J Ophthalmol 2012; 96:826e831

Small Switch Study (2010)

Conclusion:

- Preservative-free tafluprost was better tolerated than the commercially available formulation of latanoprost.
- Patients (n=158) who were recruited to the study because exhibiting symptoms / signs of ocular surface side-effects.
- The drugs appeared to have equal IOP reducing effect.
Zioptan: Decreased Osmolarity
Switch from Latanoprost

![Graph showing decreased osmolarity over time.](image)

**Result/Finding:** Decreased dry eye complaints

<table>
<thead>
<tr>
<th>Week</th>
<th>Dry eye complaints</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>10% (10/90 patients)</td>
</tr>
<tr>
<td>Week 1</td>
<td>7% (1/14 patients)</td>
</tr>
<tr>
<td>Week 2</td>
<td>3% (1/30 patients)</td>
</tr>
<tr>
<td>Week 3</td>
<td>3% (1/30 patients)</td>
</tr>
<tr>
<td>Week 4</td>
<td>3% (1/30 patients)</td>
</tr>
</tbody>
</table>

TBUT (total break-up time) decrease was noted.

www.zioptan.com

Zioptan Cost Considerations

- Newly Introduced Medications are typically not available on Formularies
- Pharma. Discount Cards are available
- Brings Price down to approximately $49 for eligible patients (includes Medicare Part D!)

No Difference in OSD for 3 PGAs (3 months)

- Xalatan
  - 0.02% BAK
- Lumigan 0.03%
  - 0.005% BAK
- Travatan Z
  - Sofzia
- Graded:
  - Ocular Tolerability
  - TBUT
  - Hyperemia

Recent Cosopt PF articles

- dorzolamide HCL - timolol maleate 2%/0.5%
- Preservative Free
- BID dosing
- 25-30% IOP reduction when used as monotherapy
- Role: COPD and other beta blocker contraindications
- Similar indications for OSD patients where BAK toxicity is a concern

Cosopt PF

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http://cosoptpf.com/consumer/index.html
Another PF Option

- TIMOPTIC® in OCUDOSE® —
  - Preservative-free Sterile Ophthalmic Solution TIMOPTIC® is supplied in OCUDOSE®, a clear, individual, unit dose container
  - Valeant Pharmaceuticals
    - Patient Care Program

BAK in Other Meds

- Simbrinza — 0.003%
- Combigan — 0.005%
- Cosopt — 0.0075%
- Rescula — 0.015%
- Azopt — 0.01%
- Trusopt — 0.0075%
- Timolol sol — 0.01%

Other Non-BAK Options for Glaucoma Patients with OSD

- Alphagan P
  - Brimonidine PURITE® 0.1%
  - Higher pH 7.8
  - Lower Concentration
- PURITE®
  - stabilized oxychloro complex) is a preservative that is effective at low concentrations.

PURITE® Is a Gentle Preservative

SEM of rabbit corneal epithelium (800X)

My Typical Approach

- Glaucoma Patient
  - New or established
- History
  - Specific for dry eye symptoms
  - Questionnaire if necessary
- Thorough slit lamp
  - TBUT and Lissamine green
- With Positive Findings or Risk Factors
  - Review Medications and Treatment Options
  - Patient Education
  - Reduce the Preservative Load

Clinical Evaluation
Summary

• Do preserved glaucoma medications have a deleterious effect on superficial eye tissues? Yes
• Are preservatives like BAK deleterious? Yes
• Are the changes dose/time dependent? Yes
• Are the changes reversible? Probably
• Is it clinically important? In many patients, especially those with OSD.

Questions

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