Rapid Fire Rounds: Treatment Glaucoma 2019

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Distinguished Alumnus

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Clinical Professor
Ocular Health Clinic

WATERLOO
OPTOMETRY & VISION SCIENCE
optometry.uwaterloo.ca
disclosures

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Carl Zeiss Meditec

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Are we ready?
Optometry and Vision Science Research Guide: Find Articles

Research resources and information for vision science.

Vision Specific Databases

These databases contain citation information (title, author, journal, volume, issue, page and associated index terms) for academic research articles on optometry and vision science. Click on the Get it@Waterloo button for the full text article.

- Contact Lens Update
  A contact lens specific resource that includes articles from experts, highlights from major contact lens meetings, clinical images, and videos of complications.
- VisionCite
- VisionNet

Systems (Point-of-Care Tools)

- UpToDate
  How to Cite UpToDate example:
  Marion DW. Diaphragmatic pacing. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on November 25, 2013.)

- RxTx (e-version of CPS, CTC, CTMA, CPMA)
  Use RxTx as a Point-of-Care tool. Refer to the therapeutics found within the CTC and CTMA.

http://subjectguides.uwaterloo.ca/optometry
Optometry Research Guide

Research resources and information for vision science.

Search Strategies

To find resources on Ocular Pharmacology, search for subject headings "in the subject" field in our catalogue. Sort the results by date to view the most current.

Subject Headings in our Catalogue

- Drug interactions
- Ocular pharmacology
- Ophthalmic drugs
- Therapeutics, ophthalmological

Library Resources for Drug Information

- RxTx (formerly: e-CPS & e-Therapeutics)
  RxTx is the new platform for e-Therapeutics+. It is a comprehensive drug information resource produced by the Canadian Pharmacists Association. Access e-CPS, Therapeutic Choices, drug interactions via Lexi-Interact, and patient information. 18 users.

- Lexicomp
  Interactions, drug identification, intravenous compatibility, patient education, toxicology, and calculators. Includes access to AHFS Drug Information (DI) and AHFS Essentials. Drug content is updated on a monthly basis. Unlimited users.

- Merck Index
  Data for chemicals, drugs, and biological substances.

- Burger's Medicinal Chemistry and Drug Discovery
  Provides a well recognized, authoritative and comprehensive source on medicinal chemistry and drug development

- Access Pharmacy
  A resource for pharmacy education. Searches across 20+ pharmacy and medical online references. Includes functional calculators, lab test information, and an integrated drug database

- Natural Standard
  An international research collaboration that systematically reviews scientific evidence on complementary and alternative medicine

- Contact Lens Compendium Contact Lenses & Solutions Available in Canada
  A collection of case reports, fitting techniques, abstracts, review papers and listing of new contact lens materials

Drug Information Websites

- Health Canada: Drugs and Health Products
- Health Canada: Adverse Reaction Database
- Health Canada: Drug Product Database
- Ontario Drug Benefit Formulary/Comparative Drug Index
- IntelHealth
- Drug Information Portal (United States National Library of Medicine)
- US. Food and Drug Administration. Center for Drug Evaluation and Research
- Medline Plus Drug Information
- Medscape
- ePocrates
- Motherisk (Toronto Hospital for Sick Children)
Critical Resources

1. Look up drugs in CPS / RxTx and in LEXICOMP (drug interactions)

2. Find out what is available in Canada (watch if it is up to date)

3. Find out what is covered in your own provincial plan (link at left is ODB in Ontario)

4. **Motherisk!** – essential resource for use of ALL drug diagnostics and therapeutics in pregnancy and breastfeeding
What is the Drug Product Database (DPD)?

The DPD contains product specific information on drugs approved for use in Canada. The database is managed by Health Canada and includes human pharmaceutical and biological drugs, veterinary drugs, radiopharmaceutical drugs and disinfectant products. It contains approximately 47,000 products that are currently approved, marketed or cancelled.

Human, veterinary, disinfectants and Schedule C drugs (e.g. radiopharmaceutical products) approved products will be available in the DPD online at the time of authorization, with the exception of three monographed product groups under Division 1, Part C of the Food and Drug Regulations: sunscreen (sunscreens, lipstick making a SPF claim, cosmetic-like products with sunscreen claims, etc.), anti-dandruff shampoo, and hard surface disinfectants. For these products, applications filed after June 15, 2015, there may be a six month delay after approval for the inclusion in the DPD online.

Health Canada is the federal regulator of therapeutic products and does not provide medical advice on the use of the products identified in this database. For information related to treatment options, choices of medications and their uses, illnesses, side effects or drug interactions, please contact your health care professional. For information on where these products are sold, please contact the individual company directly.

Information Regarding the DPD Online Query

Additional information regarding the DPD online query:
- the data found in the DPD online query is updated nightly;
- use the Search Tips to help navigate the database;
- use the Terminology to get an understanding of the words used in the DPD online query;
- use the Data Extracts to download the content of the DPD online query;
- the Frequently Asked Questions document is intended to provide readers with a better understanding of Health Canada-authorized Product Monographs (PMs).

Please note that, products that were discontinued prior to 1996 are not available in this database.

For general questions about the contents of the DPD contact: The Office of Submissions and Intellectual Property

For technical support about the database contact: DPD Data Administrator

Related Resources

- Natural Health Products Directorate (NHPD)
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<th>Company</th>
<th>Product</th>
<th>Class</th>
<th>PM</th>
<th>Schedule</th>
<th>#</th>
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<td>Prescription</td>
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<td>Prescription</td>
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<td>Prescription</td>
<td>1</td>
<td>LATANOPROST</td>
<td>50 MCG / ML</td>
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<td>PHARMASCIENCE INC</td>
<td>PMS-LATANOPROST</td>
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<td>RIVA-LATANOPROST</td>
<td>Human</td>
<td>Yes</td>
<td>Prescription</td>
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<td>2</td>
<td>LATANOPROST</td>
<td>50 MCG / ML</td>
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Beta-adrenergic Blocking Agents


Anti-anginal—Antiarrhythmic—Antihypertensive—Heart Failure Agent—Migraine Prophylaxis—Post-myocardial Infarction

CPhA Monograph

Date of Revision: February 2014

This monograph has been compiled by CPhA and reviewed by experts. It may contain information different from that found in Health Canada-approved Product Monographs. The reader is referred to the CPS Editorial Policy for more information.
<table>
<thead>
<tr>
<th>Name</th>
<th>Benefit</th>
<th>Format(s)</th>
<th>Product Subcategory</th>
<th>Generic Available</th>
<th>Years and Up</th>
<th>Discontinued</th>
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<tr>
<td>Acetazolamide (Generic) [US Name: Diamox]</td>
<td>X</td>
<td></td>
<td>Glaucoma Agents</td>
<td>Yes</td>
<td></td>
<td></td>
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<tr>
<td>Alphagan P (Allergan) [brimonidine tartrate 0.15% solution]</td>
<td>*</td>
<td>FORMAT(S)...</td>
<td>Glaucoma Agents</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Azarga (Alcon) [brinzolamide 1% with timolol 0.50% suspension]</td>
<td>*</td>
<td>PRESERVATIVE-FREE...</td>
<td>Glaucoma Agents</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Azopt (Alcon) [brinzolamide 1% suspension]</td>
<td>*</td>
<td></td>
<td>Glaucoma Agents</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Betagan (Allergan) [levobunolol hydrochloride 0.5% solution (branded), 0.25% &amp; 0.5% solution (generic)]</td>
<td>*</td>
<td></td>
<td>Glaucoma Agents</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Betoptic S (Alcon) [betaxolol hydrochloride 0.25% suspension]</td>
<td>*</td>
<td></td>
<td>Glaucoma Agents</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brimonidine (Generic) [brimonidine 0.2% solution]</td>
<td>*</td>
<td></td>
<td>Glaucoma Agents</td>
<td>Yes</td>
<td></td>
<td></td>
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Subcategory: Oral Carbonic Anhydrase Inhibitors, Alpha Agonists, Combination Agents, Topical Carbonic Anhydrase inhibitors, Beta-Blockers, Alpha Agonists
### Prostanoids/Prostaglandins

<table>
<thead>
<tr>
<th>Drug</th>
<th>Year</th>
<th>Concentration</th>
<th>Brand Name</th>
<th>Dosing</th>
<th>Bottle Size</th>
<th>Preservative</th>
</tr>
</thead>
<tbody>
<tr>
<td>latanoprost (ester)</td>
<td>1996</td>
<td>0.005%</td>
<td>XALATAN (and generics)</td>
<td>QD (hs)</td>
<td>2.5 mL</td>
<td>BAK</td>
</tr>
<tr>
<td>travoprost (ester)</td>
<td>2001</td>
<td>0.004%</td>
<td>TRAVATAN Z (and generics)</td>
<td>QD (hs)</td>
<td>2.5 mL</td>
<td>BAK</td>
</tr>
<tr>
<td>travoprost (ester)</td>
<td>2002</td>
<td>0.004%</td>
<td>LUMIGAN (and generics)</td>
<td>QD (hs)</td>
<td>3 mL</td>
<td>BAK</td>
</tr>
<tr>
<td>bimatoprost (amide)</td>
<td>2002</td>
<td>0.03%</td>
<td>LUMIGAN RC</td>
<td>QD (hs)</td>
<td>3 mL</td>
<td>0.005% BAK</td>
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<tr>
<td>bimatoprost (amide)</td>
<td>2012</td>
<td>0.01%</td>
<td>ZIOPTAN (US) or SAFLUTAN (elsewhere)</td>
<td>QD (hs)</td>
<td>10 x 0.3mL/vial</td>
<td>PF</td>
</tr>
<tr>
<td>tafluprost (ester)</td>
<td>2012</td>
<td>0.0015%</td>
<td>TIMOPTIC (and generics)</td>
<td>QD (am)</td>
<td>5, 10 mL</td>
<td>BAK</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Timoptic XE (q.d. dosing)</td>
<td>QD (am)</td>
<td>5 mL (GEL); OCUDOSE PLUS</td>
<td>benzododecimium bromide 0.012%</td>
</tr>
<tr>
<td>levobunolol</td>
<td>1978</td>
<td>0.25%</td>
<td>BETAGAN (and generics)</td>
<td>QD (am)</td>
<td>5, 10, 15 mL</td>
<td>BAK</td>
</tr>
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</table>

### Beta-Adrenoceptor Blocking Agents (non-selective; β1 & β2)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Year</th>
<th>Concentration</th>
<th>Brand Name</th>
<th>Dosing</th>
<th>Bottle Size</th>
<th>Preservative</th>
</tr>
</thead>
<tbody>
<tr>
<td>timolol</td>
<td>1978</td>
<td>0.25%, 0.5%</td>
<td>TIMOPTIC (and generics)</td>
<td>QD (am)</td>
<td>5, 10 mL</td>
<td>BAK</td>
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<tr>
<td></td>
<td></td>
<td>0.25%, 0.5%</td>
<td>Timoptic XE (q.d. dosing)</td>
<td>QD (am)</td>
<td>5 mL (GEL); OCUDOSE PLUS</td>
<td>benzododecimium bromide 0.012%</td>
</tr>
<tr>
<td>levobunolol</td>
<td>1998</td>
<td>0.5%</td>
<td>Betoptic S</td>
<td>BID</td>
<td>Susp 5, 10 mL</td>
<td>BAK</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.5%</td>
<td>(generics only)</td>
<td>BID</td>
<td>BAK</td>
<td></td>
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</table>

### Beta-Adrenoceptor Blocking Agents (cardioselective; β1)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Year</th>
<th>Concentration</th>
<th>Brand Name</th>
<th>Dosing</th>
<th>Bottle Size</th>
<th>Preservative</th>
</tr>
</thead>
<tbody>
<tr>
<td>betaxolol</td>
<td>1998</td>
<td>0.25%</td>
<td>Propine (and generics)</td>
<td>BID</td>
<td>10, 15 mL</td>
<td>BAK</td>
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<tr>
<td></td>
<td></td>
<td>0.5%</td>
<td>(generic concentrations)</td>
<td>TID (or BID if adding)</td>
<td>5, 10, 15 mL</td>
<td>Purite BAK</td>
</tr>
</tbody>
</table>

### Adrenominetics Alpha₂-selective Adrenergic Agonists (note: non-selective epinephrine, dipivefrin not used)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Year</th>
<th>Concentration</th>
<th>Brand Name</th>
<th>Dosing</th>
<th>Bottle Size</th>
<th>Preservative</th>
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</thead>
<tbody>
<tr>
<td>apraclonidine</td>
<td>1994</td>
<td>0.5%</td>
<td>Propine (and generics)</td>
<td>BID</td>
<td>10, 15 mL</td>
<td>BAK</td>
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<tr>
<td></td>
<td></td>
<td>1.0%</td>
<td>(generic concentrations)</td>
<td>TID (or BID if adding)</td>
<td>5, 10, 15 mL</td>
<td>Purite BAK</td>
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<tr>
<td>brimonidine</td>
<td>1996</td>
<td>0.15%</td>
<td>ALPHA AGAN-P (Canada)</td>
<td>TID (or BID if adding)</td>
<td>5, 10, 15 mL</td>
<td>Purite BAK</td>
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<tr>
<td></td>
<td></td>
<td>0.2%, 0.15%</td>
<td>(generic concentrations)</td>
<td>TID (or BID if adding)</td>
<td>5, 10, 15 mL</td>
<td>Purite BAK</td>
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### Carbonic Anhydrase Inhibitors – Topical

<table>
<thead>
<tr>
<th>Drug</th>
<th>Year</th>
<th>Concentration</th>
<th>Brand Name</th>
<th>Dosing</th>
<th>Bottle Size</th>
<th>Preservative</th>
</tr>
</thead>
<tbody>
<tr>
<td>dorzolamide</td>
<td>1994</td>
<td>2%</td>
<td>TRUSOPT</td>
<td>TID (or BID if adding)</td>
<td>5 mL</td>
<td>BAK</td>
</tr>
<tr>
<td>brinzolamide</td>
<td>2000</td>
<td>1%</td>
<td>AZOPT</td>
<td>TID (or BID if adding)</td>
<td>Susp – 2.5, 5, 10, 15 mL</td>
<td>BAK</td>
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### Carbonic Anhydrase Inhibitors – Oral

<table>
<thead>
<tr>
<th>Drug</th>
<th>Year</th>
<th>Concentration</th>
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<th>Dosing</th>
<th>Bottle Size</th>
<th>Preservative</th>
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<td>acetazolamide</td>
<td>1955</td>
<td>250 mg</td>
<td>DIAMOX (and generics)</td>
<td>QID</td>
<td>Tabs</td>
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<td>methazolamide</td>
<td>1955</td>
<td>50 mg</td>
<td>(generics)</td>
<td>TID</td>
<td>Tabs</td>
<td>N/A</td>
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### Miotics

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<th>Dosing</th>
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<th>Preservative</th>
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<tbody>
<tr>
<td>pilocarpine</td>
<td>Pre1900</td>
<td>1, 2, 4% (6 no longer available)</td>
<td>MIOCARPINE (and generics)</td>
<td>QID</td>
<td>15 mL</td>
<td>BAK</td>
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<tr>
<td></td>
<td></td>
<td>4%</td>
<td>PILOPINE HS</td>
<td>QD (hs)</td>
<td>Gel 5 g tube</td>
<td>BAK</td>
</tr>
<tr>
<td>Combination Anti-glaucoma Drugs</td>
<td>Year</td>
<td>Concentration</td>
<td>Brand</td>
<td>Schedule</td>
<td>Volume</td>
<td>Diluent</td>
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<td>---------------------------------</td>
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<td>---------------</td>
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<td>0.005% / 0.5%</td>
<td>XALACOM</td>
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<td>2.5mL</td>
<td>BAK</td>
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<td>0.004% / 0.5%</td>
<td>DUOTRAV PQ</td>
<td>QD (am)</td>
<td>2.5, 5mL</td>
<td>Polyquad, SofZia</td>
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<td>brimonidine / timolol</td>
<td>2006</td>
<td>0.2% / 0.5%</td>
<td>COMBIGAN</td>
<td>BID</td>
<td>5, 10mL</td>
<td>BAK</td>
</tr>
<tr>
<td>dorzolamide / timolol</td>
<td>1998</td>
<td>2% / 0.5%</td>
<td>COSOPT (and generics)</td>
<td>BID</td>
<td>5, 10mL</td>
<td>BAK</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>COSOPT PF</td>
<td></td>
<td>0.4mL x 30 vials</td>
<td>PF</td>
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<td>brinzolamide / timolol</td>
<td>2008</td>
<td>1% / 0.5%</td>
<td>AZARGA</td>
<td>BID</td>
<td>5mL</td>
<td>BAK</td>
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<tr>
<td>brinzolamide / brimonidine</td>
<td>2014</td>
<td>1% / 0.2%</td>
<td>SIMBRINZA</td>
<td>BID</td>
<td>Susp 10mL</td>
<td>BAK</td>
</tr>
</tbody>
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Available treatment strategies
Current Treatment Strategies

Available Topical Medical Therapies for OAG

IOP Reduction

**β-blockers**
- betaxolol
- timolol
- levobunolol
- metipranolol
- carteolol

**Miotics**
- pilocarpine
- carbachol
- physostigmine
- demecarium
- echothiophate

**CAIs**
- (dichlorophenamide)
- (methazolamide)
- (acetazolamide)
- dorzolamide
- brinzolamide

**α₂-agonists**
- epinephrine
dipivefrin
- apraclonidine
- brimonidine

**Prostanoids**
- latanoprost
- travoprost
- bimatoprost (tafluprost)
- unoprostone-isopropyl

WATERLOO
OPTOMETRY & VISION SCIENCE

Review - 24

(24)
Current Treatment Strategies

Available Topical Medical Therapies for OAG

IOP Reduction

**β-blockers**
- betaxolol
- timolol
- levobunolol
- metipranolol
- carteolol

**Miotics**
- pilocarpine

**CAIs**
- (dichlorophenamide)
- (methazolamide)
- (acetazolamide)
- dorzolamide
- brinzolamide

**α₂-agonists**
- apraclonidine
- brimonidine

**Prostanoids**
- latanoprost
- travoprost
- bimatoprost
- (tafluprost)

WATERLOO
OPTOMETRY & VISION SCIENCE

Review - 8
α-agonists

**COMBINATION PRODUCTS**
- Xalcom (timolol 0.5% + latanoprost 0.005%)
- Combigan (timolol 0.5% + brimonidine 0.2%)
- Azarga (timolol 0.5% + brinzolamide 1%)
- Cosopt (timolol 0.5% + dorzolamide 2%)
- DUOTRAV (timolol 0.5% + travoprost 0.004%)
- SIMBRINZA (brinzolamide 1% + brimondine 0.2%)

**Prostaglandin analogues (Prostanoids & Prostamides)**
- Xalatan
- Luigan
- Lumigan
- Advane
- Travatan
- Azarga (timolol 0.5% + brinzolamide 1%)
- CAIs
- SIMBRINZA (brinzolamide 1% + brimondine 0.2%)

**Preservative-Free**
- Timolol Cosopt, Saflutan (Zioptan), Trusopt

**Miotics...**

**Mydriatic/Cycloplegics**

**β-adrenoceptor antagonists (incl. generics)**
IZBA
(travoprost 0.003%)

- Reduced IOP to an equivalent extent as TRAVATAN Solution at all on therapy visits and time points
- An improved safety profile with IZBA
- Hyperemia was observed in 11.8% of patients on IZBA compared with 14.5% for patients using TRAVATAN
- POLYQUAD (polyquaternium-1)
  - Non-detergent, polycationic anti-microbial preservative

5. Data on file, Alcon Inc.
SAFLUTAN (or ZIOPTAN)
(tafluprost 0.0015%)

- PRESERVATIVE FREE FP agonist prostanoid
- q.d. dosed at night
- Was to be called Saflutan, as in UK/Spain etc, but changed to Zioptan in U.S. (Feb.2012)
- Canada (Purdue) was to be Saflutan (NOT coming)
  - Purdue has Trusopt, Cosopt, Timoptic and Timoptic XE
MONOPROST
(PF latanoprost 0.005%)

• Canada’s first PF prostaglandin medication!
• Approved October 2017
• Single-dose containers (0.2 mL; 1gt / eye)
• 5x single-dose containers in individual paper-aluminium sachets (Groups of 6 or 18 per box; i.e., 30 or 90 single-dose containers)
• Non-medicinal ingredients include:
  – carbomer 974 P, disodium edetate, macrogol 4000, macrogolglycerol hydroxystearate 40, sodium hydroxide (to adjust pH), sorbitol, and water for injection

http://www.labticianthea.com/about-labtician-thea/
TIOPEX

(PF timolol 0.1%)

• Not yet approved in Canada but available in UK
• Single-dose containers (0.2mL?; 1gt / eye, ie. q.d. dose)
• Compared it to b.i.d. timolol and noted that this was 10X decrease in amount of timolol administered with 90% reduction in systemic absorption
• Non-medicinal ingredients – carbomer and PVA to increase contact time

http://www.labticianthea.com/about-labtician-thea/
Combination Products

**Cosopt**
(timolol maleate 0.5% + dorzolamide 2%)
Note: also available preservative free

**Xalcom**
(timolol maleate 0.5% + latanoprost 0.005%)

**Combigan**
(timolol maleate 0.5% + brimonidine 0.2%)

**DUOTRAV**
(timolol maleate 0.5% + travoprost 0.004%)

**AZARGA***
(timolol maleate 0.5% + brinzolamide 1%)

**SIMBRINZA***
(brinzolamide 1% + brimondine 0.2%)

Compared with UFC (ie, multiple bottles), FC therapies can
- decrease cumulative patient exposure to preservatives,
- reduce risk of drug washout, and
- simplify drug administration
Advantages of FC (Fixed Combinations)

- Reduces IOP *more effectively* than their component medications used separately as monotherapy
  - May even demonstrate a more favorable safety profile and reduced ocular allergy compared to monotherapy (e.g. brimonidine)... better than BOTH taken separately, too...?
- *Eliminate* the need to instill two separate drugs, at least five minutes apart, to *prevent a washout* effect from the 2nd
- *Limits exposure to preservative* (BAK), which increases the preservation of the ocular surface
- Increase *convenience* by reducing the number of dosages and medicine bottles, which may increase *adherence*
- *Cost savings*?
# FC drugs

all 6 commonly used FC can effectively lower IOP by >30%

<table>
<thead>
<tr>
<th>Previous metanalysis [vanderValk]</th>
<th>Relative reduction of FC combinations</th>
</tr>
</thead>
<tbody>
<tr>
<td>timolol</td>
<td>22 - 27%</td>
</tr>
<tr>
<td>latanoprost</td>
<td>31%</td>
</tr>
<tr>
<td>travoprost</td>
<td>31%</td>
</tr>
<tr>
<td>bimatoprost</td>
<td>33%</td>
</tr>
<tr>
<td>brimonidine</td>
<td>25%</td>
</tr>
<tr>
<td>brinzolamide</td>
<td>17%</td>
</tr>
<tr>
<td>dorzolamide</td>
<td>22%</td>
</tr>
</tbody>
</table>

* b/c timolol dose is omitted, may not decrease as much; may also be affected by the peak decrease curves and time measures were taken (e.g. max post instillation time was 8h, but 12-24h may be the peak for prostanoids… vs 2h for betablocker)

| brinzolamide/brimonidine          | 27-35%                               |


When to change glaucoma treatment?

And how?
Glaucoma Guideline for Canadian Optometrists: Stepwise Treatment Algorithm

**STEP 1**
First-line monotherapy

**PGA**
(QD, usually hs)

- **SWITCH**
  within the PGA class

- **ADD**
  beta-blocker
  (QD, in a.m.)

  - **SWITCH**
    FC (PGA / timolol)
    (QD, a.m. preferred)

  - **ADD**
    single agent
    alpha agonist OR CAI
    (both BID)

  - **ADD**
    FC (brimonidine / timolol) OR
    FC (CAI / timolol)
    (both BID)

  - **ADD**
    single agent
    alpha agonist OR CAI
    (both BID)

**STEP 2**

**ADD**
remaining single agent
alpha agonist OR CAI
(both BID)

**STEP 3**

**ADD**
single agent
alpha agonist OR CAI
(both BID)

**STEP 4**

**ADD**
remaining single agent
alpha agonist OR CAI
(both BID)

**GO TO**
STEP 3
24 Hour Diurnal Control: timolol vs. latanoprost

24 Hour Diurnal Control: Brimonididine makes no difference at night

Figure 1. Profiles of 24-hour IOP in the habitual body positions. Measurements were taken from 15 subjects sitting during the diurnal period and supine during the nocturnal period. Open circles represent the baseline, and solid circles represent the brimonididine treatment. Error bars represent standard error of the mean. IOP = intraocular pressure.

Azopt Shows Adjunctive Nocturnal IOP Lowering; Timolol Does Not

Management Pearls

• Follow the 6 steps of treatment

• For initiating treatment:
  – Goal: to slow down progression of glaucoma
    • First line therapy generally prostanoid
    • Consider each person uniquely / follow them appropriately
BL 78 yo man (Swedish bkgnd)

Retired, world traveler, author
Diagnosed with POAG 3 years ago
No changes to vision; ‘excellent’ adherence to his treatment

**LUMIGAN RC (bimatoprost 0.01%) OU hs**
- Switched from travoprost (used 2.5 years)

**AZOPT (brinzolamide 1%) OU BID (x1 year)**

**Systemic**
- (+) family history of glaucoma (details)
- (-) diabetes, (-) smoking, (-) vascular dysregulation
- (+) cardiovascular disease (HT, dyslipidemia, MI 2010, 2017, Graves disease)
- Surgeries: Pacemaker 2017, stents 2010, 2017, thyroid radiation in 70s
- MEDS: Synthroid (levothyroxine), LIPITOR (atorvastatin), COVERSYL (perindopril), XARELTO (rivaroxaban) 15mg, Vitamin D supplement
<table>
<thead>
<tr>
<th>Structure</th>
<th>OD</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>VA</td>
<td>6/4.5</td>
<td>6/6</td>
</tr>
<tr>
<td>Rx</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pupils</td>
<td>ERLL (-) RAPD</td>
<td></td>
</tr>
<tr>
<td>Lids/Lashes</td>
<td>Trace MGD, lower lid notching, ant blepharitis</td>
<td></td>
</tr>
<tr>
<td>Tears (not volume)</td>
<td>Shallow tear prism, Oily debris</td>
<td></td>
</tr>
<tr>
<td>Conjunctiva</td>
<td>Mild hyperemia</td>
<td></td>
</tr>
<tr>
<td>Angles</td>
<td>Grade 4 (VH) 1:1 N &amp; T</td>
<td></td>
</tr>
<tr>
<td>Cornea</td>
<td>Coalesced SPK inf arcus</td>
<td></td>
</tr>
<tr>
<td>AC</td>
<td>Deep and quiet</td>
<td></td>
</tr>
<tr>
<td>Gonioscopy</td>
<td>Open to CB 360, (-) NVA/PAS/AR, Grade 2 pigment 360</td>
<td></td>
</tr>
<tr>
<td>Iris</td>
<td>Flat, blue</td>
<td></td>
</tr>
<tr>
<td>Lens</td>
<td>Grade 2 NS, vacuoles</td>
<td></td>
</tr>
<tr>
<td>IOP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pachymetry</td>
<td>653um</td>
<td>632um thick</td>
</tr>
<tr>
<td>BP/ HR</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>DFE (ON/NFL)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>OU</td>
<td></td>
</tr>
<tr>
<td>----------------</td>
<td>-----------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Macula</td>
<td>Even macular pigment</td>
<td></td>
</tr>
<tr>
<td>Vasculature</td>
<td>Normal course/calibre/ crossings for age</td>
<td></td>
</tr>
<tr>
<td>Periphery</td>
<td>No holes, tears, RD detected 360 degrees</td>
<td></td>
</tr>
<tr>
<td>Vitreous</td>
<td>PVD</td>
<td></td>
</tr>
</tbody>
</table>
Reference database: European Descent (2009)
Initiated treatment with Travatan Z qhs

Added Azopt bid
Superior Temporal: -27 from baseline
Superior Nasal: -10 from baseline
Indicative of progression
OD>OS
BL

Target IOP = 16/15

Initiated treatment with Travatan Z qhs

Added Azopt bid

IOP (mmHg)

Date

NOV-14 | MAR-15 | JUN-15 | NOV-15 | MAR-16 | JUN-16 | NOV-16 | MAR-17 | JUN-17 | NOV-17 | MAR-18

14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24

OD - OS
Early loss might be masked; later loss amplified (log scale)
Event Analysis: Likely progression OD
Trend Analysis: Rate of progression of ~0 in OD and in OS
BL

Target IOP = 16/15

Initiated treatment with Travatan Z qhs

Added Azopt bid

Analysis?
IOP (mmHg)

Date

Target IOP = 16/15

BL's IOP History

- Initiated treatment with Travatan Z qhs
- Added Azopt bid
- Switched Travatan Z to Lumigan RC, continued Azopt bid

Date

OD  OS

- NOV-14
- MAR-15
- JUL-15
- NOV-15
- MAR-16
- JUL-16
- NOV-16
- MAR-17
- JUL-17
- NOV-17
- MAR-18
- JUL-18
- NOV-18
- MAR-19

IOP (mmHg)
Inferior “arcuate-like” defect
## OCT: RNFL Thickness

<table>
<thead>
<tr>
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<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RNFL Thickness</strong> (12.0°)</td>
<td><img src="OD.png" alt="Diagram" /></td>
<td><img src="OD.png" alt="Diagram" /></td>
<td><img src="OD.png" alt="Diagram" /></td>
<td><img src="OD.png" alt="Diagram" /></td>
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</tbody>
</table>

**OD**

<table>
<thead>
<tr>
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<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RNFL Thickness</strong> (12.0°)</td>
<td><img src="OS.png" alt="Diagram" /></td>
<td><img src="OS.png" alt="Diagram" /></td>
<td><img src="OS.png" alt="Diagram" /></td>
<td><img src="OS.png" alt="Diagram" /></td>
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<td><img src="OS.png" alt="Diagram" /></td>
<td><img src="OS.png" alt="Diagram" /></td>
</tr>
</tbody>
</table>

**OS**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RNFL Thickness</strong> (12.0°)</td>
<td><img src="BL.png" alt="Diagram" /></td>
<td><img src="BL.png" alt="Diagram" /></td>
<td><img src="BL.png" alt="Diagram" /></td>
<td><img src="BL.png" alt="Diagram" /></td>
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<td><img src="BL.png" alt="Diagram" /></td>
<td><img src="BL.png" alt="Diagram" /></td>
</tr>
</tbody>
</table>

**BL**
Superior Temporal: -38 from baseline
Superior Nasal: -13 from baseline

Indicative of progression
OD>OS
Initiated treatment with Travatan Z qhs

Added Azopt bid

Switched Travatan Z to Lumigan RC, continued Azopt bid

AZOPT switched to SIMBRINZA

Target IOP = 16/15
<table>
<thead>
<tr>
<th></th>
<th>OD</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>C/D Ratio</strong></td>
<td>0.75</td>
<td>0.75</td>
</tr>
<tr>
<td><strong>ONH</strong></td>
<td>Sup rim thinning (OD&gt;OS), <strong>ODH sup</strong> temp, lamina visible</td>
<td>Sup neural retinal rim thinning, lamina visible</td>
</tr>
</tbody>
</table>
BL's IOP History

- Initiated treatment with Travatan Z qhs
- Added Azopt bid
- Switched Travatan Z to Lumigan RC, continued Azopt bid
- AZOPT switched to SIMBRINZA

Target IOP = 16/15
Questions…?

• Did we have progression?
  – Inadequate response to progression or progression on progression….?

• How did we do with our treatment/s?
  – Strategies…. 

• Any other considerations?
  – Betablocker, anyone???
### Beta-adrenergic Blocking Agents

- acebutolol HCl
- atenolol HCl
- bisoprolol fumarate
- carvedilol
- esmolol HCl
- labetalol HCl
- metoprolol tartrate
- nadolol
- nebivolol HCl
- pindolol
- propranolol HCl
- sotalol HCl
- timolol maleate

**Anti-anginal/Antiarrhythmic/Antihypertensive/Heart Failure Agent/Migraine Prophylaxis/Post-myocardial Infarction**

*CPhA Monograph*

**Date of Revision:** June 2019

---

This monograph has been compiled by CPhA and reviewed by experts. It may contain information different from that found in Health Canada-Approved Product Monographs. The reader is referred to the [CPS Editorial Policy](#) for more information.

---

### Summary Product Information

<table>
<thead>
<tr>
<th>Drug</th>
<th>Route of Administration</th>
<th>Dosage Form</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acebutolol</td>
<td>Oral</td>
<td>Tablet</td>
<td>100 mg, 200 mg, 400 mg</td>
</tr>
<tr>
<td>Atenolol[a]</td>
<td>Oral</td>
<td>Tablet</td>
<td>25 mg, 50 mg, 100 mg</td>
</tr>
<tr>
<td>Bisoprolol</td>
<td>Oral</td>
<td>Tablet</td>
<td>5 mg, 10 mg</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>Oral</td>
<td>Tablet</td>
<td>3.125 mg, 6.25 mg, 12.5 mg, 25 mg</td>
</tr>
<tr>
<td>Esmolol</td>
<td>IV</td>
<td>Solution</td>
<td>10 mg/mL</td>
</tr>
<tr>
<td>Labetalol</td>
<td>Oral</td>
<td>Tablet</td>
<td>100 mg, 200 mg</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>Solution</td>
<td>5 mg/mL</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>Oral</td>
<td>Tablet</td>
<td>25 mg, 50 mg, 100 mg</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>Slow-release tablet</td>
<td>100 mg, 200 mg</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>Solution</td>
<td>1 mg/mL</td>
</tr>
</tbody>
</table>

[a] Table includes single entity atenolol products only.

Also available in ophthalmic products.
# Beta blocker interactions

## Drug-Drug Interactions

See Table 3.

<table>
<thead>
<tr>
<th>Interacting Drug</th>
<th>Effect</th>
<th>Clinical Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha-adrenergic stimulants (e.g., phenylephrine)</td>
<td>Additive risk of hypertension</td>
<td>Monitor BP.</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>Increased bradycardia with nadolol and propranolol</td>
<td>Monitor HR.</td>
</tr>
<tr>
<td>Antacid (magnesium or aluminum)</td>
<td>Sotalol: approximate 20% decrease in absorption</td>
<td>Space doses by at least 2 h.</td>
</tr>
<tr>
<td>Antiarrhythmics</td>
<td>Additive bradycardia and heart block. Amiodarone, propafenone and quinidine can inhibit the metabolism of agents metabolized by CYP2D6. Possible additive QTc prolongation with sotalol</td>
<td>Caution, monitor HR. Wait 3–4 half-lives after other antiarrhythmic drugs before starting sotalol.</td>
</tr>
<tr>
<td>Beta₂-agonist bronchodilators (e.g., formoterol, salbutamol, salmeterol, terbutaline)</td>
<td>Antagonized bronchodilatation with nonselective <strong>beta-blockers</strong></td>
<td>Avoid nonselective <strong>beta-blockers</strong> with beta₂-agonists if possible.</td>
</tr>
<tr>
<td>Calcium channel blockers, non-dihydropyridine (e.g., diltiazem, verapamil)</td>
<td>Additive bradycardia, hypotension, heart failure and depressed AV conduction</td>
<td>Avoid intravenous diltiazem and verapamil. Monitor closely.</td>
</tr>
<tr>
<td>Cholinesterase inhibitors</td>
<td>Bradycardia</td>
<td>Monitor HR.</td>
</tr>
</tbody>
</table>

## Drug-Food Interactions

- Waterloo Optometry & Vision Science
# Beta blocker interactions

## Drug-Drug Interactions

See Table 3.

<table>
<thead>
<tr>
<th>Interacting Drug</th>
<th>Effect</th>
<th>Clinical Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cimétidine</td>
<td>Decreased metabolism of beta-blockers that are metabolized by CYP enzymes</td>
<td>Monitor. Use alternative H₂-receptor antagonist. Reduce dose of beta-blocker.</td>
</tr>
<tr>
<td>Clonidine</td>
<td>Possible worsening of the rebound hypertension that can occur when discontinuing clonidine</td>
<td>Discontinue beta-blocker several days before discontinuing clonidine.</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>Increased cyclosporine levels with carvedilol</td>
<td>Monitor cyclosporine levels and adjust dose.</td>
</tr>
<tr>
<td>CYP1A2 inhibitors or substrates (e.g., ciprofloxacin, fluvoxamine, rizatriptan)</td>
<td>Possible increased propranolol levels due to inhibited metabolism</td>
<td>Monitor HR and BP.</td>
</tr>
<tr>
<td>CYP2D6 inhibitors (e.g., cimetidine, fluoxetine, ritonavir)</td>
<td>Increased levels and toxicity of beta-blockers that are metabolized by CYP2D6</td>
<td>Monitor. Reduce dose of beta-blocker.</td>
</tr>
<tr>
<td>CYP inducers (e.g., rifampin, barbiturates)</td>
<td>Decreased levels and benefit of beta-blockers that are metabolized by CYP enzymes</td>
<td>Consider beta-blockers that are not metabolized by CYP enzymes (see Table 8).</td>
</tr>
<tr>
<td>Digoxin</td>
<td>Additive bradycardia</td>
<td>Monitor for bradycardia and arrhythmias.</td>
</tr>
</tbody>
</table>

## Drug-Food Interactions

WATERLOO OPTOMETRY & VISION SCIENCE
## Beta blocker interactions

### Drug-Drug Interactions

See Table 3.

<table>
<thead>
<tr>
<th>Interacting Drug</th>
<th>Effect</th>
<th>Clinical Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digoxin</td>
<td>Additive bradycardia</td>
<td>Monitor for bradycardia and arrhythmias.</td>
</tr>
<tr>
<td></td>
<td>30% increase in digoxin levels with carvedilol; increased arrhythmias with sotalol</td>
<td></td>
</tr>
<tr>
<td>Dipyridamole</td>
<td>Additive bradycardia and asystole</td>
<td>Withhold beta-blocker before dipyridamole testing.</td>
</tr>
<tr>
<td>Disopyramide</td>
<td>Possible severe bradycardia</td>
<td>Avoid if possible.</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>Epinephrine: risk of severe hypertension and reflex bradycardia with nonselective beta-blockers. Epinephrine may be less effective in the treatment of anaphylaxis</td>
<td>Monitor. Selective agents preferred. Caution if large doses of epinephrine are used for local anesthesia. Avoid esmolol in patients who require epinephrine to maintain BP and cardiac output.</td>
</tr>
<tr>
<td>Ergot alkaloids</td>
<td>Peripheral ischemia leading to hypertension</td>
<td>Monitor for signs of peripheral ischemia (tingling or cold extremities).</td>
</tr>
<tr>
<td>Fingolimod</td>
<td>Additive bradycardia</td>
<td>Caution is recommended.</td>
</tr>
</tbody>
</table>

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**WATERLOO**  
**OPTOMETRY & VISION SCIENCE**
# Beta blocker interactions

## Drug-Drug Interactions

See Table 3.

<table>
<thead>
<tr>
<th>Interacting Drug</th>
<th>Effect</th>
<th>Clinical Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fingolimod</td>
<td>Additive bradycardia</td>
<td>Caution is recommended.</td>
</tr>
<tr>
<td>Insulin</td>
<td>If hypoglycemia occurs, there is a prolonged recovery time, greater increase in BP, and masking of tachycardia and tremors (but not sweating); hyperglycemia is possible</td>
<td>Beta₁-selective agents are preferred. Masking of the warning signs of hypoglycemia can occur with both selective and nonselective agents.</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>Increased lidocaine levels</td>
<td>Monitor lidocaine levels. Avoid combining propranolol with lidocaine infusion.</td>
</tr>
<tr>
<td>MAOIs</td>
<td>Increased risk of hypotension and bradycardia</td>
<td>Avoid if possible. Monitor BP and HR.</td>
</tr>
<tr>
<td>Methacholine</td>
<td>Increased effect of methacholine</td>
<td>Avoid or use with caution.</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>Decreased norepinephrine-related rise in BP</td>
<td>Avoid esmolol in patients who require norepinephrine to maintain BP and cardiac output.</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Decreased antihypertensive effect since NSAIDs can increase BP</td>
<td>Monitor BP.</td>
</tr>
<tr>
<td>Phenothiazines</td>
<td>Possible additive hypotension. Combining chlorpromazine with propranolol results in increased levels of both drugs</td>
<td>Avoid combining sotalol with phenothiazines. Monitor BP. A lower dose of both propranolol and the phenothiazine may be needed.</td>
</tr>
</tbody>
</table>
# Beta blocker interactions

**Drug-Drug Interactions**

*See Table 3.*

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<thead>
<tr>
<th>Interacting Drug</th>
<th>Effect</th>
<th>Clinical Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prazosin</td>
<td>Increased first-dose hypotension with prazosin</td>
<td>Minimize first prazosin dose. Inform patient.</td>
</tr>
<tr>
<td>Rizatriptan</td>
<td>Propranolol can increase rizatriptan levels by 75% due to inhibition of MAO-A metabolism</td>
<td>Within the triptan class, this effect appears to be specific to rizatriptan. Reduce rizatriptan dose.</td>
</tr>
<tr>
<td>Succinylcholine</td>
<td>Prolonged neuromuscular blockade with esmolol</td>
<td>Caution is recommended.</td>
</tr>
<tr>
<td>Sulfonylureas</td>
<td>Decreased effect of sulfonylureas. If hypoglycemia occurs, there is a prolonged recovery time, greater increase in BP, and masking of tachycardia and tremors (but not sweating); hyperglycemia is possible</td>
<td>Beta₁-selective agents are preferred. Masking of the warning signs of hypoglycemia can occur with both selective and nonselective agents.</td>
</tr>
<tr>
<td>Theophylline</td>
<td>Increased theophylline levels with propranolol. Antagonism of bronchodilation, mainly with nonselective beta-blockers</td>
<td>Monitor theophylline levels. Avoid nonselective beta-blockers in patients with reactive airway disease.</td>
</tr>
<tr>
<td>Tricyclic antidepressants</td>
<td>Increased hypotension. Increased risk of QTc interval prolongation with sotalol</td>
<td>Avoid sotalol.</td>
</tr>
</tbody>
</table>

**Drug-Food Interactions**

**WATERLOO OPTOMETRY & VISION SCIENCE**
Interactions

Drug Search Results

- PARoxetine
- PARoxetine-10 (CAN)
- PARoxetine-20 (CAN)
- PARoxetine-30 (CAN)

Duplicate Drug Therapy

Analyze Clear

Help

Drug Interactions. Information regarding the drug interaction between two or more drugs can be found. For example, some drugs may interfere with each other or with certain patients.

Common Interactions include:
- Dizziness
- Headache
- Nausea
- Vomiting

Presence of Interactions:

- Mild
- Moderate
- Severe

Potential Complications:

- Hypotension
- Respiratory depression
- Cardiac arrest

Side Effects:

- Drowsiness
- Sedation
- Dry mouth

Prescription Antidepressants may cause side effects such as dyes, preservatives,

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Lexicomp Interaction Analysis

A = No known interaction  C = Monitor therapy
B = No action needed    D = Consider therapy modification
X = Avoid combination

View interaction detail by clicking on link.

Drugs in this analysis: PARoxetine; Timolol (Ophthalmic)

Drug-Drug Interactions

PARoxetine (CYP2D6 Inhibitors (Strong)) – Timolol (Ophthalmic)

Display Drug-Drug Interaction Monograph

Created on June 14, 2019 7:14:14 AM EDT

Disclaimer: Readers are advised that decisions regarding drug therapy must be based on the independent judgment of the clinician, changing information about a drug (eg, as reflected in the literature and manufacturer's most current product information), and changing medical practice.
**Summary**  CYP2D6 Inhibitors (Strong) may increase the serum concentration of Timolol (Ophthalmic). **Severity** Moderate **Reliability Rating** Good

**Patient Management**  Monitor closely for evidence of systemic beta-blocker effects, including but not limited to orthostatic hypotension, bradycardia, and exercise intolerance.

**CYP2D6 Inhibitors (Strong) Interacting Members**  BuPROPion; Dacomitinib; FLUoxetine; PARoxetine; QuiNIDine; Tipranavir

**Discussion**  The AUC and maximum serum concentrations of timolol were increased by 1.6- to 1.8-fold and 1.5-fold, respectively, with concurrent administration of the strong CYP2D6 inhibitors (BuPROPion and Dacomitinib) at usual clinical dosages (0.1-0.5 mg/day). CYP2D6 inhibitors that inhibit the CYP2D6 enzyme (e.g., Dacomitinib) could be associated with higher risk of clinical adverse effects such as bradycardia.}

**Risk Rating**  C: Monitor therapy

**Summary**  CYP2D6 Inhibitors (Strong) may increase the serum concentration of Timolol (Ophthalmic). **Severity** Moderate **Reliability Rating** Good

**Patient Management**  Monitor closely for evidence of systemic beta-blocker effects, including but not limited to orthostatic hypotension, bradycardia, and exercise intolerance.

**CYP2D6 Inhibitors (Strong) Interacting Members**  BuPROPion; Dacomitinib; FLUoxetine; PARoxetine; QuiNIDine; Tipranavir
Betablocker advances?

- Drug delivery – liposomes…
- Sustained drug release with gelatinized core liposomes
- 0.1% timolol being developed
- (we need our PF formulations back)
OSD + glaucoma?
When to go PF?
So, what’s *new* in treatment?
With all this talk of MIGS and novel treatments, are topical eyedrops for glaucoma going to be obsolete?
“Despite all the advances, our medical therapy fails not only for compliance reasons, but just fails… We need to continue to have new alternatives for treatment that are more effective, that last longer, and that have simple dosing requirements.”

-Dr. Louis Cantor
(Indiana University)
High outflow resistance in OAG

Uveal meshwork
Corneoscleral meshwork
Juxtacanalicular Tissue (JCT)
Major source of outflow resistance


New drugs focus on TM outflow

- **Remember *pilocarpine***?
  - used CB contraction to pull on SS, increasing drainage through the TM

- **Rho kinase (ROCK) inhibitors**
  - Uncouple actin and myosin, proteins that work together to control CM contractility, and relax the cells in the TM, increasing outflow

- **Adenosine agonists**
New wave of drugs shaking up the glaucoma pipeline

Had been no new class of medications since Pfizer’s latanoprost entered the market and the clinics in 1996! Until 2017

- **VYZULTA (VESNEO)** (Bausch & Lomb) combines latanoprost with nitric oxide donating molecule in Nov.2017 (US)
- **RHOPRESSA** (Aerie Pharmaceuticals Inc) in Dec.2017 (US)
- **ROCLATAN** (Aerie) in 2019 (US) (FC of Rhopressa and latanoprost)
- **Trabodenoson** (Inotek Pharmaceuticals) trials expected to be completed by 2018 (no red eye ADRs) (failed phase 3)
- **Devices/implants:**
  - devices are being developed; inserted into the eye to deliver regular medication is in mid-stage clinical trials. (Ocular Therapeutix Inc, pSivida and Mati Therapeutics all working on implants)
  - **bimatoprost SR** (Allergan) is a long-acting implant in late-stage clinical trials

FDA Approved Drugs for Ophthalmology

Drugs Approved in 2019

Rocklatan (netarsudil and latanoprost ophthalmic solution); Aerie Pharmaceuticals; For the treatment of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension, Approved March 2019

Drugs Approved in 2018

Oxervate (cenegermin-bkbj); Dompe Pharmaceuticals; For the treatment of neurotrophic keratitis, Approved August 2018

Drugs Approved in 2017

Luxturna (voretigene neparvovec); Spark Therapeutics; For the treatment of vision loss due to confirmed biallelic RPE65-mediated inherited retinal disease, Approved December 2017

Rhopressa (netarsudil ophthalmic solution); Aerie Pharmaceuticals; For the treatment of glaucoma or ocular hypertension, Approved December 2017

Vyzulta (latanoprostene bunod ophthalmic solution); Bausch & Lomb; For the reduction of intraocular pressure in patients with open-angle glaucoma or ocular hypertension, Approved November 2017

Zerviate (cetirizine ophthalmic solution 0.24%); NicOx; For the treatment of ocular itching associated with allergic conjunctivitis, Approved May 2017

VISION SCIENCE
New Drug Delivery?
Drug Delivery to the eye

- Drug delivery to targeted ocular tissues has been a major challenge to ocular scientist, for decades
- Administration of drug solutions as topical drop with conventional formulations was associated with certain drawbacks which initiated the introduction of different carrier systems for ocular delivery
- Tremendous efforts are being put into ocular research toward the development of safe and novel drug delivery strategies that will improve adherence and QoL
  - *in vivo* performance of conventional formulations
  - Nanotechnology, new techniques, devices and their applications in drug delivery
Fig. 1. Routes of drug administration to eye
A typical eyedrop is three to four times the size of the liquid capacity of the average human eye. Most of the drop is often wasted. (Craig Chivers/CBC)

... Allisa Song, 26, a medical student from Seattle, wanted a more immediate solution "I was thinking, how do we circumvent these drug companies who won't budge?"

So she and three friends, all with biomedical or engineering backgrounds, came up with a plastic adapter that screws onto the tip of any bottle and turns those wasteful blobs of eye medicine into a precise, little 9.4-μl drop... the Nanodropper, extends the life of a one-month supply of drops to three or four months.

https://apple.news/AIfqR3hKQwGHbMDBBcOTw
SMART. PRECISE. BRILLIANT.

Eyenovia is a clinical stage, ophthalmic biopharmaceutical company transforming the delivery of therapeutics for the treatment of prominent eye diseases, such as glaucoma, dry eyes, allergic eye disease and many others. Eyenovia’s breakthrough piezo-dispersion and microdosing technology enable a portfolio of first-in-class, next-generation, micro-therapeutics for the eye designed to reduce ocular and systemic toxicity and improve the risk-benefit profile of both new and existing therapeutics.

At Eyenovia, we believe that when it comes to your eyes, smaller is better.

Microdrops: smaller is better!

Eyenovia is leading the charge in how eye care is delivered with its microtherapeutic technology. Eyenovia’s microdrops and high-precision microdosing are designed for more efficient and gentler treatments for the eye with the delivery of 80% less unnecessary drug and preservatives.

Beat the Blink

Don’t wait for the drop to fall. Fast piezo-print delivery ensures microdrops gently coat the ocular surface at the speed of your blink, avoiding inconveniences such as overflow down the cheek and into the nose.

Pixel-sharp precision for your eyes

Eyenovia is bringing ocular drug delivery into focus. Our proprietary solution uses piezo-print electronics and microfluidics to generate tiny droplets for high-precision delivery of eye therapies. Applying high-resolution inkjet technology towards the development of microtherapeutics for the eye, Eyenovia can achieve gentle and precise micro-dosing at 6-8 μL volumes—dosing far less than the traditional eye drops which overdose the eye with 30-50 μL and often lead to adverse side effects such as redness, irritation and pain.

Smart technology: be smart... eye-smart!

Eyenovia’s intelligent electronic system is one of the first smart technologies to enter FDA clinical trials for ophthalmic use. Smart sensors and mobile cloud connectivity can help patients and physicians stay on top of treatment plans.

https://eyenovia.bio/?cmp=apple_news_cbc_news
What’s new in drug delivery???
Intracanalicular Implants
Ocular Surface Inserts
Drug-Delivering CLs

External

Intraocular Depot Implants
Nanoliposomes
Microparticles

Internal
External eye delivery

**Implants (intracanalicular), contact lenses, ocular insert**

Internal eye delivery

*More than 6 are being investigated with prostanoids alone!*

Figure 1. A range of sustained-release drug delivery innovations are in various stages of development.
OTX-TP

*travoprost* sustained release

- Lacrimal insert (intracanalicular depot)
- Composed of PEG hydrogel + microparticles of *travoprost*
- Sustained release (up to 3 months) of drug to lower IOP
- **Advantages**: are potential for improved adherence, and NO preservative!
bimatoprost SR
Sustained-release Ring

- Topical ocular insert
  - Rests in the fornices

- Up to 6 months of prostaglandin analogue
bimatoprost SR
Sustained-release Implant

• Intracameral injection
  (pre-filled single-use applicator)

• Advantages:
  – Reduces ocular ADRs
  – Adherence
  – Located closer to the site of action
Compounded formulations

• **OMNI** - Ocular Science, has 503 A status
  – patient-specific compounding pharmacy
  – combinations of latanoprost and timolol, but have all 4 glaucoma agents (timolol/brimonidine/dorzolamide/latanoprost) in one bottle
  – Also have p/o Cataract formulation (pred phosphate/ketorolac/gatifloxacin qid x 2 weeks, then bid x 2 weeks), LASIK formulation, etc.

• **Simple drops** - Imprimis is a 503 B compounding pharmacy
  – manufactures preservative-free glaucoma formulations
Rapid Fire Rounds: Treatment Glaucoma 2019

WATERLOO
OPTOMETRY & VISION SCIENCE
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