Glaucoma Therapy Update

Murray Fingeret, OD
Chief, Optometry Section
Dept of Veterans Affairs NYHHCS Brooklyn, NY
Clinical Professor, SUNY Optometry
Disclosures

• Consultant
  • Alcon, Aerie Pharmaceuticals, Allergan, Bausch & Lomb, Carl Zeiss Meditec, Diopsys, Heidelberg Engineering, Reichert, Topcon
Glaucoma Therapy
An Overview

• Chronic disease that can be difficult to control
  • Person has the disease for the rest of their life
• Treatment often requires multiple medications and surgeries
• Treatment endpoints are poorly defined
• Treatment endpoints often difficult to achieve, even when defined
• Medication adherence challenges are common
  • Patients have difficulties taking medications for long periods of time
• Continuing need for new therapies and drug delivery techniques
What’s New and What’s Next in Glaucoma

• Therapy
  • Generics
  • Do glaucoma medications work around the clock
    • FDA does not require 24 hour testing
  • Fixed combination agents have moved up to 2\textsuperscript{nd} line agents
  • New glaucoma surgical devices such as Xen implant, Cypass, iStent
    • MIGS type devices
  • New Medications
  • New drug delivery devices
Glaucoma Therapy Update

• In future, similar to cardiologists we may discuss with our patients smoking cessation, altering diet, weight loss, and increased physical activity as additional therapies for glaucoma

• Many of the new therapies will revolve around drug delivery directly into the eye via some form of injection (doctor) or insertion (patient)
Glaucoma Therapy Update

- There are currently 5 main classes of IOP-lowering medications
- Each works by altering 1 or more aspects of aqueous humor flow
- Beta-blockers and carbonic anhydrase inhibitors reduce the rate of aqueous production
- Prostaglandins increase outflow through the uveoscleral pathway
- Alpha-adrenergic agonists lower IOP by a dual mechanism
  - reducing aqueous production and increasing uveoscleral outflow
- None of these drugs works at the site of outflow impairment—the TM
- Miotic class of drugs do increase trabecular outflow, but only indirectly through actions on the ciliary muscle
  - not through any direct effects on the TM itself
  - generally poorly tolerated and not widely used in modern practice
- There has been an unmet need for an IOP-lowering medication that works at the TM
  - the main site of outflow obstruction in glaucomatous eyes
Glaucoma Therapy Update

• Trend in topical eyedrop therapeutics is combination compounds with multiple targets and mechanisms of action (MOA) with single daily dosing
• Targets will include trabecular meshwork and uveoscleral outflow, aqueous humor production and episcleral venous pressure (EVP)
• Stem cell and gene therapy are being developed but are years away from clinical use
What about quadruple therapy?
How Can This Medication be Prescribed?

- Does the medication(s) work?
  - Little data to support its efficacy
- Made by compounding pharmacy but needs a prescription
- Need to order the medication by calling the pharmacy
- They can send it to your office, or can call patient, get credit card info and mail direct to patient
- Need to pay for medication at time of order
Quadruple Therapy

• We don't know anything about the side effect profile of putting those 4 medications together in one bottle

• And what about effectiveness?
  • Is there an added benefit of having the 4 medications together compared to just 3 of them.... or even just two of them
  • We have seen that adding timolol to a prostaglandin in the same bottle really does not add any effectiveness to the prostaglandin alone
    • hence the lack of FDA approval of Xalcom, DuoTrav and Ganfort

• And how would you dose this?
  • There are two bid-tid medications, and two once a day medications in the same bottle

• Adherence should improve
## Topical Glaucoma Treatments

<table>
<thead>
<tr>
<th>BRAND NAME/ MNFR</th>
<th>GENERIC NAME</th>
<th>CONCENTRATION/ BOTTLE SIZE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Beta Blockers</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Betagan/Allergan</td>
<td>levobunolol HCL</td>
<td>0.25% - 5mL, 10mL; 0.5% - 2mL, 5mL, 10mL, 15mL</td>
</tr>
<tr>
<td>Betimol/Vistakon</td>
<td>timolol hemihydrate</td>
<td>0.25% - 5mL; 0.5% - 5mL, 10mL, 15mL</td>
</tr>
<tr>
<td>Betoptic-S/Alcon</td>
<td>betaxaolol HCL</td>
<td>0.25% - 2.5mL, 5mL, 10mL, 15mL</td>
</tr>
<tr>
<td>Istalol/Ista</td>
<td>timolol maleate</td>
<td>0.5% - 5mL</td>
</tr>
<tr>
<td>Timoptic/Aton Pharma</td>
<td>timolol maleate</td>
<td>0.25% - 5mL, 10mL, 15mL; 0.5% - 5mL, 10mL, 15mL</td>
</tr>
<tr>
<td>Timoptic (preservative-free)/Aton Pharma</td>
<td>timolol maleate</td>
<td>0.25% - unit dose; 0.5% - unit dose</td>
</tr>
<tr>
<td>Timoptic-XE/Aton Pharma</td>
<td>timolol maleate</td>
<td>0.25% - 2.5mL, 5mL; 0.5% - 2.5mL, 5mL</td>
</tr>
<tr>
<td><strong>Prostaglandin Analogs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lumigan/Allergan</td>
<td>bimatoprost</td>
<td>0.01% - 2.5mL, 5mL, 7.5mL</td>
</tr>
<tr>
<td>Rescula/Sucampo</td>
<td>unoprostone</td>
<td>0.15% - 2.5mL, 5mL</td>
</tr>
<tr>
<td>Travatan Z/Alcon</td>
<td>travoprost</td>
<td>0.004% - 2.5mL, 5mL</td>
</tr>
<tr>
<td>Generic</td>
<td>latanoprost</td>
<td>0.005% - 2.5mL</td>
</tr>
<tr>
<td>Zioptan/Merck</td>
<td>tafluprost</td>
<td>2.5mL</td>
</tr>
<tr>
<td><strong>Prostaglandin + Nitric Oxide</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vyzulta/Bausch + Lomb</td>
<td>latanoprostene Bunod</td>
<td>0.024% - 5 mL</td>
</tr>
<tr>
<td><strong>Prostaglandin + Rhopressa</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rocklatan/Aerie</td>
<td>Latanoprost + netarsudil</td>
<td>0.005% + 0.02% - 2.5 mL</td>
</tr>
</tbody>
</table>
## Topical Glaucoma Treatments

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<thead>
<tr>
<th>BRAND NAME/ MNFR</th>
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<th>CONCENTRATION/ BOTTLE SIZE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alpha Agonists</strong>&lt;br&gt;Generic</td>
<td>brimonidine</td>
<td>0.1%, 0.15% - 5mL, 10mL, 15mL</td>
</tr>
<tr>
<td><strong>Alphagan P/Allergan</strong></td>
<td>brimonidine</td>
<td>0.1%, 0.15% - 5mL, 10mL, 15mL</td>
</tr>
<tr>
<td><strong>Iopidine/Alcon</strong></td>
<td>apraclonidine</td>
<td>0.5% - 5mL, 10mL; 1% - unit dose</td>
</tr>
<tr>
<td><strong>Carbonic Anhydrase Inhibitors</strong>&lt;br&gt;Azopt/Alcon</td>
<td>brinzolamide</td>
<td>1% - 5mL, 10mL, 15mL</td>
</tr>
<tr>
<td><strong>Trusopt/Merck</strong></td>
<td>dorzolamide</td>
<td>2% - 5mL, 10mL</td>
</tr>
<tr>
<td><strong>Rho kinase Inhibitors (ROCK inhibitor)</strong>&lt;br&gt;Rhopressa/Aerie</td>
<td>Netarsudil</td>
<td>0.02% - 2.5mL</td>
</tr>
<tr>
<td><strong>Combination Glaucoma Medications</strong>&lt;br&gt;Combigan/Allergan</td>
<td>brimonidine/timolol</td>
<td>0.2%/0.5% - 5mL, 10mL</td>
</tr>
<tr>
<td><strong>Simbrinza/Alcon</strong></td>
<td>Brinzolamide/brimonidine</td>
<td>1%/0.2% - 8 mL</td>
</tr>
<tr>
<td><strong>Cosopt PF/Merck Generic</strong></td>
<td>dorzolamide/timolol</td>
<td>2%/0.5% - 5mL, 10mL</td>
</tr>
</tbody>
</table>
New Drugs

• Latanoprost bunod
  • Approved November 2017
  • Nitric oxide donating Prostaglandin F2α
  • Vyzulta Bausch & Lomb

• Rho Kinase Inhibitors
  • Approved December 2017
  • Netarsudil 0.02%
  • Rhopressa
  • Aerie

• Rho Kinase Inhibitors and latanoprost
  • Rocklatan
  • Aerie
  • March 2019

• Lumigan SR
  • Sustained release bimatoprost implant
  • Phase III

• OTX-TP
  • Sustained release travoprost punctal plug
  • Ocular Therapeutix

• Xelpros (latanoprost BAK-free eye drops)
  • Sun Ophthalmics
  • 1st quarter 2018
  • Multi-dose PF bottle
Latanoprostone bunod (Vyzulta)

- 0.024% used once daily to reduced IOP
  - Bausch & Lomb
  - Waiting for FDA approval
- Metabolized to latanoprost acid plus butanediol mononitrate
- Butanediol mononitrate is a nitric-oxide donating moiety NO molecule attached to latanoprost backbone to provide dual action
- Works over 24 hour period with >35% IOP reduction
- One molecule leads to IOP reduction via the uveoscleral and trabecular meshwork pathways

- NO is a signaling molecule that regulates outflow facility via the TM
- Can dilate blood vessels
- Modulates TM contractility, cell adhesion and the cytoskeleton leading to reduced IOP
- Medication acts on both the
  - Uveoscleral outflow pathway by altering the extracellular matrix in the ciliary muscle and the sclera
  - Trabecular meshwork outflow by inhibiting actomyosin contractility in trabecular meshwork cells thereby relaxing the meshwork
A randomised, controlled comparison of latanoprostene bunod and latanoprost 0.005% in the treatment of ocular hypertension and open angle glaucoma: the VOYAGER study

Robert N Weinreb, Tuyen Ong, Baldo Scassellati Sforzolini, Jason L Vittitow, Kuldev Singh and Paul L Kaufman

Br J Ophthalmol published online December 8, 2014

Phase II

In conclusion, LBN 0.024% dosed once daily was the lower of the two most effective LBN doses evaluated with significantly greater IOP lowering compared with latanoprost 0.005% solution. To the best of our knowledge, this is the first phase II study that demonstrates a drug that is more effective for IOP lowering, without increased ocular hyperaemia and with comparable overall side effects, than the commercially available latanoprost 0.005% solution.

ABSTRACT

Aim To assess the efficacy and safety of latanoprostene bunod (LBN) compared with latanoprost 0.005%, and to determine the optimum drug concentration(s) of LBN in reducing intraocular pressure (IOP) in subjects with open angle glaucoma or ocular hypertension.

Methods Randomised, investigator-masked, parallel-group, dose-ranging study. Subjects instilled one drop of study medication in the study eye once daily each evening for 28 days and completed five study visits. The primary efficacy endpoint was the reduction in mean diurnal IOP at Day 28.

Results Of the 413 subjects randomised (LBN 0.006%, n=82; LBN 0.012%, n=85; LBN 0.024%, n=83; LBN 0.040%, n=81; latanoprost, n=82), 396 subjects completed the study. Efficacy for LBN was dose-dependent reaching a plateau at 0.024%–0.040%. LBN 0.024% led to significantly greater reductions in diurnal IOP compared with latanoprost at the primary endpoint, Day 28 (p<0.005), as well as Days 7 (p=0.033) and 14 (p=0.015). The incidence of adverse events, mostly mild and transient, was numerically higher in the LBN treatment groups compared with the latanoprost group. Hyperaemia was similar across treatments.

Conclusions LBN 0.024% dosed once daily was the lower of the two most effective concentrations evaluated, with significantly greater IOP lowering and comparable side effects relative to latanoprost 0.005%. LBN dosed once daily for 28 days was well tolerated.

Clinical trial number NCT01223378.
Latanoprostene Bunod 0.024% versus Timolol Maleate 0.5% in Subjects with Open-Angle Glaucoma or Ocular Hypertension

The APOLO Study

Robert N. Weinreb, MD,1 Baldo Scassellati Sforzolini, PhD,2 Jason Vittitow, PhD,2 Jeffrey Liebmann, MD3

Purpose: To compare the diurnal intraocular pressure (IOP)-lowering effect of latanoprostene bunod (LBN) ophthalmic solution 0.024% every evening (qPM) with timolol maleate 0.5% twice daily (BID) in subjects with open-angle glaucoma (OAG) or ocular hypertension (OHT).

Design: Phase 3, randomized, controlled, multicenter, double-masked, parallel-group clinical study.

Participants: Subjects aged ≥18 years with a diagnosis of OAG or OHT in 1 or both eyes.

Methods: Subjects were randomized (2:1) to a 3-month regimen of LBN 0.024% qPM or timolol 0.5% 1 drop BID. Intraocular pressure was measured at 8 AM, 12 PM, and 4 PM of each postrandomization visit (week 2, week 6, and month 3). Adverse events were recorded throughout the study.

Main Outcome Measures: The primary efficacy end point was IOP in the study eye measured at each of the 9 assessment time points. Secondary efficacy end points included the proportion of subjects with IOP ≤18 mmHg consistently at all 9 time points and the proportion of subjects with IOP reduction ≥25% consistently at all 9 time points.

Results: Of 420 subjects randomized, 387 completed the study (LBN 0.024%, n = 264; timolol 0.5%, n = 123). At all 9 time points, the mean IOP in the study eye was significantly lower in the LBN 0.024% group than in the timolol 0.5% group (P ≤ 0.002). At all 9 time points, the percentage of subjects with mean IOP ≤18 mmHg and the percentage with IOP reduction ≥25% were significantly higher in the LBN 0.024% group versus the timolol 0.5% group (mean IOP ≤18 mmHg: 22.9% vs. 11.3%, P = 0.005; IOP reduction ≥25%: 34.9% vs. 19.5%, P = 0.001). Adverse events were similar in both treatment groups.

Conclusions: In this phase 3 study, LBN 0.024% qPM demonstrated significantly greater IOP lowering than timolol 0.5% BID throughout the day over 3 months of treatment. Latanoprostene bunod 0.024% was effective and safe in these adults with OAG or OHT. Ophthalmology 2016;119:1–9 © 2016 by the American Academy of Ophthalmology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
Efficacy of Latanoprostene Bunod 0.024% Compared With Timolol 0.5% in Lowering Intraocular Pressure Over 24 Hours

JOHN H.K. LEE, JOHN R. SigHt, JASON L. VITTITOW, BALDO SCASSELLATI SFORZOLINI, AND ROBERT N. WEINREB

PURPOSE: To compare the diurnal and nocturnal effects of latanoprostene bunod 0.024% solution with timolol maleate 0.5% solution on intraocular pressure (IOP) and ocular perfusion pressure.

METHODS: Prospective, open-label randomized crossover trial.

RESULTS: Twenty-five patients (aged 43–82 years) with ocular hypertension or early primary open-angle glaucoma were enrolled. Baseline IOP and blood pressure were measured in a sleep laboratory every 2 hours in the sitting and supine positions during the 16-hour diurnal/wake period and in the supine position during the 8-hour nocturnal/sleep period. Subjects were randomly assigned to bilateral treatments of latanoprostene bunod at 8 PM or timolol at 8 AM and 8 PM. The second laboratory recording occurred after the 4-week treatment. Subjects were crossed over to the comparator treatment for 4 weeks before the third laboratory recording. Mean IOP and calculated ocular perfusion pressure were compared for the diurnal and nocturnal periods.

RESULTS: Twenty-one subjects completed the study. Both treatments reduced diurnal sitting and supine IOP compared to baseline by 2.3–3.9 mm Hg (all P < .05) with no statistically significant difference between the 2 treatments. Nocturnal IOP under latanoprostene bunod treatment was 2.5 ± 3.1 mm Hg (mean ± SD) less than baseline (P = .002) and 2.3 ± 3.0 mm Hg less than timolol treatment (P = .024). Latanoprostene bunod treatment resulted in greater diurnal sitting and supine ocular perfusion pressures compared with baseline (P ≤ .006) and greater nocturnal ocular perfusion pressure compared with timolol treatment (P = .010).

CONCLUSIONS: During the nocturnal period, latanoprostene bunod caused more IOP reduction and more increase of ocular perfusion pressure than timolol. (Am J Ophthalmol 2016;162:71-76. © 2016 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license [http://creativecommons.org/licenses/by-nc-nd/4.0/].)

Lowering intraocular pressure (IOP) may delay the onset of glaucoma in ocular hypertensive patients and slow the disease progression in patients with existing glaucoma.1 Whereas the highest IOP in patients with ocular hypertension and primary open-angle glaucoma frequently occur outside the diurnal/wake period,1,2 currently available topical medications to treat these patients have shown variable IOP-lowering efficacies during the nocturnal/sleep period compared to their diurnal efficacies.3-10 Prostaglandin analogues (including latanoprost, travoprost, and bimatoprost) applied once daily in the evening were shown to be effective in lowering IOP for 24 hours, but with less nocturnal efficacy than the diurnal efficacy.3,4,11 Timolol, a beta-adrenergic antagonist, applied in gel form once daily in the morning had very limited IOP reduction during the nocturnal period compared to its diurnal efficacy.11,12 Latanoprostene bunod (Bausch & Lomb, Bridgewater, New Jersey, USA) is a new nitric oxide-donating prostaglandin F2α analogue with unique biological properties. In vitro, latanoprostene bunod is rapidly metabolized to latanoprost acid, a prostaglandin agonist, and butanediol mononitrate, a nitric oxide (NO)-donating moiety.13 Latanoprost acid (as the active moiety of latanoprost 0.005% [Xalatan Pfizer, New York, NY]) is reported to reduce IOP by primarily increasing aqueous outflow.12,13 In contrast, NO released from the NO-donating moiety of latanoprostene bunod may lower IOP by increasing the trabecular meshwork outflow.12,13 Nitric oxide is also a biological messenger for other physiological functions, including vasodilation and, on systemic administration, a reduction of blood pressure.14

A recent report showed that latanoprostene bunod was well tolerated and efficacious in lowering IOP in patients with primary open-angle glaucoma or ocular hypertension.15 There was a dose-dependent reduction in diurnal IOP over 28 days at concentrations of 0.006% to 0.04%, reaching a maximum effect with the 0.024% and 0.04%...
New Medication
Rho Kinase Inhibitors

• Rho kinase inhibitors - Rhopressa
• Reduce cellular stiffness in trabecular meshwork
  • Target trabecular meshwork cells to enhance outflow
  • May offer neuroprotective as well as anti-inflammatory effects
• Approved December 2017
• Aerie
Rho Kinase Inhibitors as a Novel Treatment for Glaucoma and Ocular Hypertension

Angelo P. Tanna, MD,1 Mark Johnson, PhD1,2,3

In an elegant example of bench-to-bedside research, a hypothesis that cells in the outflow pathway actively regulate conventional outflow resistance was proposed in the 1990s and systematically pursued, exposing novel cellular and molecular mechanisms of intraocular pressure (IOP) regulation. The critical discovery that pharmacologic manipulation of the cytoskeleton of outflow pathway cells decreased outflow resistance placed a spotlight on the Rho kinase pathway that was known to regulate the cytoskeleton. Ultimately, a search for Rho kinase inhibitors led to the discovery of several molecules of therapeutic interest, leaving us today with 2 new ocular hypotensive agents approved for clinical use: ripasudil in Japan and netarsudil in the United States. These represent members of the first new class of clinically useful ocular hypotensive agents since the US Food and Drug Administration approval of latanoprost in 1996. The development of Rho kinase inhibitors as a class of medications to lower IOP in patients with glaucoma and ocular hypertension represents a triumph in translational research. Rho kinase inhibitors are effective alone or when combined with other known ocular hypotensive medications. They also offer the possibility of neuroprotective activity, a favorable impact on ocular blood flow, and even an antifibrotic effect that may prove useful in conventional glaucoma surgery. Local adverse effects, however, including conjunctival hyperemia, subconjunctival hemorrhages, and cornea verticillata, are common. Development of Rho kinase inhibitors targeted to the cells of the outflow pathway and the retina may allow these agents to have even greater clinical impact. The objectives of this review are to describe the basic science underlying the development of Rho kinase inhibitors as a therapy to lower IOP and to summarize the results of the clinical studies reported to date. The neuroprotective and vasoactive properties of Rho kinase inhibitors, as well as the antifibrotic properties, of these agents are reviewed in the context of their possible role in the medical and surgical treatment of glaucoma. Ophthalmology 2018;11-16 © 2018 by the American Academy of Ophthalmology
New Glaucoma Medications

• Aerie Pharmaceuticals
  • Two compounds
    • Dual action Rho kinase (ROCK) + norepinephrine transport (NET) inhibitor (Netarsudil 0.02%) - Rhopressa
      • AR-13324 lowers IOP by enhance outflow through TM (ROCK) and inhibit aqueous production (NET)
      • Also believed to reduce episcleral venous pressure which may allow it to better reduce IOP when it is below 21 mm Hg
    • Triple action ROCK + NET + latanoprost (Rocklatan)
      • PG324 fixed combination of AR-13324 and latanoprost
        • Additional IOP reduction through uveoscleral outflow
  • Both agents are once per day dosage
  • Hyperemia is most common side effect found in studies to date
Rocklatan

• Combination of Rhopressa with latanoprost
• Dosed once daily with significant IOP lowering
• Few systemic side effects
• Limited ocular side effects
Safety/Tolerability Overview of Rocklatan™

- There were no drug-related serious adverse events (SAEs).
- The most common adverse event was conjunctival hyperemia with ~50% incidence*, the majority mild on biomicroscopy.
- Other ocular AEs:
  - AEs occurring in ~5-11% of subjects receiving Rocklatan™ included: conjunctival hemorrhage, eye pruritus, lacrimation increased and cornea verticillata.

* Incidence of conjunctival hyperemia ~50% including baseline at ~20%
Rocklatan™ Phase 3 Safety Profile

<table>
<thead>
<tr>
<th>Adverse Events (≥5.0% in any group)</th>
<th>Rocklatan™ n=238</th>
<th>Rhopressa™ n=244</th>
<th>Latanoprost n=236</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Eye Disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conjunctival Hyperemia</td>
<td>126 (52.9%)</td>
<td>99 (40.6%)</td>
<td>33 (14.0%)</td>
</tr>
<tr>
<td>Conjunctival Hemorrhage</td>
<td>25 (10.5%)</td>
<td>34 (13.9%)</td>
<td>1 (0.4%)</td>
</tr>
<tr>
<td>Eye Pruritus</td>
<td>18 (7.6%)</td>
<td>17 (7.0%)</td>
<td>3 (1.3%)</td>
</tr>
<tr>
<td>Lacrimation Increased</td>
<td>14 (5.9%)</td>
<td>15 (6.1%)</td>
<td>1 (0.4%)</td>
</tr>
<tr>
<td>Cornea Verticillata</td>
<td>12 (5.0%)</td>
<td>9 (3.7%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td><strong>Administration Site Conditions</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Instillation site pain</td>
<td>45 (18.9%)</td>
<td>51 (20.9%)</td>
<td>15 (6.4%)</td>
</tr>
</tbody>
</table>

Patients with known contraindications or hypersensitivity to latanoprost were excluded.
Rocklatan™ Summary

- Demonstrated superiority over both latanoprost and Rhopressa™ for the primary efficacy analysis at all 9 time points (p<0.0001)

- IOP-lowering effect was greater (1-3 mmHg) than monotherapy with either latanoprost or Rhopressa™ throughout the duration of the study

- There were no drug-related serious adverse events

- The main adverse event was conjunctival hyperemia, ~50% of patients and was scored as mild for the large majority of these patients
Xelpros emulsion

• While Xelpros® does NOT contain BAK, it is preserved with potassium sorbate
• XELPROS (latanoprost ophthalmic emulsion) 0.005% is a sterile, isotonic, buffered aqueous emulsion of latanoprost with a pH approximately 7.0 and an osmolality of approximately 375mOsmol/kg
• Each mL of XELPROS contains 50 micrograms of latanoprost
• Potassium sorbate 0.47% is added as a preservative.
• Sun Pharma in-licensed XELPROS™ from SPARC in June 2015
• Developed using SPARC’s proprietary Swollen Micelle Microemulsion (SMM) technology
  • helps to solubilize drugs that have limited or no solubility
  • eliminating the need for benzalkonium chloride (BAK)