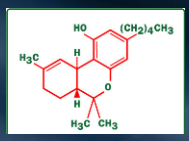
Pharmacology A to Z



TOA
TEXAS OPTOMETRIC ASSOCIATION

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Disclosures

- Allergan/AbbVie
- BioTissue
- Katena/Corza
- Dompé
- Oyster Point / Viatris
- Kala
- Merakris Therapeutics
- Bausch&Lomb
- Zeiss

There are no conflicts of interest in this program as all conflicts have been mitigated.

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FDA Pregnancy Categories

- The Pregnancy and Lactation Labeling Final Rule (PLLR) went into effect on June 30, 2015
  - Prescription drugs submitted for FDA approval after June 30, 2015 will use the new format immediately
- Prescription drugs approved on or after June 30, 2001 will be phased in gradually
- Medications approved prior to June 29, 2001 are not subject to the PLLR rule; however, the pregnancy letter category must be removed by June 29, 2018
- The A, B, C, D and X risk categories, in use since 1979, are now replaced with narrative sections and subsections to include:
- Pregnancy (includes Labor and Delivery):
  - Pregnancy Exposure Registry
  - Risk Summary
  - Clinical Considerations
  - Data
- Lactation (includes Nursing Mothers)
  - Risk Summary
  - Clinical Considerations
  - Data
- Females and Males of Reproductive Potential
  - Pregnancy Testing
  - Contraception
  - Infertility

Autologous Serum

- Use first described in 1984 by Fox et al (for keratoconjunctivitis sicca)
  - Fox RI, Chan R, Michelson J, et al. *Beneficial effect of artificial tears made with autologous serum in patients with keratoconjunctivitis sicca. Arthritis Rheum1984;29:577-83.*
- DEWS / ITF - Severity Level 3 Treatment
- Unpreserved
- Utilizes patients own blood serum
- Blood is drawn and serum is spun down and mixed with artificial tears / 0.9% sodium chloride
  - Doesn't contain red blood cells

Autologous Serum

- Contains essential components in tears
  - growth factors (EGF, NGF)
  - fibronectin
  - Vitamins
  - pH
  - nutrient content
  - Inhibits release of inflammatory cytokines
  - Increase number of goblet cells and mucin expression
- Potential complications
  - Immunoglobulin deposits
  - Corneal infiltrates
  - Conjunctivitis
  - Decreased corneal sensitivity

Autologous Serum

- 20% vs 50% concentration
  - TGF-β (transforming growth factor) known to have anti-proliferative effects
  - High concentrations can suppress healing on ocular surface
    - Tsubota (2000) recommended keeping equivalent to natural tears at 20%
- 50% concentration found to be more effective in treating dry eye patients
  - Schirmer scores and NaFL stain improved over time
  - No complications

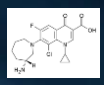
Hussain M[1], Shtein RM, Sugar A, Soong HK, Woodward MA, DeLoss K, Mian SI Cornea. 2014 Dec;33(12):1245-51. ***Long-term use of autologous serum 50% eye drops for the treatment of dry eye disease.***

Autologous Serum

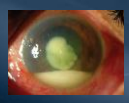
- Concerns:
  - Costly - $150-300 time, 2-4x /year
    - Typically not covered by insurance
  - Inconvenient - Requires blood donation from patient
  - Need to store frozen for up to three months at −20°C
  - Kept away from light to avoid degradation of vitamin A
  - Possible risk of infection
    - Cornea and systemic

Besivance (0.6 % besifloxacin)

- FDA approved in Dec 2008
- Not considered a 5th generation FQ
- First chlorinated fluoroquinolone
  - Has a chlorine atom at the C8 position
  - 4th generations have a methoxy group which diminishes the known photosensitivity in systemic use



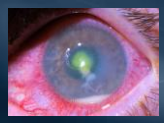
- Developed specifically for topical ophthalmic use
  - No widespread systemic, agriculture, or animal feed usage
  - Greatly reducing chance for resistance
- Formulated in the DuraSite mucoadhesive vehicle.
  - provides enhanced ocular surface contact time, potentially allowing greater concentration of the active drug on the ocular surface.



Besivance

- MIC 2-4x lower than other Ab's tested including other Fluoroquinolones
- Potent broad spectrum activity
  - Esp against gram + and – organisms showing resistance to other Ab's (including moxi, levo and cipro)
  - Effective against MRSA, MRSE
  - C7 addition of aminoazepinyl
- Specific approval for Pseudomonas Aeruginosa Oct 2012

- Research has pointed to potential anti-inflammatory properties
  - May be why so well tolerated by patients
- Suspension rather than a solution
- Dosed three times a day, 4-12 hours apart, for 7 days
- Safe to use in patients over 12 months of age
- Pregnancy Category C



Cyclosporin ophthalmic

- Topical anti-inflammatory that has been widely used to treat inflammatory ocular surface diseases
- Immunomodulator that possesses clinical efficacy in the presence of an excellent safety profile. It acts as a selective T-cell immunosuppressive agent.
- Several topical formulations
  - Restasis (0.05%)
  - Cequa (0.09%)
  - Vevye (0.1%)
  - Verkazia (0.1%)
  - Klarity-C (0.1%)

Cyclosporin ophthalmic

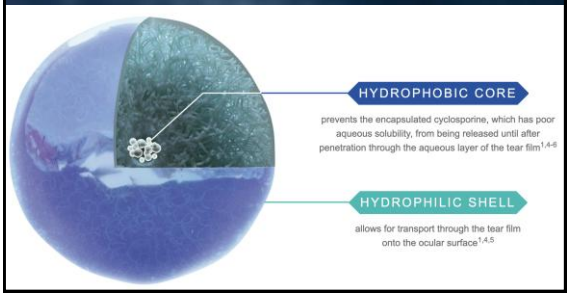
- Restasis (0.05%)
  - calcineurin inhibitor immunosuppressant indicated to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca. Increased tear production was not seen in patients currently taking topical anti-inflammatory drugs or using punctal plugs
  - Current challenges with Restasis

Cyclosporin ophthalmic

- Cequa (0.09%)
  - Historically, the poor aqueous solubility of cyclosporine can limit ocular tissue penetration
  - First and only FDA-approved treatment to combine cyclosporin with NCELL technology
    - Improved delivery and increased penetration
    - NCELL uses nanomicelles composed of polymers that encapsulate the cyclosporin molecules

Cyclosporin ophthalmic

- Cequa



Cequa

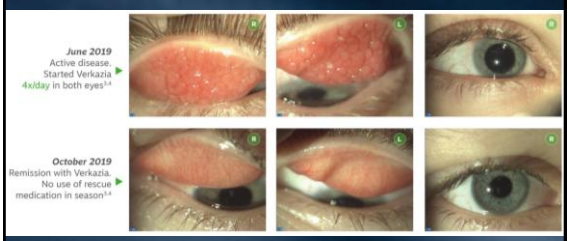
- Phase 4 multi-center study
- Enrolled 124 patients uncontrolled on Restasis
  - Average length of 3+ years
- Looked at tCFS and frequency/severity of symptoms
  - Statistically significant improvement at 4 weeks

Cyclosporin ophthalmic

- Verkazia (0.1%)
  - Harrow Pharmaceutical
  - FDA Approval June 2021
  - Calcineurin inhibitor immunosuppressant indicated for the treatment of vernal keratoconjunctivitis in children and adults
  - Dosing: 1 gtt QID in the affected eye(s)

Cyclosporin ophthalmic

- Verkazia



Cyclosporin ophthalmic

- Klarity-C (0.1%)
  - Imprimis Rx
  - 5.5 mL bottle
- Klarity CL
  - 0.1 % cyclosporin / 0.2% loteprednol etabonate
  - 5.5 mL bottle

Cyclosporin ophthalmic

- Vevye 0.1%
  - Harrow Pharmaceuticals
  - Approved June 8, 2023
  - first and only cyclosporine solution indicated for the treatment of signs and symptoms of dry eye disease with efficacy demonstrated after 4 weeks of treatment
    - 66% of subjects had 3 or more grades of tCFS improvement by Day 29
    - 57% of patients showed at least 3 grades of improvement in tCFS at Day 15

Dextenza (dexamethasone ophthalmic insert 0.4mg)

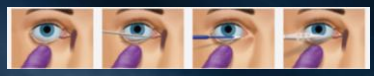
- Ocular Therapeutix
  - Originally approved November 2018 to treat ocular pain after ophthalmic surgery
  - In June 2019 added approval to treat ocular inflammation after ophthalmic surgery
  - October 2021 added approval to treat ocular itching that is associated with allergic conjunctivitis
    - Category 1 CPT Code 68841 for DEXTENZA Effective January 1, 2022
- Dextenza is the first, FDA-approved, physician-administered intracanalicular insert that delivers a preservative-free drug to treat ocular itching associated with allergic conjunctivitis with 1 administration lasting up to 30 days
- Delivers a tapering dose of 20mg / day at start down to 10mg /day at end of month

Dextenza (dexamethasone ophthalmic insert 0.4mg)

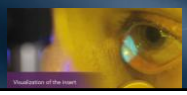
- Approval was based on the results of 3 randomized, multicenter, vehicle-controlled studies that included 255 patients with a positive history of ocular allergies and positive skin test reaction to perennial and seasonal allergens
- The results of the 3 studies showed that Dextenza had lower mean ocular itching scores compared with the vehicle group at all time points throughout the study duration of up to 30 days
- In 2 of the studies, higher percentages of patients had significant reductions in ocular itching on day 8 after the start of treatment, at 3, 5, and 7 minutes post-challenge in the Dextenza group compared to the vehicle group

Dextenza (dexamethasone ophthalmic insert 0.4mg)

- Insertion



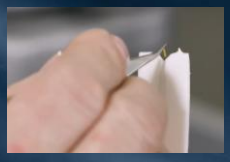
  - 1.Carefully remove foam carrier and transfer to a clean and dry area
  - 2. If necessary, dilate the punctum with an ophthalmic dilator
  - 3. **After drying the punctal area**, using blunt (non-toothed) forceps, grasp DEXTENZA and insert into the lower lacrimal canaliculus
  - 4. Ensure DEXTENZA is placed just below the punctal opening
    - Excessive squeezing with forceps may cause deformation
  - 5. To aid in the hydration of DEXTENZA, 1 to 2 drops of balanced salt solution can be instilled into the punctum
  - 6. DEXTENZA can be visualized when illuminated by a blue light source (e.g., slit lamp or hand held blue light) with yellow filter
- Dry insert dimensions:
  - Approx 0.55mm in diameter
  - 3mm in length



Dextenza (dexamethasone ophthalmic insert 0.4mg)

Dextenza was well tolerated

- Most common ocular adverse reactions in DEXTENZA patients (≥1%)
  - Intraocular pressure increase 3%
  - Lacrimation increased 1%
  - Eye discharge 1%
  - Visual acuity reduced 1%

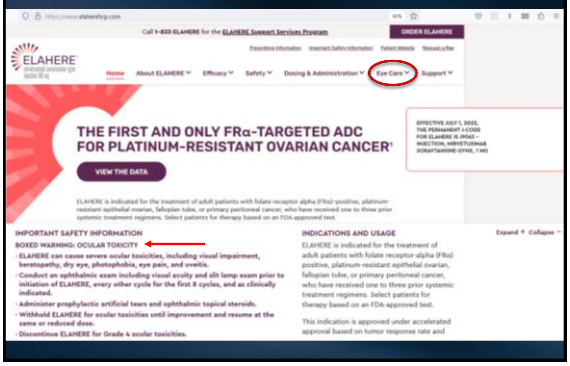


- Most common non-ocular adverse reaction that occurred in patients treated with DEXTENZA was headache (1%)

Elahere (mirvetuximab soravtansine-gynx)

- Indications
  - treatment of adult patients with FRα positive, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer and
    - have not responded to or are no longer responding to treatment with platinum-based chemotherapy
    - have received 1 to 3 prior types of chemotherapy
- Dosage and administration
  - IV infusion after dilution every 3 weeks until disease progression or unacceptable toxicity
    - Ultimately dictated by prescribing doctor

Elahere (mirvetuximab soravtansine-gynx)



Elahere (mirvetuximab soravtansine-gynx)

- Patients should receive a baseline ophthalmic exam from an eye care provider, including visual acuity and slit lamp exam, prior to treatment initiation, and follow-up exams during every other cycle for the first 8 cycles and as clinically indicated
- Tell your patients to avoid use of contact lenses
- The use of ophthalmic topical steroids and preservative-free lubricating eye drops is recommended. The initial prescription and renewals of any corticosteroid medication should be made only after examination with a slit lamp

Elahere (mirvetuximab soravtansine-gynx)

Recommended schedule for eye drops

Steroid eye drops[1]

- 6x — Instruct patients to administer 1 drop of ophthalmic topical steroid in each eye 6 times daily starting the day prior to each infusion of ELAHERE until day 4
- 4x — Then patients should administer 1 drop in each eye 4 times daily on days 5–8 of each cycle of ELAHERE

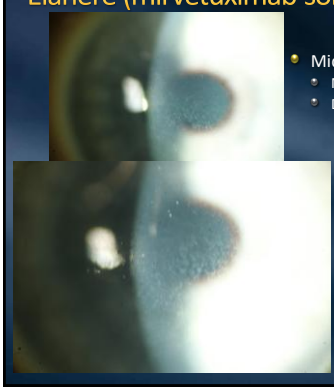
Lubricating eye drops[1-4]

- 4x — The use of preservative-free* lubricating eye drops at least 4 times daily and as needed is recommended during treatment with ELAHERE
- Advise patients to wait at least 10 minutes after ophthalmic topical steroid administration before instilling lubricating eye drops*

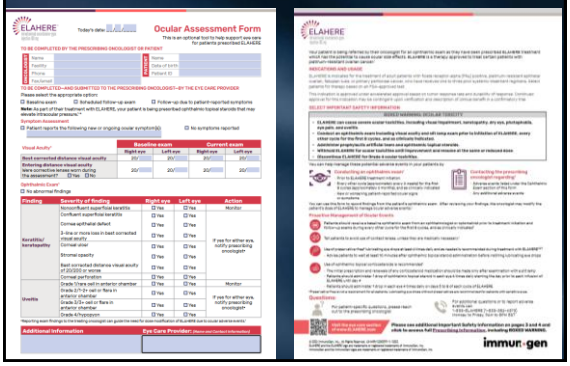
Elahere (mirvetuximab soravtansine-gynx)

- Can cause severe ocular adverse reactions, including visual impairment, keratopathy (corneal disorders), dry eye, photophobia, eye pain, and uveitis
  - occurred in 61%
- Most common reactions were:
  - visual impairment (49%)
  - keratopathy (36%)
  - dry eye (26%)
  - cataract (15%)
  - photophobia (13%)
  - eye pain (12%)

Elahere (mirvetuximab soravtansine-gynx)



- Microcystic epithelial changes
  - MECs
  - Do not stain



Faricimab (Vabysmo)

- FDA approved Genetech's faricimab for the treatment of (nAMD) and (DME)
  - Jan 31, 2022
- Faricimab is the first bispecific antibody designed for the eye
- It targets two distinct pathways – via angiopoietin-2 (Ang-2) and vascular endothelial growth factor-A (VEGF-A) – that drive a number of retinal conditions
  - Ang-2 and VEGF-A contribute to vision loss by destabilizing blood vessels, causing new leaky blood vessels to form and increasing inflammation
- By independently blocking both pathways, faricimab is designed to stabilize blood vessels, potentially resulting in better vision outcomes, for longer, for people living with retinal conditions

Faricimab

- Across four phase III studies, approximately half of patients receiving faricimab could extend treatment time to every four months – the first time this level of durability has been achieved in phase III nAMD and DME studies
- More than half of participants in the faricimab personalized dosing arms had extended time between treatments to 16 weeks at year one – the first time this level of durability has been achieved in a phase III diabetic macular edema study
- Faricimab was generally well-tolerated, with no new safety signals identified

Gabapentin

- Gabapentin (Neurontin, Gabarone)
  - GABA analog
  - initially synthesized to mimic the structure of gamma-aminobutyric acid (GABA)
  - Mechanism of Action: unknown

Gabapentin

- Indications
  - Management of post-herpetic neuralgia in adults
  - Adjunctive therapy in the treatment of partial onset seizures, with and without secondary generalization, in adults and pediatric patients 3 years and older with epilepsy
- Contraindications/Cautions
  - Impaired renal function
  - Elderly patients
  - Hypersensitivity to drug/class/compound
- Off label uses
  - Migraines
  - Neuropathic pain
  - Bipolar disorder
  - ADD, restless leg syndrome
  - Insomnia

Gabapentin

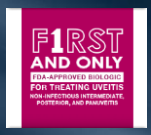
- Neuropathic pain
  - Post-PRK use
    - 100-300 mg TID 1-2 days prior, 3-4 days after
  - HZO
- Maximum daily dose 3600 mg
- 10th most widely prescribed medication in US

Gabapentin

- New link noted between gabapentinoid use and incidence of acute angle closure
- Looked at all adult patients that developed AAG between 1/1/06 and 12/31/16
  - PharMetrics Plus Database
  - Results were found to be statistically significant if gabapentin was used the year before diagnosis
    - Not statistically significant with current use
  - Pregabalin did not show statistical significance the year before diagnosis or with current use

Humira (adalimumab)

- Indications
  - Rheumatoid Arthritis
  - Juvenile Idiopathic Arthritis
  - Psoriatic Arthritis
  - Ankylosing Spondylitis
  - Pediatric Crohn's Disease
  - Ulcerative Colitis
  - Plaque Psoriasis
  - Hidradenitis Suppurativa
  - Uveitis
    - Non-infectious intermediate, posterior, or panuveitis in adult patients



Humira (adalimumab)

- Contraindications
  - None
- Cautions / Warnings
  - Not to be started during active infection
- Treatment
  - Initial dose of 80 mg followed by 40 mg given every other week starting 1 week after initial dose

Humira (adalimumab)

- Mechanism of Action
  - TNF-α and other pro-inflammatory cytokines drive chronic inflammation of NI uveitis
  - TNF-α is overexpressed in the serum and ocular fluid in patients with NI uveitis
  - The relationship between these pharmacodynamic activities and the mechanism(s) by which HUMIRA exerts its clinical effects is unknown
- One of the top selling drugs in US
  - Over $19.8 Billion in sales in 2020
  - Over $20.7 Billion in sales in 2021
  - Over $21.2 Billion in sales in 2022

Humira (adalimumab)

- Pregnancy
  - Benefits outweigh risks in 1st and 2nd trimester
  - Weigh risk:benefit ratio in 3rd trimester
- Lactation
  - May use while breastfeeding
  - No known risk of infant harm

Iyuzeh (latnoprost ophthalmic 0.05% PF)

- Thea Pharma
- Approved September 26, 2023
- prostaglandin F2α analog indicated for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension
- Bottled without BAK and other preservatives
- 1 gtt QHS OU

Iyuzeh (latnoprost ophthalmic 0.05% PF)

- Does not need to be manufactured, distributed, or stored at refrigerated temperatures
- Consistent IOP-lowering effects and tolerability
  - lowered IOP by 3 to 8 mmHg in patients with OAG or OHT (mean baseline of 19 to 24 mmHg)
  - BAK-preserved Xalatan lowered IOP 4 to 8 mmHg
- Pivotal trial comparing Iyuzeh with Xalatan
  - 334 patients over 84 days
  - demonstrated that Iyuzeh had similar clinically meaningful reductions in IOP from baseline with fewer ocular adverse events
  - Less than 2% of patients in the Iyuzeh group experienced instillation site pain, pruritis,or conjunctival hyperemia

Jetrea (ocriplasmin)

- FDA-approved non-surgical treatment for symptomatic VMA
- FDA approved October 2012
- Indication
  - For the treatment of symptomatic vitreomacular adhesion
  - Intravitreal injection
- More than 35,000 eyes treated globally

Jetrea (ocriplasmin)

Jetrea (ocrmiplasmin)

- **Apr 30, 2020 — As part of a global transfer of commercial rights for JETREA to ThromboGenics, the decision has been taken to discontinue the manufacture for the United States and cease the commercialization of JETREA in this market, effective May 31, 2020. ... JETREA can be used until the end of the expiry date, which is January 31, 2021**.
  - The decision to discontinue the sale of Jetrea is being taken for business reasons and is not because of any safety or efficacy concerns.

But…….

In March 2020, Oxurion and Inceptua Group signed a global commercial license agreement for Jetrea®
- still being used in EU, United Kingdom

Ketotifen

- Non-competitive H1 anti-histamine and mast cell stabilizer
- Temporarily prevents itching of the eye caused by a condition known as allergic conjunctivitis
- OTC Products
  - Zaditor
  - Alaway
  - Other generic versions

Ketotifen

- Acuvue TheraVision
  - First drug-eluting CL
- Approved March 2022 by FDA
- Available in Europe, Canada, Japan

Ketotifen (Acuvue TheraVision)

- Daily disposable
- 0.019 mg ketotifen per CL
- exhibited a clinically and statistically meaningful reduction in itching in as fast as 3 minutes after lens insertion and lasted up to 12 hours
- J&J has not released US launch plans

Lumify (brimonidine tartrate 0.025%)

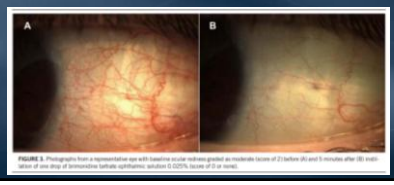
- Dec. 22, 2017 Bausch + Lomb
- (FDA) has approved LUMIFY™ (brimonidine tartrate ophthalmic solution 0.025%) as the first and only over-the-counter (OTC) eye drop developed with low-dose brimonidine tartrate for the treatment of ocular redness.
- Brimonidine, which was first approved by the FDA in 1996 for intraocular pressure (IOP) reduction in glaucoma patients, is available at higher doses in prescription eye care products.

Lumify (brimonidine tartrate 0.025%)

- OTC for treatment of ocular redness
- For adults and children >5 years old
  - 1 drop every 6-8 hours
  - Not to be used more than 4x daily
- 6 clinical studies in over 600 patients
  - included both pediatric and geriatric subjects
  - double-blinded, randomized, placebo-controlled
  - Phase 3 efficacy study
    - 95% of subjects reported significant symptom improvement at 1 minute
    - 79% of respondents maintained significant redness reduction at 8 hours
    - low-risk of allergic reactions among all patient groups

Lumify (brimonidine tartrate 0.025%)

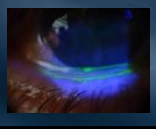
- Selective alpha-2 adrenergic receptor agonist
  - No rebound hyperemia
  - No dependency
  - No tachyphylaxis
- Constricts veins and increases availability of oxygen to surrounding tissue



Lumify (brimonidine tartrate 0.025%)

Lumify (brimonidine tartrate 0.025%)

- 20 patients with more than 0.5 mm of conjunctival chalasis who were experiencing ocular pain
- measured the chalasis with the Oculus Keratograph 5M prior to the instillation of LUMIFY and 3 minutes afterward
- revealed a trend of early tightening of the conjunctiva, on average approximately 20% tighter



Miebo (perfluorohexyloctane)

- Bausch & Lomb
- FDA Approval May 19, 2023

- First in class eye drop to treat signs and symptoms of dry eye disease
- May prevent excessive tear evaporation and has the ability to restore tear film balance
- Has a unique mode-of-action: It stabilizes the lipid layer for hours to protect the tear film and has the ability to penetrate the Meibomian glands

Miebo (perfluorohexyloctane)

- No inactive ingredients
  - Water free
  - Preservative free
  - Steroid free
- 2 large clinical trials (Gobi and Mojave)
  - Improvement in signs and symptoms of DED
    - Total corneal fluorescein staining
    - Eye dryness score
  - Change from baseline at Day 57 (primary endpoint) and Day 15 (secondary endpoint)

Miebo (perfluorohexyloctane)

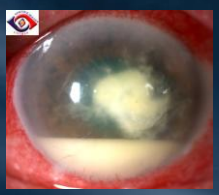
- Instill one drop of MIEBO four times daily into each eye
- No serious ocular adverse events
- Low rate of discontinuation (n=1)
- Side Effects 1-3%
  - Eye redness
  - Temporary blurred vision

Miebo (perfluorohexyloctane)

- PLLR
  - There are no adequate and well controlled studies with MIEBO in pregnant women
  - There is no data on the presence of perfluorohexyloctane in human milk, the effects on the breastfed infant, or the effects on milk production

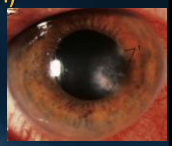
Natacyn (5% Natamycin Suspension)

- Indicated for the treatment of fungal blepharitis, conjunctivitis and keratitis
  - Feathery borders
  - Satellite lesion
  - Dry Rough texture
  - Hx of CL wear
- Culture on sabouraud dextrose agar



- Only commercially available antifungal
  - Works well against Fusarium and Aspergillus most common pathogen

Natacyn (5% Natamycin Suspension)



- Fungal keratitis is relatively uncommon
  - 6-20% of all microbial keratitis
  - Makes up 5% of all CL related infections
- 2005 outbreak of Fusarium keratitis was linked to MPS
  - B+L ReNu with MoistureLoc
- CDC found cases starting June 2005, peaking April 2006
  - 164 confirmed cases over 33 states and 1 US territory
  - 71% reported using MoistureLoc
    - Withdrawn from US Market on April 13, 2006
      - World market on May 15, 2006
    - Post-recall surveillance found sharp decline of Fusarium within 2 mo of outbreak

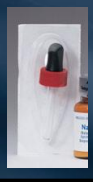
Natacyn (5% Natamycin Suspension)

- Despite resolution of outbreak, the number of contact lens related fungal infections are still on the rise
  - Mass Eye and Ear study (excluded data from outbreak)
    - 19 cases from 1999-2002
    - 40 cases from 2004-2007
- Increased to the point that the proportion of infections related to CL wear (20-35%), has supplanted trauma (10-20%) as the most common cause of fungal keratitis
  - Despite Fusarium levels going back to baseline after outbreak, non-Fusarium increased in both CL and non-CL wearers

Jurkunas U, Behlau I, Colby K. Fungal keratitis: changing pathogens and risk factors. Cornea 2009; 28:638–643.

Natacyn (5% Natamycin Suspension)

- Dosage: q1-2h, shake well
  - Taper to 6x/d after 3-4d Tx - progresses over epi
  - Tx continued for 14-21d
  - Tx should include debridement prior if no defect exists
- MOA
  - Predominately fungicidal
  - Binding of fungal cell membrane depleting cellular constituents
- Suspension adheres to epi ulcer and in fornices
- Limited usage, limited data
  - Monitor pt twice a week
- Pregnancy Category C

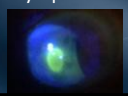


Oxervate (cenegermin)

- Dompé Pharmaceutical
- First treatment specifically indicated for neurotrophic keratitis
- First ever topical biological medication in the ophthalmic space
- First ever application of a human nerve growth factor as a drug or treatment
- Was authorized in Europe in 2017
- Received Orphan Drug Designation, Fast Track Status, Breakthrough Therapy Designation
  - Ultimately Priority Review

Oxervate

- Neurotrophic Keratitis
  - rare condition that affects fewer than 65,000 people in US
  - results from impaired function of corneal nerves
    - herpetic or other infections, ocular surface injuries, ocular or neurologic surgeries, and some systemic conditions that can impair corneal sensation
    - treatment options were limited to symptomatic treatments



Oxervate

- 151 patients in 2 studies
  - 8 week, randomized controlled
  - Multi-center, double masked
- Drops used 6x/day in affected eye(s) for 8 weeks
  - Compared drops to placebo or different concentration (Study 1)
  - Compared drops to placebo (Study 2)
- Results: Complete corneal healing in 8 weeks in up to 72% of patients (Oxervate) vs. 28% (without Oxervate)

Pilocarpine 1.25% (Vuity)

- An optimized formulation of pilocarpine 1.25%, a cholinergic muscarinic receptor agonist
  - The presbyopia treatment works through pupil modulation — constricting the pupil to create a “pinhole effect” and increase depth of focus, improving near vision
  - Approved October 29, 2021

Pilocarpine 1.25% (Vuity)

- Allergan, an AbbVie Company
- Bilateral, once-daily dosing had a rapid onset (15 minutes) of near vision improvement, with a duration of up to 6 hours
  - Now approved as BID dosing, 3-6 hours after initial dose
  - 20/40 or better vision in photopic, high-contrast, binocular DCNVA Improvement compared with vehicle for intermediate vision for at least 10 hours
  - ≥2-line gains in mesopic, high-contrast, binocular DCNVA
  - Pupillary response and the return to baseline were maintained from Day 1 to Day 30, with no tachyphylaxis

Pilocarpine 1.25% (Vuity)

Adverse Events

System Organ Class Preferred Term	AGN-190584 (N=163) % (n)	Vehicle (N=159) % (n)
Eye disorders		
Visual impairment	4.3% (7)	0.6% (1)
Conjunctival hyperemia	2.5% (4)	2.5% (4)
Vision blur	2.5% (4)	1.3% (2)
Eye irritation	2.5% (4)	0.6% (1)
Eye pain	2.5% (4)	0.6% (1)
Lacrimation increased	2.5% (4)	0.0% (0)
Punctate keratitis	0.6% (1)	3.1% (5)
Nervous system disorders		
Headaches	14.1% (23)	9.4% (15)
Gastrointestinal disorders		
Nausea	2.5% (4)	0.0% (0)
Discontinuations due to AEs	1.2% (2)	0.6% (1)

Reported by at least 2% of patients in either group.

- Participants were **prompted** to report adverse events (AEs) of headaches
- In the study arm, headaches were mostly mild (87%) and transient, requiring no treatment
- **No participants discontinued AGN-190584 due to headaches**
- **No serious AEs were reported**
- **No retinal detachments were observed**

Nijm LM, et al. Presented at: WSO 2021; August 26-29, 2021; Amelia Island, FL.

Presbyopia Treatment

Potential new presbyopia treatments in development

Product name	Active ingredients	Mechanism of action	Dosage	Onset/ duration
US FDA Trials				
AGN-190584 AGN-190591	• Pilocarpine • Dorzolamide	Miosis Myalgias and Redness	Multiple different combinations, QD and BID	Unknown / Study notes 10 hours
Brimochol	• Carbachol • Brimonidine	• Miotic	• QD	• 30 minutes/All day
CSF-1	• Parasympathomimetic • NSAID • (proprietary)	• Miotic • Mitigate Discomfort	• BID	• Unknown/Unknown
Nyxol	• Low-dose pilocarpine • Phenylephrine mesylate	• Miotic • Pupil constriction	• Kit format with PM and pilocarpine and phenylephrine dosage separately	• Unknown/Unknown
PRX-100	• Apraclidine • Tropicamide	Miotic Mitigate accommodation	QD for 4 hrs/BID for "all day"	30 min/ 5-7 hours'
Qelosi	• Pilocarpine	Miotic	micro-dose array print Tpt.	PRN /3-4 hours
Non-US FDA				
FOV Tears	• Pilocarpine • Phenylephrine • Nepafenac • Phentolamine • Naphazoline • Polyethylene glycol	Miotic Reduce redness CM muscle spasm Myalgias Reduce redness Increase comfort	BID	10 minutes/ 4-6 hours

BID = twice daily; CM = ciliary muscle; NSAID = non-steroidal anti-inflammatory drug; PM = phentolamine mesylate; PRN = as needed; QD = daily

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Pilocarpine 1.25% (Vuity)

- Allergan, an AbbVie Company
  - GEMINI 1 Phase 3 Clinical Trial • Primary efficacy endpoint:
    - proportion of participants gaining ≥3 lines from baseline in mesopic, high-contrast, binocular DCNVA at Day 30, Hour 3 •
    - Secondary efficacy endpoints: – Proportion of participants achieving DCNVA 20/40 (functional vision) or better in photopic illumination – Proportion of participants gaining ≥2 lines from baseline in mesopic, high-contrast, binocular DCNVA – Change from baseline in photopic, distance-corrected intermediate visual acuity (DCIVA

Pilocarpine

- Qlosi (pilocarpine 0.4%)
  - Orasis Pharmaceuticals
  - FDA approval 10/18/23
    - expected to be commercially available in the U.S. in the first half of 2024
  - Miotic-based eye drops as a potential alternative to reading glasses
  - Preservative Free
    - This drop combines a parasympathomimetic with an NSAID in an oil-based vehicle to preclude discomfort due to ciliary spasm and minimize the risk of uveitis
  - The company claims that the drug has a fast onset of action and its effects are long-lasting
  - Instill one drop of QLOSI in each eye. This can be repeated a second time after 2 to 3 hours for an effect up to 8 hours.
  - Similar potential side effects and risks as other miotics

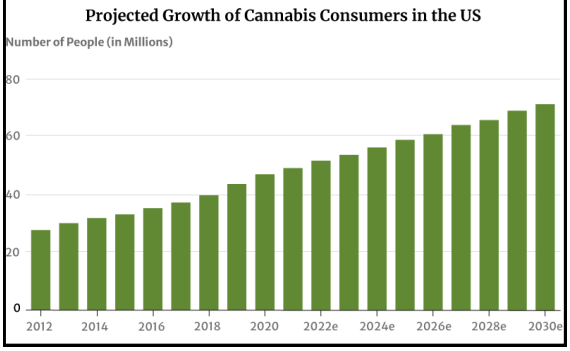
Q

Queen Ann's Lace

- Slang term for marijuana

Cannabis
Ganja
Hash
Hashish
Hemp
Mary Jane
Pot
Reefer
Weed
Acapulco
Gold/Red
Ace
Catnip
Ditch Weed
Fatty
Fine Stuff
Flower
Fu
Gash
Haircut
Hanhich
Hocus

Queen Ann's Lace



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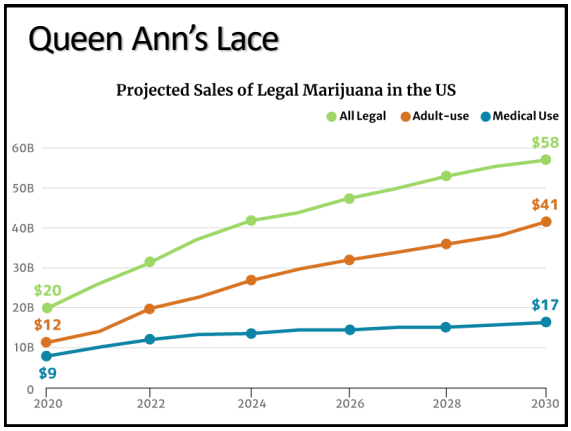
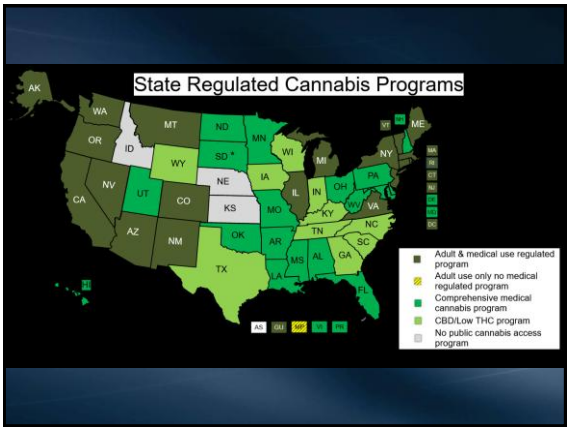


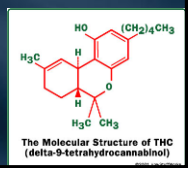


Queen Ann's Lace

- 37 states and DC, Guam, Puerto Rico, and USVI have medical marijuana laws
- 19 states, 2 territories, and DC have enacted recreational use laws (non-medical)
- 18 have limited use laws that allow for some extracts to be used medicinally
  - "[T]he Department shall issue a registry identification card to a qualifying patient with intractable epilepsy or involuntary muscle contractions that cause slow, repetitive movements or abnormal postures, such as dystonia, who is younger than 18 years of age, but only for the use of medical marijuana oil [that is not more than 7% THC]."

Queen Ann's Lace

- Binds to cannabinoid receptors in brain
  - Highest density in areas responsible for influencing
    - Pleasure
    - Memory
    - Thinking
    - Concentrating
    - Sensory and time perception
    - Coordinated movement



Queen Ann's Lace

- Potential systemic effects
  - cardiac arrhythmias
  - coronary insufficiency
  - myocardial infarction
- Potential ocular effects
  - Decreased tracking
  - Delay processing of information across retinal ganglion cells
  - Dilated pupils
  - IOP lowering capabilities
    - The high dose of marijuana necessary to produce a clinically relevant effect on IOP in the short term requires constant inhalation, as much as every three hours.
      - - Glaucoma Research Foundation

Queen Ann's Lace

- Studies show marijuana may lower IOP by up to 45%
  - Peaks at 30 minutes
  - Decreases at 60 minutes
- Two main types of cannabinoids
  - CBD (cannabidiol)
    - May have neuro-protective and anti-oxidant properties
  - THC (delta-9-tetrahydrocannabinol)
    - High-inducing

Queen Ann's Lace

- Exact MOA unknown
  - 2 different cannabinoid receptors (CB1 and CB2)
  - CB1 main receptor at ocular level
  - Greatest density found in trabecular meshwork, non-pigmented ciliary epithelium, and ciliary muscles
  - Location of CB1 receptors as well as its effect on cyclic adenosine monophosphate suggests its influence on aqueous production

Rhopressa (Netarsudil)

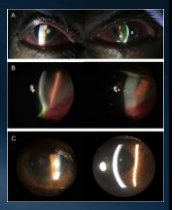
- Aerie Pharmaceuticals FDA approval Dec 2017
  - Launched May 2018
- Netarsudil ophthalmic solution 0.02%
  - The first US FDA-approved Rho Kinase / ROCK inhibitor
  - Rho kinases are serine/threonine protein kinases expressed in the trabecular meshwork
  - Rho kinase inhibitors have been shown in human, and animal models to decrease IOP
- MOA distinct from all other therapies
  - Works as both a Novel Rho kinase inhibitor, and a norepinephrine transporter (NET) inhibitor
- Recommended dosage is one drop in the affected eye(s) once daily in the evening – QHS
  - as effective as timolol BID in lowering IOP
  - But less effective than latanoprost (about 1mmHg)

Rhopressa

- Adverse reactions
  - Conjunctival hyperemia (53%) of patients
    - More than latanoprost
  - Corneal verticillata, instillation site pain, and conjunctival hemorrhage (20%)
  - Instillation site erythema, corneal staining, blurred vision, increased lacrimation, erythema of eyelid, and reduced visual acuity (5-10%)

Rhopressa

- Adverse reactions
  - New reports of Epithelial Keratopathy
    - Conjunctival hyperemia
    - Corneal epithelial bullae
    - Keratic precipitates without hypopyon
  - Resembles microcystic edema and bullous keratopathy and were predominantly in the inferior cornea
  - Starts days after exposure to netarsudil and resolves after discontinuation



Netarsudil-associated epithelial keratopathy. Meera S. Ramakrishnan, Victoria M. Addis, Amanda Y. Lehman, , Prithvi S. Sankar. American Journal of Ophthalmology Case Reports Volume 19, September 2020, 100800

Rhopressa

- Use in patients with Corneal Edema:
  - Ripasudil (used in Japan for OcHTN) has shown efficacy against corneal endothelial dysfunction like Fuch's corneal dystrophy
  - Variety of underlying pathologies for endothelial dysfunction can resolve with netarsudil use
  - Both focal endothelial dysfunction and diffuse endothelial dysfunction can be improved with the addition of netarsudil
  - Successful corneal clearance typically occurs within the first 1 month of treatment (QHS)

Cornea Volume 40, Number 1, January 2021

Before 6/9/22

Before cell counts 2217 OD, 2445 OS
Before pachy 656 OD, 656 OS

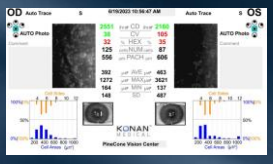
After 12/11/23

After cell counts 2315 OD, 2262 OS
After Pachy 624 OD, 645 OS

Before 11/1/21

Before cell counts 2208, OD 1835 OS
Before pachy 616 OD, 624 OS

After 6/19/23



After cell counts 2551 OD, 2160 OS
After Pachy 556 OD, 606 OS

Syfovre (pegcetacoplan injection)

- Apellis Pharmaceuticals
- First FDA-approved treatment for GA secondary to macular degeneration
  - February 17, 2023
  - 1 injection into affected eye every 25-60 days
- Contraindications
  - Active ocular or periocular infections
  - Active intraocular inflammation
- Warnings/Precautions
  - Endophthalmitis and Retinal Detachments
    - Neovascular AMD
    - Intraocular inflammation
    - Increased Intraocular Pressure

Syfovre (pegcetacoplan injection)

- multi-center, randomized, double-masked Phase 3 clinical trials
  - OAKS and DERBY
    - Syfovre EOM (420)
    - Syfovre Monthly (419)
    - Sham EOM (211)
    - Sham Monthly (208)
  - Trial Assessment
    - Change in baseline of rate of GA lesion area growth measured by FAF

Syfovre (pegcetacoplan injection)

- OAKS and DERBY
  - Lesions with and without subfoveal involvement
  - With and without history of active CNV in the fellow eye
  - Unilateral and bilateral GA
  - Unifocal and multifocal lesions
  - Broad range of lesion sizes (2.5 mm^2 to 17.5 mm^2)
- 2 year trials
- 1200 patients
- ~12,000 injections

Syfovre (pegcetacoplan injection)

After 2 years, compared to those who did not receive Syfovre

- Trial 1
  - Slowed lesion growth by 22% when taken monthly (n=202)
  - Slowed lesion growth by 18% when taken every other month (n=205)
- Trial 2
  - Slowed lesion growth by 18% when taken monthly (n=205)
  - Slowed lesion growth by 17% when taken every other month (n=205)

Syfovre (pegcetacoplan injection)

Syfovre (pegcetacoplan injection)

- There are no adequate and well-controlled studies of SYFOVRE administration in pregnant women to inform a drug-associated risk. The use of SYFOVRE may be considered following an assessment of the risks and benefits.
- It is not known whether intravitreal administered pegcetacoplan is secreted in human milk or whether there is potential for absorption and harm to the infant. Animal data suggest that the risk of clinically relevant exposure to the infant following maternal intravitreal treatment is minimal Because many drugs are excreted in human milk, and because the potential for absorption and harm to infant growth and development exists, caution should be exercised when SYFOVRE is administered to a nursing woman.
- It is recommended that women of childbearing potential use effective contraception methods to prevent pregnancy during treatment with intravitreal pegcetacoplan. Advise female patients of reproductive potential to use effective contraception during treatment with SYFOVRE and for 40 days after the last dose. For women planning to become pregnant, the use of SYFOVRE may be considered following an assessment of the risks and benefits

Topical Losartan

- Losartan is an Angiotensin II Receptor Blocker (ARB)
  - Relaxes the blood vessels
    - Oral med Used to treat high blood pressure (hypertension) and to help protect the kidneys from damage due to diabetes
    - It is also used to lower the risk of strokes in patients with high blood pressure and an enlarged heart
  - Has potential to augment pharmacological therapeutics for ocular diseases where transforming growth factor (TGF) beta plays a central role in pathophysiology

Topical Losartan

- Has potential to treat numerous diseases of cornea and anterior segment that are mediated by TGF beta-dependent myofibroblasts bec of its effect on TGR beta signal transduction
  - Could possibly decrease corneal deposits in TGFB1-related corneal dystrophies
  - Intraocular fibrotic diseases could potentially be treated
- .8mg/ml losartan in BSS treated 6x day for at least 6 months

Topical Losartan

- Some potential uses of topical losartan include:
- Corneal scarring
  - Losartan can prevent or reverse scarring in the cornea caused by myofibroblasts. It can also be used to treat scarring after refractive surgery, microbial keratitis, herpes simplex and zoster keratitis, and thermal or chemical burns
- Conjunctival fibrotic diseases
  - Losartan can be used to treat conjunctival fibrotic diseases like ocular cicatricial pemphigoid and Stevens–Johnson syndrome
- Glaucoma surgical procedures
  - Losartan could be used to reduce conjunctival bleb scarring and shunt encapsulation after glaucoma surgical procedures

Topical Losartan

- For three decades, Dr. Steve Wilson's lab (CCF) has been funded by the National Institutes of Health and/or Department of Defense to study corneal wound healing
- A focus of their research has been controlling scar-causing myofibroblasts, the main type of cell that causes corneal opacity after injury, infection and some surgeries
- Myofibroblasts develop during a process driven by two growth factors:
  - transforming growth factor (TGF) beta-1
  - TGF beta-2
- Losartan is known to hinder TGF beta signaling by inhibiting a signal transduction molecule, extracellular signal-regulated kinase (ERK)

Topical Losartan

- More severe, persistent scarring is almost always caused by myofibroblasts
- However, those cells are continually dying by apoptosis and being replaced with new myofibroblasts in scars in the cornea, even years after the original injury
- If we interrupt the process, with losartan
  - myofibroblasts that are dependent on TGF beta for regeneration and survival will instead be replaced with new, normal corneal cells that restore corneal transparency

Topical Losartan

- Losartan dosing
  - Dr. Wilson advises investigators to limit concentrations of losartan to no more than 0.8 mg/mL in a balanced salt solution (pH 6.7-7.0) because different formulations have not been tested in animal models
- "Higher doses could interfere with normal TGF beta functions and lead to unforeseen complications," he says
- "We need to proceed with caution until higher dosages are carefully evaluated"

Topical Losartan

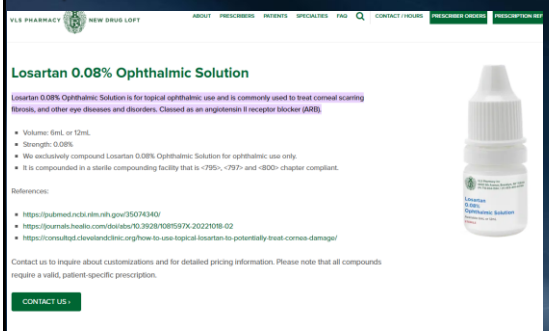
Slitlamp biomicroscopy of the patient's right eye in May 2023 (A), premedication, August 2023 (B), after 2 months of losartan application, and September 2023 (C), after 3 months of losartan application. A marked reduction in opacity was noted after topical losartan treatment.

*Topical Losartan for Treating Corneal Haze After Ultraviolet-A/Riboflavin Collagen Cross-Linking. Rodgers, Emily Grace BS*Link to author's ORCID page: Rodgers, Emily Grace BSAI-Mohtaseb, Zaina MD*Chen, Allison J. MD, MPH†Link to author's ORCID page: Chen, Allison J. MD, MPH *Whitsett Vision Group, Houst*

Topical Losartan

- Losartan must be compounded by a pharmacy that specializes in ophthalmic compounding
- These pharmacies use specialized equipment and a sterile environment to prepare the medication

Topical Losartan



Upneeq (0.1% Oxymetazoline hydrochloride)

- Oxymetazoline hydrochloride ophthalmic solution 0.1%
  - Approved July 8, 2020
  - RVL Pharmaceuticals
- Indication
  - First and only treatment of acquired blepharoptosis in adults
  - Non-surgical treatment
  - 1 gtt in affected eye(s) daily

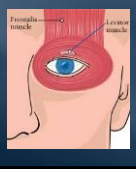
Upneeq (oxymetazoline hydrochloride ophthalmic solution) 0.1%

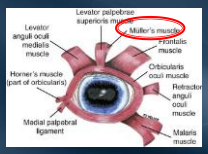
Upneeq

- Mechanism of Action - Alpha adrenergic agonist
  - Likely inspired by its cousin apraclonidine, which has been used as off-label treatment
  - Botox-induced ptosis
  - Horner's syndrome diagnosis and treatment
- Upneeq at once a day dosing works to similarly engage Müller's muscle, lifting the upper lids 1-2 mm for 8-10 hours, with minimal side effects

Upneeq

- 3 Muscles responsible for upper eyelid retraction
  - Levator palpebrae superioris
  - Frontalis muscle
  - *Müller's muscle*





Upneeq

- Overall safe and effective alternative to surgery
- No insurance coverage, only available through RVL Pharmacy
- Effective monthly price is ~ $150/month

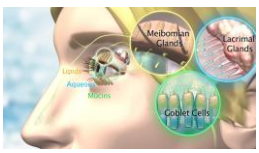
Varenicline (Tyrvaya)

- Viatris
  - Previously Oyster Point Pharma
  - Approved October 18th, 2021
- Highly selective nicotinic acetylcholine receptor agonist (nAChR)
- Activates the trigeminal parasympathetic nervous system to stimulate the LFU to re-establish tear film homeostasis
- Novel compound developed as preservative-free nasal spray (BID) to treat signs and symptoms of dry eye disease

Parasympathetic Nervous System Controls Tear Film Homeostasis

The trigeminal nerve is **accessible within the nasal cavity**, and is activated by OC-01 (varenicline) by stimulating **cholinergic receptors**.

The trigeminal nerve provides the pathway for **parasympathetic stimulation** of the lacrimal functional unit (LFU) to activate **complete natural tear film**.

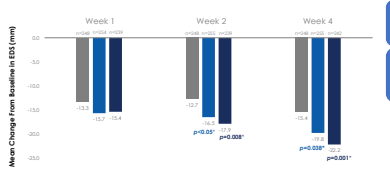


34% of basal tear production is due to inhaling air through the nose[1]

1. Gupta A, Heigle T, and Pflugfelder SC. Nasolacrimal stimulation of aqueous tear production. Cornea. 1997;16(6):645-648.

OC-01 (varenicline) Nasal Spray Improved Symptoms as Early as Week 2 in ONSET-2

ONSET 2



OC-01 (varenicline) Nasal Spray demonstrated EDS improvements in the in-clinic environment (mm) as early as Week 2 and at Week 4

"Smoldering activation" of cholinergic receptors (some receptors in a desensitized state while others in an activated state) occurs over many hours with cholinergic agonist activity[1]

- Vehicle Control
- OC-01: 0.6 mg/mL
- OC-01: 1.2 mg/mL

Data presented with imputation for missing assessments; observed data does not alter interpretation
All comparisons made to control group.
*Nominal p-value

ONSET-1 Adverse Event Profile

ONSET 1

Treatment-Emergent Adverse Events in >5% of Subjects Potentially Related to OC-01 (varenicline)

	Control (n=43)	OC-01 0.12 mg/mL (n=47)	OC-01 0.6 mg/mL (n=48)	OC-01 1.2 mg/mL (n=44)	Total (n=182)
Sneeze After Any Instillation	0	29 (62)	38 (79)	37 (84)	104 (57)
Cough After Any Instillation	0	4 (9)	6 (13)	11 (25)	21 (12)
Throat Irritation After Any Instillation	0	0	7 (15)	9 (20)	16 (9)
Instillation Site Irritation	0	3 (6)	8 (17)	8 (18)	19 (10)

All events mild (82%) or moderate (18%) in severity. No severe events

No serious adverse events related to study drug

Subjects reporting more than 1 event are only counted once at the maximum relationship reported.
A TEAE is defined as an AE that is new or worsened in severity compared to the first dose of study drug.
Safety population.
AE records were cut off at 28-day treatment period.

Wellbutrin (buproprion)

- Indications
  - Treatment of major depressive disorder
  - Prevention of Seasonal Affective Disorder (SAD)
- Formulations
  - Wellbutrin XL (150mg, 300mg)
  - Wellbutrin (75mg, 100mg)
  - Wellbutrin SR (100mg)
- Almost 30 million Rx (2020)
- Contraindications

Wellbutrin (buproprion)

- Contraindications
  - WELLBUTRIN XL is contraindicated in patients with seizure disorder
  - WELLBUTRIN XL is contraindicated in patients with a current or prior diagnosis of bulimia or anorexia nervosa as a higher incidence of seizures was observed in such patients treated with WELLBUTRIN XL
  - WELLBUTRIN XL is contraindicated in patients undergoing abrupt discontinuation of alcohol, benzodiazepines, barbiturates, and antiepileptic drugs
  - The use of MAOIs (intended to treat psychiatric disorders) concomitantly with

WARNING: SUICIDAL THOUGHTS AND BEHAVIORS; AND NEUROPSYCHIATRIC REACTIONS
See full prescribing information for complete boxed warning.

- **Increased risk of suicidal thinking and behavior in children, adolescents, and young adults taking antidepressants. (5.1)**
- **Monitor for worsening and emergence of suicidal thoughts and behaviors. (5.1)**
- **Serious neuropsychiatric events have been reported in patients taking bupropion for smoking cessation. (5.2)**

  - The use of WELLBUTRIN XL within 14 days of discontinuing treatment with an MAOI is also contraindicated.
  - Starting WELLBUTRIN XL in a patient treated with reversible MAOIs such as linezolid or intravenous methylene blue is contraindicated WELLBUTRIN XL is contraindicated in patients with known hypersensitivity to bupropion or other ingredients of WELLBUTRIN XL.
  - Anaphylactoid/anaphylactic reactions and Stevens-Johnson syndrome have been reported

Wellbutrin (buproprion)

- Ophthalmic Concerns
  - Angle-closure glaucoma
    - has occurred in patients with untreated anatomically narrow angles treated with anti-depressants who do not have a patent iridotomy
  - Case control study from health claims database
    - Over 6 million patients
    - Looked for patients with angle closure, instituted controls
    - Risk of angle closure (<50 years old) was twice as high if they were taking Wellbutrin
      - Symes RJ, Etminan M, Mikelberg FS. Risk of Angle-Closure Glaucoma With Bupropion and Topiramate. *JAMA Ophthalmol.* 2015;133(10):1187-1189. doi:10.1001/jamaophthalmol.2015.2180
- Take home point?
- Pregnancy Category C

Xdemvy (lotaliner ophthalmic solution 0.25%)

- Tarsus Pharmaceuticals
- Approved July 25, 2023
- First and only approved therapeutic for Demodex blepharitis

Xdemvy (lotaliner ophthalmic solution 0.25%)

- Demodex blepharitis
  - Affects 25 million patients in US
  - Common cause of itching, grittiness and eye dryness
    - leads to lash thinning, lash loss, evaporative dry eye, hordeola, chalazion, meibomian gland atrophy and rosacea
  - Evaluate lids at slit lamp by having patient look down and examine base of upper lid margin

Xdemvy (lotaliner ophthalmic solution 0.25%)

- Anti-parasitic that works by paralyzing the mite's nervous system
- Two phase III trials met primary endpoints
  - Collarette cure rate and mite eradication
- 89% of patients achieved clinically meaningful collarette cure rate (<10/eye)
- 56% of patients showed a complete collarette cure rate and 31% showed a complete resolution of erythema
- BID for 6 weeks

Xdemvy (lotaliner ophthalmic solution 0.25%)

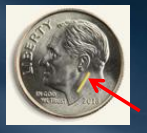
- The most common side effect in clinical trials was stinging and burning in 10% of patients
- Other side effects in less than 2% of patients were chalazion/hordeolum and punctate keratitis
- XDEMVY contains potassium sorbate, which may discolor soft contact lenses. Contact lenses should be removed prior to instillation of XDEMVY and may be reinserted 15 minutes following its administration.

Xdemvy (lotaliner ophthalmic solution 0.25%)

- Pregnancy
  - There are no available data on XDEMVY use in pregnant women to inform any drug associated risk; however, systemic exposure to lotilaner from ocular administration is low
- Lactation
  - There are no data on the presence of XDEMVY in human milk, the effects on the breastfed infant, or the effects on milk production. However, systemic exposure to lotilaner following 6 weeks of topical ocular administration is low and is >99% plasma protein bound, thus it is not known whether measurable levels of lotilaner would be present in maternal milk following topical ocular administration.

Yutiq

- flucinolone acetonide .18 mg intravitreal implant
- Indication
  - Treatment of chronic non-infectious uveitis affecting the posterior segment of the eye
- Contraindications
  - Ocular / periocular infections
  - Hypersensitivity
- Warnings & Precautions
  - Endophthalmitis, increased IOP, retinal detachment
- Adverse Reactions
  - Cataract development and increased IOP



Yutiq

- Was shown to reduce uveitis recurrence
  - Study 1/2 (at 6 months)
    - 18% Yutiq / 79% sham
    - 22% Yutiq / 54% sham
  - Study 1/2 (at 12 months)
    - 28% Yutiq / 86% sham
    - 33% Yutiq / 60% sham

Yutiq

- Pregnancy
  - Risk Summary : Adequate and well-controlled studies with YUTIQ have not been conducted in pregnant women to inform drug associated risk. Animal reproduction studies have not been conducted with YUTIQ. It is not known whether YUTIQ can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Corticosteroids have been shown to be teratogenic in laboratory animals when administered systemically at relatively low dosage levels. YUTIQ should be given to a pregnant woman only if the potential benefit justifies the potential risk to the fetus.
  - All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the United States general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively
- Lactation
  - Risk Summary: Systemically administered corticosteroids are present in human milk and can suppress growth, interfere with endogenous corticosteroid production. Clinical or nonclinical lactation studies have not been conducted with YUTIQ. It is not known whether intravitreal treatment with YUTIQ could result in sufficient systemic absorption to produce detectable quantities of fluocinolone acetonide in human milk, or affect breastfed infants or milk production. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for YUTIQ and any potential adverse effects on the breastfed child from YUTIQ.

Zerviate (cetirizine ophthalmic solution 0.24%)

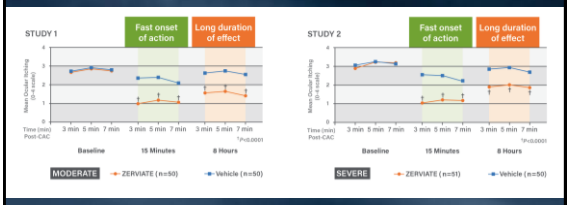
- Launched March 30, 2020
  - Approved May 30, 2017 to Nicox
  - Eyevance Pharmaceuticals
- First novel prescription-only treatment for allergic conjunctivitis in 10 years
- Cetirizine is active ingredient found in Zyrtec
  - Cetirizine is a well-established treatment for allergic inflammation. Its availability in a topical form facilitates localized, targeted treatment – which can have significant patient benefits over systemic options
  - As a topical agent, Zerviate provides ~100-fold lower systemic exposure than cetirizine tablets, potentially lowering incidence rates for antihistamine-related systemic side effects (e.g., somnolence, fatigue and dry mouth)
- Zerviate is formulated with Hydrella, a vehicle that contains glycerin and hydroxypropyl methylcellulose (HPMC)
  - two common ingredients found in tear lubricants;
  - delivering the cetirizine molecule to the eye with optimal ocular comfort

Zerviate (cetirizine ophthalmic solution 0.24%)

- Indications
  - histamine-1 (H1) receptor antagonist indicated for treatment of ocular itching associated with allergic conjunctivitis
- Dosage
  - 1 drop in each affected eye twice daily
- Contraindications
  - None
- Warnings and Precautions
  - To prevent contaminating the dropper tip and solution, advise patients not to touch the eyelids or surrounding areas with the dropper tip of the bottle or tip of the single-use container
- Adverse Reactions
  - The most common adverse reactions (1–7%) were ocular hyperemia, instillation site pain, and visual acuity reduced
- Appropriate for children >2 years

Zerviate

- Reduction in ocular itch



Zerviate

- Comfortable delivery with Hydrella
  - Composed of glycerin and HPMC
  - Neutral pH of 7.0
- Mean comfort score of <1 at all time points
  - Over 500 adult and pediatric patients
  - Drop comfort assessed upon instillation, 30 seconds post-dose, and 1 minute post-dose
  - 11 point scale (0=very comfortable, 10=very uncomfortable)

Zerviate

Pregnancy

- **Risk Summary** There were no adequate or well-controlled studies with ZERVIATE™ (cetirizine ophthalmic solution) 0.24% in pregnant women. Cetirizine should be used in pregnancy only if the potential benefit justifies the potential risk to the fetus.
- **Animal Data** Cetirizine was not teratogenic in mice, rats, or rabbits at oral doses up to 96, 225, and 135 mg/kg, respectively (approximately 1300, 4930, and 7400 times the maximum recommended human ophthalmic dose (MRHOD), on a mg/m 2 basis).

Lactation

- **Risk Summary** Cetirizine has been reported to be excreted in human breast milk following oral administration. Multiple doses of oral dose cetirizine (10 mg tablets once daily for 10 days) resulted in systemic levels (Mean C max = 311 ng/mL) that were 100 times higher than the observed human exposure (Mean C max = 3.1 ng/mL) following twice-daily administration of cetirizine ophthalmic solution 0.24% to both eyes for one week. Comparable bioavailability has been found between the tablet and syrup dosage forms. However, it is not known whether the systemic absorption resulting from topical ocular administration of ZERVIATE could produce detectable quantities in human breast milk.
- There is no adequate information regarding the effects of cetirizine on breastfed infants, or the effects on milk production to inform risk of ZERVIATE to an infant during lactation. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ZERVIATE and any potential adverse effects on the breastfed child from ZERVIATE.

Pediatric Use

- The safety and effectiveness of ZERVIATE has been established in pediatric patients two years of age and older. Use of ZERVIATE in these pediatric patients is supported by evidence from adequate and well-controlled studies of ZERVIATE in pediatric and adult patients.

Geriatric Use

- No overall differences in safety or effectiveness have been observed between elderly and younger patients.

Thank you

Please feel free to contact us:

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