Complications of Pharmaceuticals
Every Optometrist Should Know!

Greg Caldwell, OD, FAAO
PSS Eyecare
Saturday, September 6, 2025

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Disclosures- Greg Caldwell, OD, FAAO
All relevant relationships have been mitigated

- Lectured for: Alcon, B&L, Dompé, Lenz
  - Disclosure: Receive speaker honorariums
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- Healthcare Registries – Chairman of Advisory Council for Diabetes and AMD
- The content of this activity was prepared independently by me - Dr. Caldwell
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All of these cases have entered my practice, or great friends have shared their cases with me to present

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Which of these ocular complications have you seen?

- Hydroxychloroquine / chloroquine: Retinopathy
- Amiodarone: Corneal whorls or optic neuropathy
- Tetracycline: Pseudotumor cerebri or other complications
- Ethambutol: Optic neuropathy

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Thoughts

- Always check the medication list
  - Review it with the patient
- Medications to H.A.T.E in neuro-op (Andy Lee, MD)
  - Hydroxychloroquine / chloroquine retinopathy
  - Amiodarone optic neuropathy - Anterior ischemic optic neuropathy
  - Tetracycline: pseudotumor cerebri
  - Ethambutol optic neuropathy
  - The Erectile dysfunction agents (Viagra) -Anterior ischemic optic neuropathy

Andy Lee, MD

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Antibiotics (anti-inflammatory)
Adverse Drug Reactions

- Tetracycline analogs
  - Doxycycline
  - Minocycline
- Enhanced photosensitivity
- Avoid in children and pregnancy (Category D), and in breastfeeding women
  - Stained teeth
  - Small incisors
- Enhances the effects of
  - Coumadin
    - Comment on antibiotic drug interactions…
  - Digoxin
- Idiopathic intracranial hypertension
  - Pseudotumor cerebri
- Hyperpigmentation

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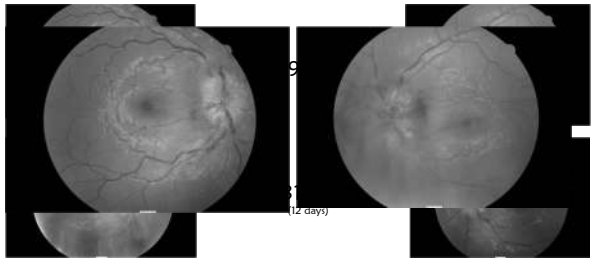
Benign intracranial hypertension

"It's not rare if it's in your chair"



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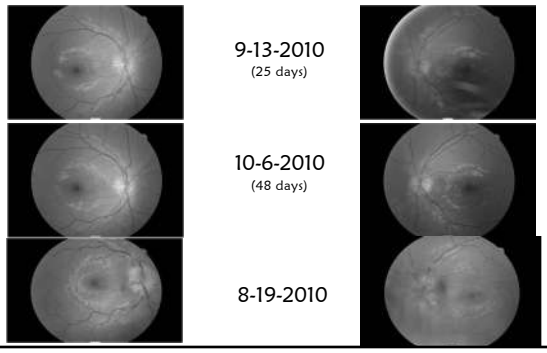

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PTC VS. IIH (THANKS DR. JOE SOWKA)

- **Pseudotumor Cerebri (PTC)**
  - Increased intracranial pressure in the absence of an intracranial mass lesion
  - Many causative agents have been identified
    - IIH, venous sinus thrombosis, drugs
- **Primary PTC** - IIH
- **Secondary PTC** - venous sinus thrombosis, drugs
- **Idiopathic Intracranial Hypertension (IIH)**
  - Increased intracranial pressure without an identifiable cause
  - Young, obese females are at risk
  - Poor CFS drainage
- **Secondary Intracranial Hypertension (IIH)**
  - venous sinus thrombosis, drugs
    - ex. doxycyline

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Minocycline Optic Nerve Edema

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Minocycline Optic Nerve Edema

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OMG

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6 Months Later


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1 Year Later


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Dacryocystitis

Patient as a severe allergic reaction to Penicillin and Keflex (EpiPen)
Which antibiotic would you use?

A. Augmentiin
B. Azithromycin
C. Cephalexin
D. Bactrim
E. Cipro

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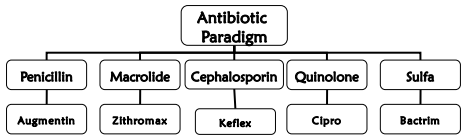
Antibiotic Paradigm Thru 2019



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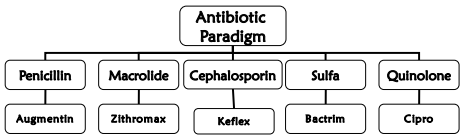
Antibiotic Paradigm Changed 2020



Oral (9:32) Antibiotic Review in Eye Care YouTube – By Greg Caldwell, OD, FAAO

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Ciprofloxacin (Cipro) Levofloxacin (Levaquin)

- Quinolone - In my opinion, an end of the line, antibiotic to use…allergic to PCN, cephlosporins, macrolides…
- Really effective, because they are BROAD
- Would avoid if pregnant, BF, and in kids
  - Only use 18 years or older (oral)
- Cipro and Levaquin available in 250, 500 and 750 mg
  - Cipro 750 mg for only severe infections (usually life-threatening pneumonia)
- 500 mg bid x 1 week-Cipro
- 500 mg qd x 1 week-Levaquin
- Levaquin-tendon ruptures

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Fluoroquinolone ADRs

- Retinal detachment (1 per 2,500 pts)
  - WHAT?!?
    - Mechanism is possible through destruction of collagen and connective tissue…
- QT prolongation in newer agents
- Photosensitivity
- Tendon rupture
  - Watch shoulders, wrists, Achilles

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Have you Rxed Trusopt/Azopt/Cosopt successfully to a patient with a "Sulfa allergy"?

- Yes
- Yes – glad it worked, not sure how
- No

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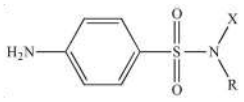
"Sulfa Antibiotic Allergy"

- If a true allergy: Mast cell and IgE mediated, causing hives, itch, congestion, lip and tongue swelling, tightness in throat, and bronchial constriction
  - Anaphylaxis
- The "S" is typically not the hapten/antigen
- The arylamine group is the hapten/antigen



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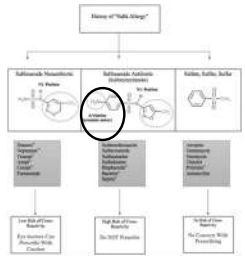
What to ask about allergies

- For the patient
  - When did you react?
  - What was the reaction?
    - Systemic versus topical
- For you…
  - For sulfa allergic patients
    - Antibiotic structure sulfa allergy
      - Sulfamethoxazole/trimethoprim
    - Non-antibiotic structure agents
      - Carbonic anyhydrase inhibitors
      - Hydrochlorothiazide
      - Celecoxib (Celebrex)
      - Glipizide, glyburide, glimepiride



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Antivirals

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Beside the dosing frequencies…

- What is different about the oral antivirals?

- Main reason for early discontinuation of oral acyclovir in HEDS
  - Gastrointestinal side effects
  - Rash

Many patients on oral acyclovir have GI symptoms

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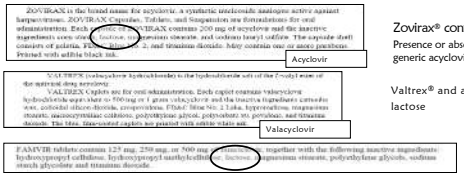
Acyclovir vs. Valacyclovir vs. Famciclovir

What is the difference?



Zovirax® contains lactose

Presence or absence of lactose in generic acyclovir varies

Valtrex® and all generics are free of lactose

Generics available in the US contain lactose

* In Europe you can get generic famciclovir without lactose (Teva Pharmaceuticals, Israel)

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Acyclovir versus Valacyclovir versus Famciclovir

What is the difference?

CNS Effects in Elderly Patients

- Acyclovir and valacyclovir carry a higher risk of CNS adverse effects in the elderly:
  - Agitation
  - Hallucinations
  - Confusion
- Clinical Take Home Point:
- Consider famciclovir in older patients who CNS side effects with acyclovir or valacyclovir
- Other major concern with elderly patients is age-related reduced kidney function

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Alpha 1 Blockers

- Floppy iris syndrome!
- Treatment of enlarged prostate:
  - Uroxatrol™ (Alfuzosin)
  - Flomax™ (Tamsulosin)
    - These two agents LIKELY have the highest incidence of causing floppy iris syndrome, as they are selective for alpha 1a receptors, which also predominate in the eye
    - Complications can be intraoperative (eg. iris trauma) or postoperative (eg. intraocular pressure increases)
      - 57-100% incidence with tamsulosin
      - there may also be a correlation with higher doses?
- Treatment of CHF and/or hypertension
  - Coreg™ (Carvedilol)
    - Alpha1/beta 2 blocker
  - Hytrin™ (Terazosin)
    - Alpha 1 blocker

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Alpha 1 Blockers

- Floppy iris syndrome and miosis!
- After 4 rounds of phenylephrine, tropicamide, and cyclopentolate, if poor dilation
  - Iris hooks
- What happens at the time of making the incision?
  - Tricks with different viscoelastic agents
- Post op day 1, IOP 43
  - What's the caution?

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Pentosan Polysulfate (Elmiron)

- Used to relieve bladder pain and discomfort related to interstitial cystitis
- Interstitial cystitis
  - Disease that causes swelling and scarring of the bladder wall
- Pentosan polysulfate is similar to a class of medications called low molecular weight heparins
  - It works by preventing irritation of the bladder walls
- Ocular adverse events
  - Blurred vision, changes in color vision perception, prolonged dark adaptation, and pigmentary maculopathy

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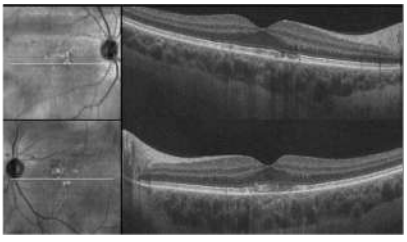
Pentosan Polysulfate (Elmiron)

Pigmentary Maculopathy



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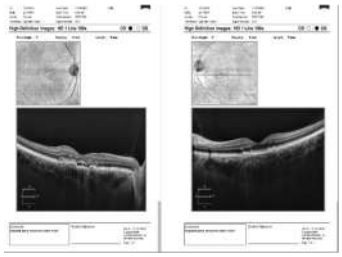
Pentosan Polysulfate (Elmiron)

Pigmentary Maculopathy



Courtesy of Joe Shovlin, OD, FAAO

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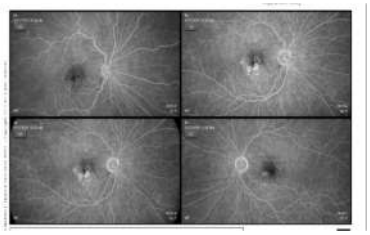
Pentosan Polysulfate (Elmiron)

Pigmentary Maculopathy



Courtesy of Joe Shovlin, OD, FAAO

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I have seen cornea verticillata cause vision loss?

- Yes
- No
- It doesn't cause vision loss

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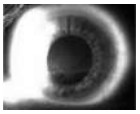
Anti-arrhythmics



- Treatment of cardiac arrhythmia
  - Cordarone™ (amiodarone)
    - Corneal deposits - nearly universal in patients on amiodarone
      - usually bilateral with 10% complaining of blurred vision and halos around lights
    - Optic neuritis - 2% incidence
      - can occur anytime after starting amiodarone

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Stages

Grade I	Punctate opacities in a horizontal linear pattern in the inferior cornea
Grade II	More aligned deposits in a linear pattern that extend into the inferior pupillary margin toward the limbus
Grade III	Increased numbers of branching patterns in the inferior pupillary area into the visual axis
Grade IV	Deposits form additional clumps compared with grade III

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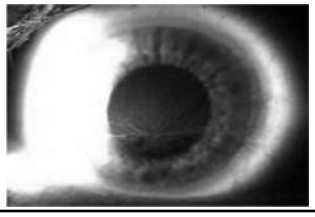
65-year-old woman

- Patient reports decreasing vision over past 6-9 months.
  - Especially at near
- Vision 20/50 OU



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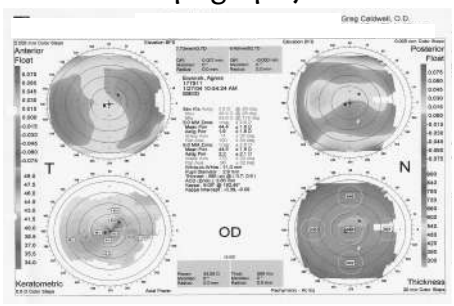
Topography



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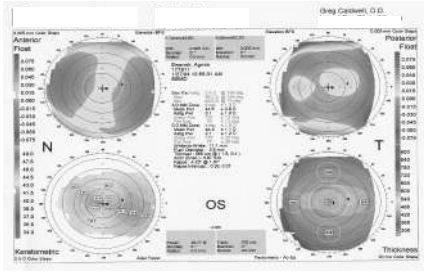
Topography



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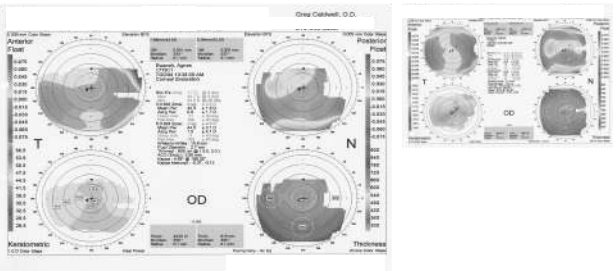
6 Months Later



20/25 BVA

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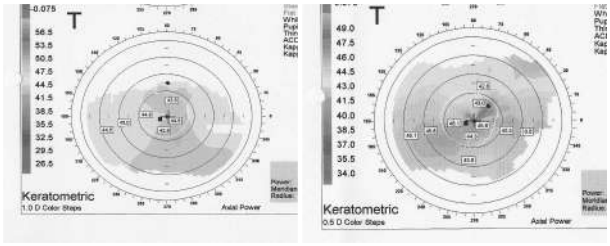
OD



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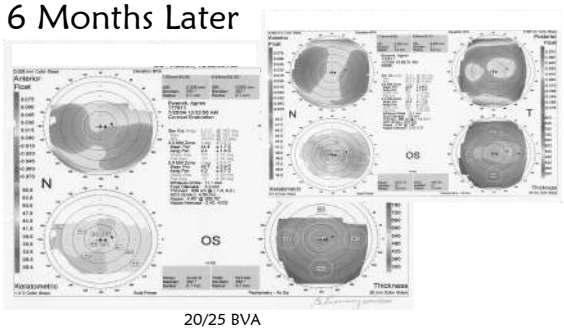
6 Months Later



20/25 BVA

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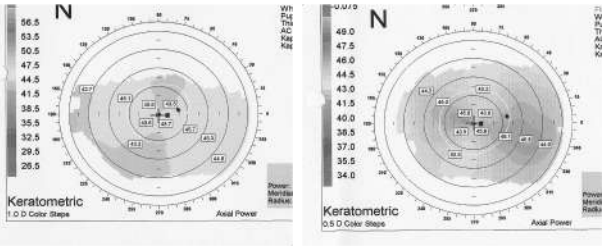
OS



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67-year-old man complains of vision slowly deteriorating over the past 8 months

- History of NA-ION 10 months ago OD
- Patient sees family physician for physical due to recent NA-ION
  - Patient has not been to PCP for 35 years
  - Patient started Cardarone™
  - VA 20/80 OD 20/25 OS (9 months ago)
- VA 20/400 OD 20/200 OS (today)
- CF: severe constriction OU
- SLE: vortex corneal whorls OU

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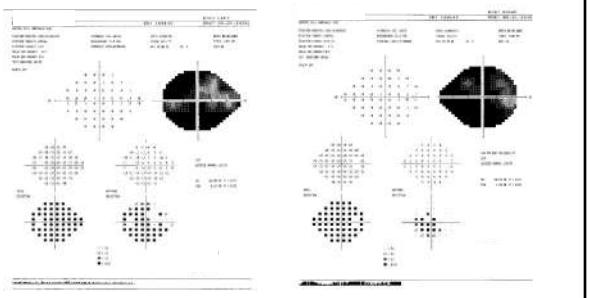

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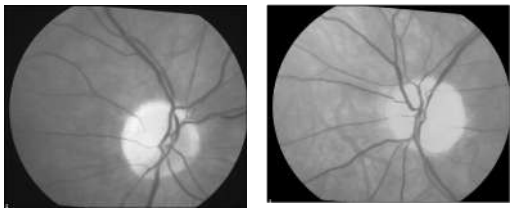
Amiodarone Optic Neuropathy

(Toxic Optic Neuropathy)



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Rhopressa™ 0.02% (netarsudil ophthalmic solution)

- Aerie Pharmaceuticals - asset is now with Alcon
  - Approved December 2017
  - Treatment of glaucoma or ocular hypertension
  - Rho kinase inhibitor
    - ROCK-NET Inhibitor
  - Once daily in the evening
    - Twice a day dosing is not well tolerated and is not recommended
  - Side Effects
    - Conjunctival hyperemia
    - Corneal verticillata
    - Conjunctival hemorrhage

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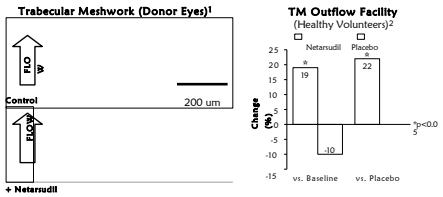
Rhopressa™ 0.02% (netarsudil)

Causes Expansion of TM in Donor Eyes

Increases TM Outflow Facility in Clinic



TM: Trabecular Meshwork; SC: Schlemm's Canal; Control: buffered saline solution; EVS: Episcleral Vein

1. Ren R et al. Invest Ophthalmol Vis Sci. 2016;57(14):6197-6209. 2. Sit AJ et al. Presented at AGS 2017.

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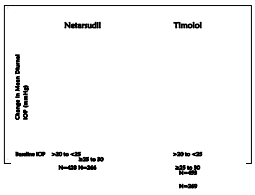
Netarsudil is Similarly Effective at Baseline IOPs <25 mmHg and ≥25 mmHg

Pooled Analysis Rocket 1, Rocket 2, Rocket 4



Baseline IOP >20 to <25 mmHg	Netarsudil QD	Timolol BID
Median	-4.2	-4.3
Mean	-4.1	-4.3
Max	-10.7	-10.8

Baseline IOP ≥25 to <30 mmHg	Netarsudil QD	Timolol BID
Median	-4.0	-5.3
Mean	-3.7	-5.3
Max	-12.3	-12.0

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Rhopressa™ 0.02%

- No labeled contraindications for Rhopressa™
- No clinically relevant effects on vital signs
  - Blood Pressure
    - Changes were generally small and not clinically relevant in both groups
  - Heart Rate
    - Timolol caused statistically significant reduction in the phase 3 studies by an average of 2-3 beats per month

1. RHOPRESSA® (netarsudil ophthalmic solution) 0.02% Prescribing Information. 2. Khouri et al. Association for Research in Vision and Ophthalmology annual meeting 2017 [Br-abstract 2461].

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Conjunctival Hemorrhage was Sporadic and Severity did not Increase with Continued Dosing

Adverse Events	Netarsudil 0.02% QD (N=839) n (%)	Timolol 0.5% BID (N=839) n (%)
TEAE Conjunctival Hemorrhage	144 (17.2)	15 (1.8)
AE Resulting in Discontinuation	8 (1.0)	0

Majority 92.4% (133/144) of the conjunctival hemorrhage in netarsudil QD group was mild, 6.3% (9/144) was moderate and 1.4% (2/144) was severe

Self-resolving with continued dosing

Images were taken from netarsudil subjects
Source: Courtesy of study investigators AR-13324-CS301, -CS302

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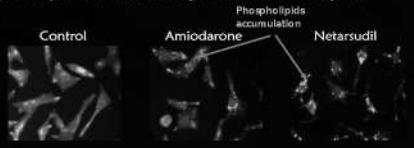
Cornea Verticillata Due to Phospholipidosis

Medications known to cause verticillata: amiodarone, chloroquine, naproxen, phenothiazine, ocular gentamicin and tobramycin*



Due to phospholipidosis where the parent drug is complexed with phospholipids in the lysosomes

Literature review suggested it is an adaptive response by the body rather than an adverse pathology*

Data on File Based on AR-13324-IPH07
* Rasmen M B et al. Surv. Ophthalmol. 2017; 62:286-301

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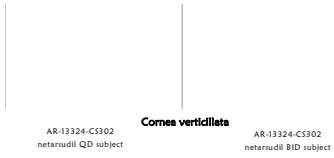
Cornea Verticillata Observed in Phase 3 Studies

- Cornea verticillata refers to a whorl-like pattern of deposits typically localized to the basal corneal epithelium
- Subjects are asymptomatic
- The onset was ~6 to 13 weeks (netarsudil QD)



Images were taken from netarsudil subjects
Source: Courtesy of study investigators AR-13324-CS302

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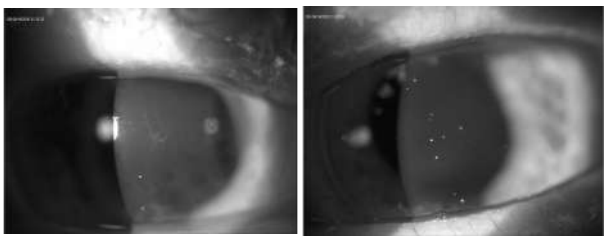
My Experience

OD treated OS gtts



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Summary of the Most Common Netarsudil Ocular TEAEs

Conjunctival Hyperemia
- 54.4% TEAE
- Severity did not increase with continued dosing
- Sporadic

Cornea Verticillata
- 20.9% TEAE
- Asymptomatic
- 7.4% experienced reduced visual acuity (not clear to a directly associated), all resolved after 13 weeks of D/C

Conjunctival Hemorrhage
- 17.2% TEAE
- Mild in severity and transient
- Self-resolving with continued dosing

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Drugs Causing ACG – Angle Closure Glaucoma

- Acetazolamide
- Hydrochlorothiazide
- Trimethoprim-sulfamethoxazole
- Indapamide
- Promethazine
- Spironolactone
- Isosorbide dinitrate
- Viagra
- Bromocriptine
- Tetracycline
- Corticosteroids
- Penicillamine
- Quinine
- Metronidazole
- Isotretinoin
- Aspirin
- *Topiramate**

Thank you, Joe Sowka, OD, FAAO

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Ciliary Effusion

- Anterior Rotation of the Ciliary Body
  - Reduces tension on the zonules
    - Lens Thickening
      - Induces myopia
  - Iris-Lens diaphragm shifts anteriorly
    - Induces myopia by changing effectivity
  - Shallowing of Anterior Chamber
    - Potential for angle closure

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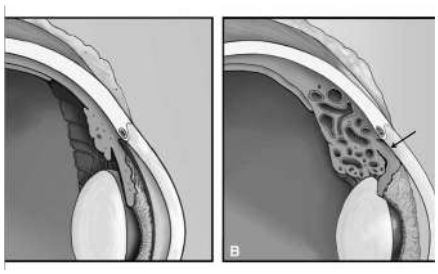

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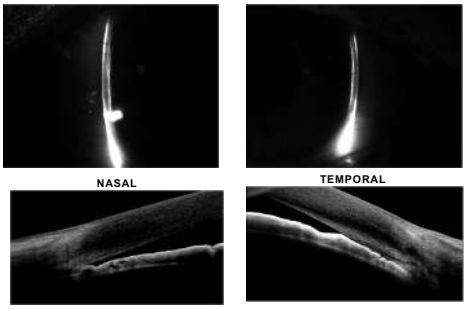

Thank you, Joe Sowka, OD, FAAO

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Case

- 39 YOF
- Recently started on Topamax for migraine
- Sudden onset blurred vision and eye pain
- Formerly emmetropic, now - 6.00 DS
- IOP 44 mm Hg

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What's the Best Management?

- **Cycloplegic and topical steroids**
- **Oral Diamox**
- **Cosopt and Lumigan**
- **Immediate LPI**
- **I'm not sure. That's why I'm here.**

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Case

- 39 YOF
- Recently started on Topamax for migraine
- Sudden onset blurred vision and eye pain
- Formerly emmetropic, now (-) 6.00 DS
- IOP 44 mm Hg
- D/C Topamax; add PF Q1H, scopolamine BID, beta blocker BID

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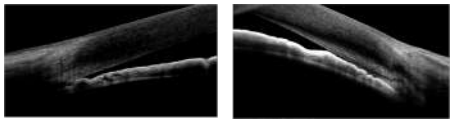
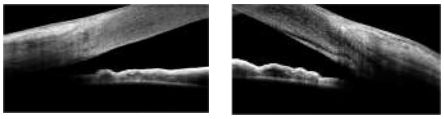


Initial Presentation



Resolution

67

Choroidal Involvement in ACG

- Drug-induced choroidal expansion
- Choroidal expansion in ACG associated with shallowing of chamber
- Malignant glaucoma may not be aqueous misdirection, but poor fluid permeability and choroidal expansion
- Atropine may work by moving ciliary body and improving forward diffusional area for fluid
  - Atropine may be a better choice than pilocarpine

68

Toxic Optic Neuropathy

- Causes
  - Ethambutol (TB)
  - Isoniazid
  - Antimicrobials
    - chloramphenicol, streptomycin, penicillamine
  - Halogenated hydroxyquinolones
  - Vigabatrin
  - Disulfiram
  - Tamoxifen
  - Sildenafil
- Causes
  - Methanol
  - Heavy metals
  - Fumes
  - Solvents
  - Alcohol abuse
  - Tobacco abuse

Clinical Pearl: When you encounter a pt with these pharmaceuticals, consider and evaluate for toxic optic neuropathy (TON)

69

Ethambutol

- Still used in the 4-drug treatment plan for active *Mycobacterium tuberculosis* ("TB")
  - Patients will take isoniazid + rifampin + pyrazinamide + ethambutol for ABOUT 2 months
    - Organism sensitivities come back
    - Non-resistant TB = discontinuation of pyrazinamide and ethambutol
- Toxic optic neuropathy
- 2 cases in the past 12 months (2019)

70

81-year-old woman

- Calls the office reporting decreased vision (3-13-19)
  - Was warned vision could decrease due her medications
  - Glaucoma patient
- Mycobacterium avium infection
- Ethambutol, rifampin, and azithromycin
  - Ethambutol started October 2017
- Glaucoma patient
  - Was on latanoprost and Rhopressa
  - Had KDB
    - No glaucoma drops currently

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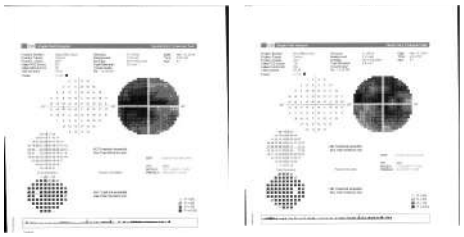
3/13/19 20/30, 20/100, 20/25



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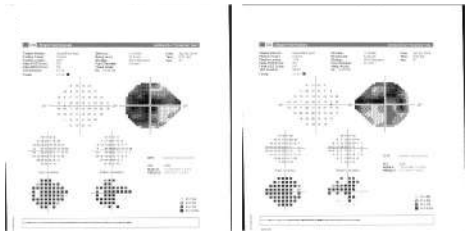
4/29/19 20/25, 20/50, 20/20



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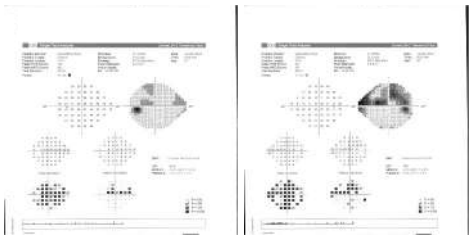
7/29/19 20/20, 20/25, 20/20



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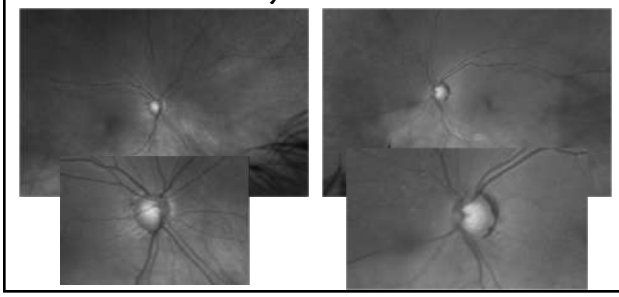
May 9, 2022



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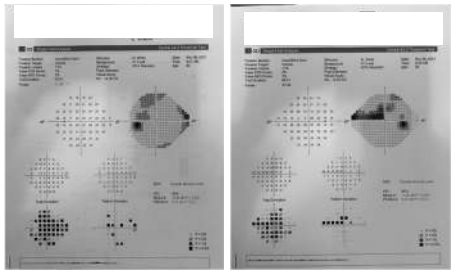
November 21, 2021



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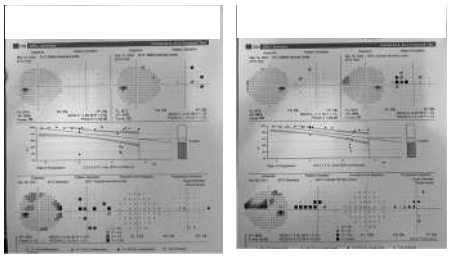
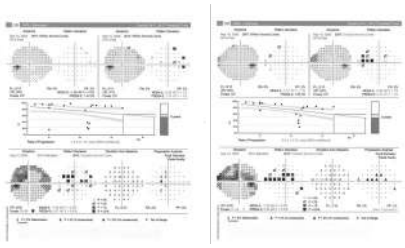
Progression thru 11-08-2021



77

Greg Caldwell, OD, FAAO
Greg@optometricedu.com 814-931-2030 cell #

Last Update August 14, 2024



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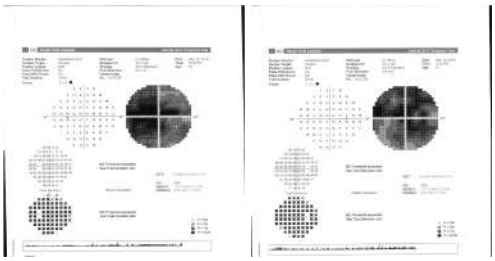
Reminder: 3/13/19 20/30, 20/100, 20/25



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Dupixant (dulipumab) injection

- **Atopic Dermatitis:** indicated for the treatment of adult and pediatric patients aged 6 months and older with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable
  - DUPIXENT can be used with or without topical corticosteroids
- **Asthma:** indicated as an add-on maintenance treatment of adult and pediatric patients aged 6 years and older with moderate-to-severe asthma characterized by an eosinophilic phenotype or with oral corticosteroid dependent asthma. Limitation of Use: DUPIXENT is not indicated for the relief of acute bronchospasm or status asthmaticus.
- **Chronic rhinosinusitis with nasal polyposis (CRSwNP):** DUPIXENT is indicated as an add-on maintenance treatment in adult patients with inadequately controlled CRSwNP.
- **Eosinophilic Esophagitis:** DUPIXENT is indicated for the treatment of adult and pediatric patients aged 12 years and older, weighing at least 40 kg, with eosinophilic esophagitis (EoE).

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Dupixant (dulipumab) injection

Warnings and Precautions

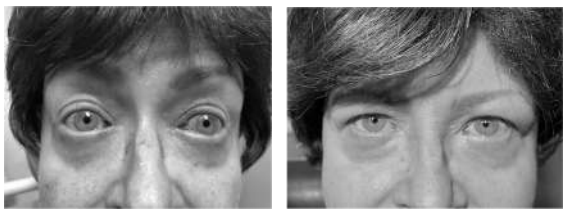
- **Conjunctivitis and Keratitis: (ocular warning and precautions of many)**
  - Conjunctivitis and keratitis occurred more frequently in atopic dermatitis subjects who received DUPIXENT versus placebo, with conjunctivitis being the most frequently reported eye disorder.
  - Conjunctivitis also occurred more frequently in chronic rhinosinusitis with nasal polyposis subjects who received DUPIXENT compared to those who received placebo.
  - Conjunctivitis and keratitis have been reported with DUPIXENT in postmarketing settings, predominantly in atopic dermatitis patients.
  - Some patients reported visual disturbances (e.g., blurred vision) associated with conjunctivitis or keratitis.
  - Advise patients to report new onset or worsening eye symptoms to their healthcare provider.
  - Consider ophthalmological examination for patients who develop conjunctivitis that does not resolve following standard treatment or signs and symptoms suggestive of keratitis, as appropriate.

82

Before and After

83

Before and After



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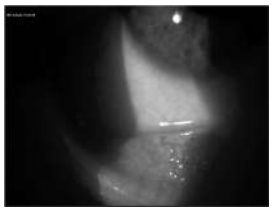
Dupixant

85



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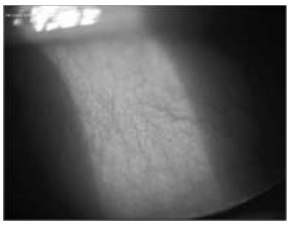

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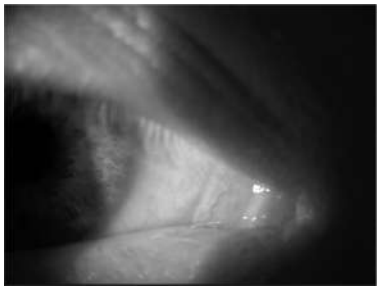

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Why Your Patients Are on ELAHERE

Eye Care Considerations for Patients Treated With ELAHERE

89

Optometry's role with Elahere - Mirvetuximab Soravtansine gynx (MIRV)

- Antibody-drug conjugate (ADC) comprising an FR-binding antibody, cleavable linker, and maytansinoid DM4 payload
- Primary ocular events with MIRV include corneal disorder, corneal epithelial defect, keratitis, keratopathy, corneal deposits, and punctuate keratitis
- Exam and clear patient for treatment

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Elahere - Mirvetuximab Soravtansine

Mirvetuximab soravtansine (MIRV) is the first biomarker-directed agent showing antitumor activity in patients with FRα-positive[a] platinum-resistant ovarian cancer (PROC)[1]

- **MIRV is an antibody-drug conjugate (ADC) comprising an FRα-binding antibody, cleavable linker, and maytansinoid DM4 payload[1]**
- **A phase 3 clinical study, SORAYA, evaluated MIRV in patients with FRα-high PROC who had received 1 to 3 prior therapies, including required bevacizumab[b,1]**

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Why Your Patients Are on ELAHERE

ELAHERE is a therapy approved to treat certain patients with advanced ovarian cancer

- ELAHERE is indicated for the treatment of adult patients with folate receptor-alpha (FR□) positive, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer
- Who have received one to three prior systemic treatment regimens
- This indication is approved under accelerated approval based on tumor response rate and durability of response

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Why Eye Care Is Important for Patients Receiving ELAHERE™

You play a critical role in patient management as ocular adverse events have been observed in patients treated with ELAHERE

BOXED WARNING: OCULAR TOXICITY

- **ELAHERE can cause severe ocular toxicities, including visual impairment, keratopathy, dry eye, photophobia, eye pain, and uveitis.**
- **Conduct an ophthalmic exam including visual acuity and slit lamp exam prior to initiation of ELAHERE, every other cycle for the first 8 cycles, and as clinically indicated.**
- **Administer prophylactic artificial tears and ophthalmic topical steroids.**
- **Withhold ELAHERE for ocular toxicities until improvement and resume at the same or reduced dose.**
- **Discontinue ELAHERE for Grade 4 ocular toxicities.**

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Proposed MOA for Ocular Events Associated With MIRV

- The underlying mechanisms of ocular toxicities remain poorly understood, but it is hypothesized to be an off-target effect on the corneal epithelium due to the lack of FRα receptors in that part of the eye
- Anti-microtubule payloads such as DM4 have been previously associated with resolvable ocular toxicity, such as blurred vision, dry eye, and keratopathy
- One hypothesis for toxicity seen with anti-microtubule payloads is that symptoms arise from a change in curvature of the cornea due to transient alterations in corneal epithelial thickness or corneal biomechanical properties, associated with the presence of microcysts
- Additionally, prolonged retention in circulation associated with MIRV's stable linker may lead to enhance exposure in normal tissues

The ocular AE profile of MIRV is a dose-dependent toxicity limited to the corneal epithelium of the eye, with resolvability observed in both non-clinical and human studies

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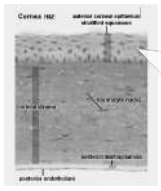
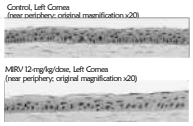
Microscopic Analysis of the Corneal Epithelium



Non-clinical Microscopic Analysis (Control and MIRV 12-mg/kg Dose)[1]



Key Observations With MIRV 12-mg/kg Dose

- **Fewer and larger** epithelial cells
- Overall **thinner** epithelial layer
- Basal layer appearing disorganized as **gaps** noted between visible nuclei
- **No visible nuclei** in places across the thickness of the epithelial layer, suggesting no cells other than those of the basal layer were present[1]
- **Lesions only at the periphery** of the cornea

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Due to the Possibility of Ocular Adverse Events With ELAHERE Eye Care Is Necessary

- Ophthalmic Exams
- Preventive Measures
- Lubricating Eye Drops
- Ophthalmic Topical Steroids

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Proactive Management of Ocular Adverse Events

- Patients should receive a baseline ophthalmic exam from an ophthalmologist or optometrist prior to treatment initiation and follow-up exams during every other cycle for the first 8 cycles, and as clinically indicated
- Tell patients to avoid use of contact lenses, unless they are medically necessary
- Use of preservative-free[a] lubricating eye drops at least 4 times daily and as needed is recommended during treatment with ELAHERE
- Use of ophthalmic topical corticosteroids is recommended
  - The initial prescription and renewals of any corticosteroid medication should be made only after examination with a slit lamp

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Recommended Schedule for Eye Drops

Ophthalmic Topical Corticosteroids

6x — **Starting the day before ELAHERE infusion until 3 days after infusion (Days 1–4)**
- Advise patients to apply 1 drop in each eye 6 times daily

4x — **On Days 5–8**
- Advise patients to apply 1 drop in each eye 4 times daily

Lubricating Eye Drops
The use of preservative-free lubricating eye drops is also recommended at least 4 times daily and as needed during treatment. Advise patients to wait at least 10 minutes after administering ophthalmic topical corticosteroids before using lubricating eye drops

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What to Look for in the Baseline Ophthalmic Exam

- A baseline ophthalmic examination should include a visual acuity test and slit lamp exam
- Document the patient's current symptoms and visual acuity prior to the initiation of ELAHERE™

Symptom Assessment
Inquire about ocular symptoms (eg, vision impairments, dry eye, photophobia, eye pain), and treat as appropriate

Visual Acuity
Measure best corrected visual acuity at baseline to help understand whether changes have occurred during follow-up exams

Slit Lamp Exam
Assess corneal health (eg, keratopathy, superficial punctate keratitis) is recommended before initiation of treatment with ELAHERE

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What to Monitor During Scheduled Follow-up Ophthalmic Exams

Monitor patients every other cycle (~every 6 weeks) for the first 8 cycles (~6 months) of ELAHERE™ for any changes from the baseline ophthalmic exam, and as clinically indicated[1]

Symptom Assessment[1]
- Inquire about any new or worsening ocular symptoms since the most recent ophthalmic exam

Visual Acuity[1]
- Compare against baseline measurement to determine whether best corrected visual acuity has changed

Slit Lamp Exam[1]
- Document any ocular findings, including keratopathy and uveitis

Note: As part of their treatment with ELAHERE, your patient is being prescribed ophthalmic topical steroids that may elevate intraocular pressure

1. ELAHERE. [illegible] *J Cataract Refract Surg.* 2021;47(1):53-64. 3. Palacio-Pastrana C, et al. *Clin Ophthalmol.* 2020;14:1581-1589.

9

100

Presentation of Keratopathy (Microcyst-like Corneal Epithelial Changes)

- Microcyst-like corneal epithelial changes (MECs) may be identified during ophthalmic slit lamp exams[1]
- MECs can appear in both symptomatic and asymptomatic patients[2]
- Document whether MECs are[3]:
  - Confluent (ie, merging or clumped)
  - Nonconfluent (ie, separated or distinct)

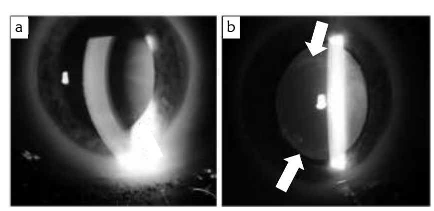

Figure. Arrows denote corneal microcysts observed in a 57-year-old patient 5 weeks after receiving ELAHERE™.[4]

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What to Expect With Ocular Events Associated With ELAHERE™

Integrated Safety Analysis of Patients Treated With ELAHERE (N=464)[a]

Timing of Onset

- Median onset to the first ocular adverse event was ~5 weeks (range, 1 day–55.3 weeks)[1]

Impact

- Ocular adverse events of any grade occurred in 61% of patients[1]
  - Grade 1 or 2: >90% of patients
  - Grade 3: 9% of patients
  - Grade 4: 0.2% of patients[b]

Resolution

- No patients had permanent ocular sequelae[2]
- Ocular adverse events led to permanent discontinuation of ELAHERE in 0.6% of patients[1]

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Monitoring Ocular Adverse Events

Ophthalmic Exam Findings Requiring Dose Modifications

Ophthalmic exam finding	Severity of finding	Action
Keratitis/ keratopathy	Nonconfluent superficial keratitis	Monitor
	Confluent superficial keratitis, a cornea epithelial defect, or 3-line or more loss in best corrected visual acuity	Notify treating oncologist[a]
	Corneal ulcer or stromal opacity or best corrected distance visual acuity of 20/200 or worse	
	Corneal perforation	
Uveitis	Grade 1/rare cell in anterior chamber	Monitor
	Grade 2/1-2+ cell or flare in anterior chamber	Notify treating oncologist[a]
	Grade 3/3+ cell or flare in anterior chamber	
	Grade 4/hypopyon	

Ocular adverse events should be treated by the eye care provider per standard clinical guidelines

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Coordinating With the Treating Oncologist

ELAHERE™ Ocular Assessment Form to Guide Ophthalmic Exams and Communicate With Treating Oncologists

- Reporting exam findings to the treating oncologist can guide the need for dose modification due to ocular events
- Dose reductions or modifications may help resolve ocular events
- Ocular adverse events led to permanent discontinuation of ELAHERE in 0.6% of patients

For questions or information about billing and coding, reference the ELAHERE Ocular Billing & Coding Guide

Scan this code to download a copy of the ELAHERE Ocular Assessment Form

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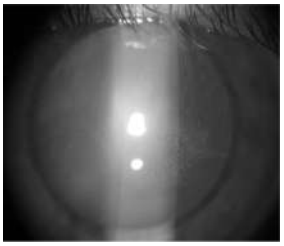
Elahere Corneal Deposits/Toxicity



Courtesy of Joe Shovlin, OD, FAAO

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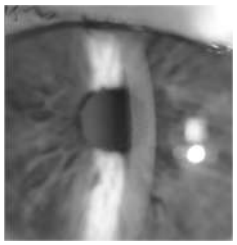
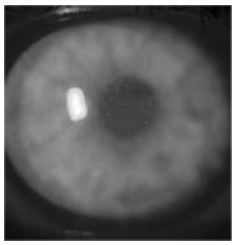
Elahere Corneal Deposits/Toxicity





Courtesy of Joe Shovlin, OD, FAAO

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Checkpoint Inhibitor for Breast Cancer
Bilateral Artery Occlusion

Courtesy of Joe Shovlin, OD, FAAO

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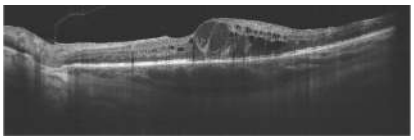
52-year-old woman

- History of MS was switched from Tysabri (natalizumab) to Gilenya (fingolimod)
- Blurred vision in her left eye, BVA 20/40
  - Noticed blurred vision 7-8 weeks after starting Gilenya



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Gilenya (fingolimod) & FAME

- All patients on fingolimod appear to have a mild increase in macular volume on OCT
- A small subset of patients develop cystoid or diffuse macular edema
- Discontinuation of the medication typically resolves the edema
- Highest period of risk is during the first year of treatment
- *Patients should have baseline macular OCT with repeat 3 months after treatment, followed by 6 months, then yearly*
- Newer drugs in this class have similar risks:
  - Mayzent (siponimod), in 2019
  - Zeposia (ozanimod) in 2020
  - Ponvory (ponesimod) in 2021

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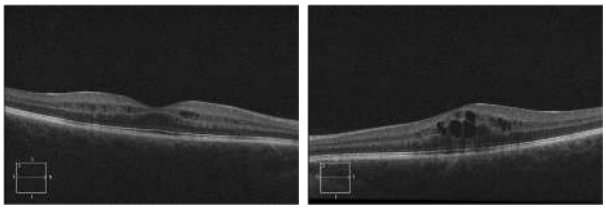
Another Gilenya™(fingolimod) and FAME



Courtesy of Joe Shovlin, OD, FAAO

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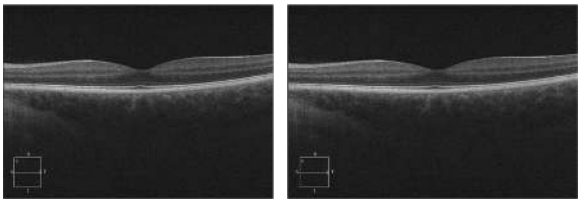
After D/C Gilenya™(fingolimod)



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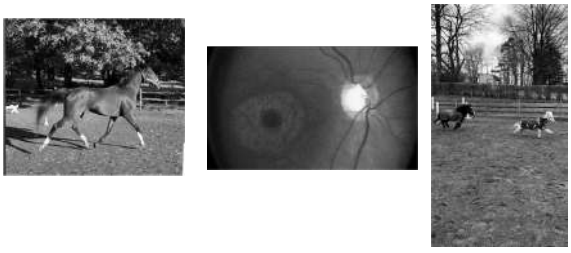
"Horse Is Out of the Barn"



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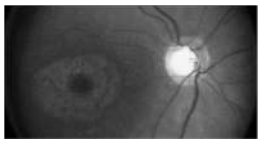
Autoimmune Agents

- Treatment of rheumatologic conditions
  - Rheumatoid arthritis, systemic lupus erythematosis
- Plaquenil™ (hydroxychloroquine)
  - Bull's eye maculopathy



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Immunosuppressive Medications

Disease-Modifying Anti-Rheumatic Drugs (DMARDs)
Traditional Meds and Biologics

Methotrexate +/-
Hydroxychloroquine (Plaquenil™)

⍰

Tumor Necrosis Factor α Inhibitors
- Adalimumab (Humira™)
- Infliximab (Remicade™)
- Etanercept (Enbrel™)
- Certolizumab (Cimzia™)

⍰

Additional Agents
- Abatacept (Orencia™)
- Tocilizumab (Actemra™)
- Tofacitinib (Xeljanz™)
- Rituximab (Rituxan™)

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Plaquenil

Hydroxychloroquine (Plaquenil) - Anti-malarial

- Ophthalmic side effects (infrequent with current dosing ranges):
  - Irreversible retinal damage has been observed ("chloroquine retinopathy").
  - If there are any indications of abnormality in the color vision, visual acuity, visual field, or retinal macular areas, or any visual symptoms (eg, light flashes or streaks), d/c drug stat

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Revised Recommendations on Screening for Chloroquine and Hydroxychloroquine Retinopathy

- Recommendations were 2002 by the American Academy of Ophthalmology
- Improved screening tools and new knowledge about prevalence of toxicity have prompt the change
  - 1% after 5-7 years of use or a cumulative dose of 1000 grams (Plaquenil)
- There is no treatment for this condition
  - Therefore must be caught early
- Screening for the earliest hints of functional or anatomic change
- Plaquenil toxicity is not well understood


American Academy of Ophthalmology Update

Revised Recommendations on Screening for Chloroquine and Hydroxychloroquine Retinopathy

Ophthalmology · Volume 123, Number 2, February 2016

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American Academy of Ophthalmology Statement

Recommendations on Screening for Chloroquine and Hydroxychloroquine Retinopathy (2016 Revision)

Revised Again

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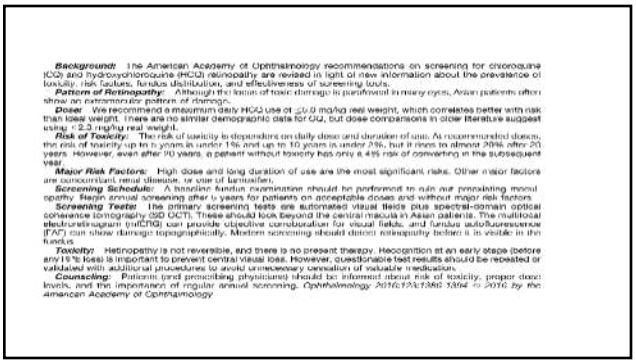

Background: The American Academy of Ophthalmology recommendations on screening for chloroquine (CQ) and hydroxychloroquine (HCQ) retinopathy are revised in light of new information about the prevalence of toxicity, risk factors, fundus distribution, and effectiveness of screening tools.

Pattern of Retinopathy: Although the locus of toxic damage is parafoveal in many eyes, Asian patients often show an extramacular pattern of damage.

Dose: We recommend a maximum daily HCQ use of ≤5.0 mg/kg real weight, which correlates better with risk than ideal weight. There are no similar demographic data for CQ, but dose comparisons in older literature suggest using ≤ 2.3 mg/kg real weight.

Risk of Toxicity: The risk of toxicity is dependent on daily dose and duration of use. At recommended doses, the risk of toxicity up to 5 years is under 1% and up to 10 years is under 2%, but it rises to almost 20% after 20 years. However, even after 20 years, a patient without toxicity has only a 4% risk of conversion in the subsequent year.

Major Risk Factors: High dose and long duration of use are the most significant risks. Other major factors are concomitant renal disease, or use of tamoxifen.

Screening Schedule: A baseline fundus examination should be performed to rule out preexisting maculopathy. Begin annual screening after 5 years for patients on acceptable doses and without major risk factors.

Screening Tests: The primary screening tests are automated visual fields plus spectral-domain optical coherence tomography (SD OCT). These should look beyond the central macula in Asian patients. The multifocal electroretinogram (mfERG) can provide objective corroboration for visual fields, and fundus autofluorescence (FAF) can show damage topographically. Modern screening should detect retinopathy before it is visible in the fundus.

Toxicity: Retinopathy is not reversible, and there is no present therapy. Recognition at an early stage (before any VF or VA loss) is important to prevent central visual loss. However, questionable test results should be repeated or validated with additional procedures to avoid unnecessary cessation of valuable medication.

Counseling: Patients (and prescribing physicians) should be informed about risk of toxicity, proper dose limits, and the importance of regular annual screening. *Ophthalmology* 2016;123:1386–1394 © 2016 by the American Academy of Ophthalmology

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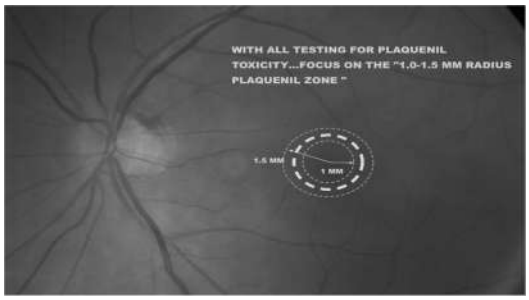
PLAQUENIL ZONE



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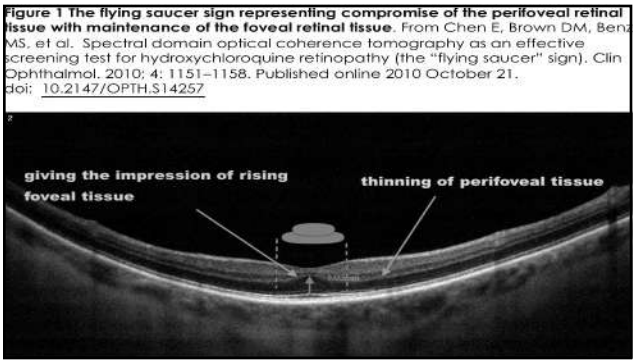

Figure 1 The flying saucer sign representing compromise of the perifoveal retinal tissue with maintenance of the foveal retinal tissue. From Chen E, Brown DM, Benz MS, et al. Spectral domain optical coherence tomography as an effective screening test for hydroxychloroquine retinopathy (the "flying saucer" sign). Clin Ophthalmol. 2010; 4: 1151–1158. Published online 2010 October 21. doi: 10.2147/OPTH.S14257

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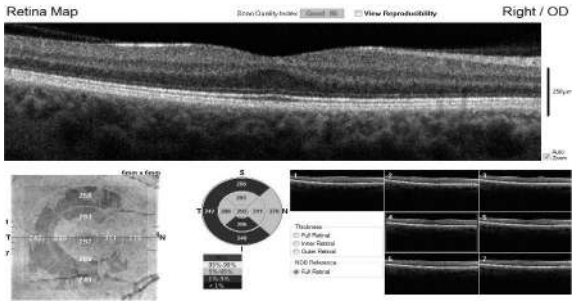
AUGUST 2014



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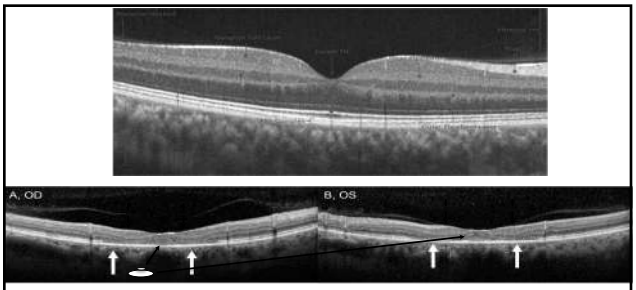

BILATERAL COMPROMISE OF THE PIL (WHITE ARROWS) AFTER COLLAPSE OF PERIFOVEAL RETINA (RED DASHED ARROWS) WITH FLYING SAUCER ATTACK (BLUE ARROWS)

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71 yo woman

- With Lupus and hypertension
- Medications:
  - Clonazepam™
  - Plaquenil™ 200 mg BID, 15 years
  - 81 mg ASA
  - Prednisone
  - Losartan™
- VA 20/25 OD/OS (mild cataracts)
- Patient was told to see an ophthalmologist in 2013

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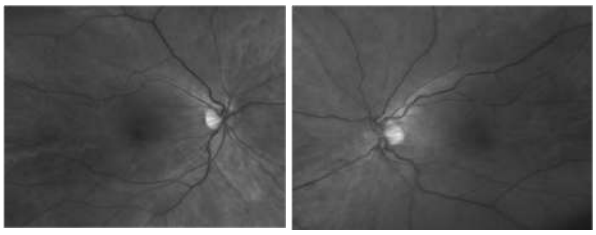
2016



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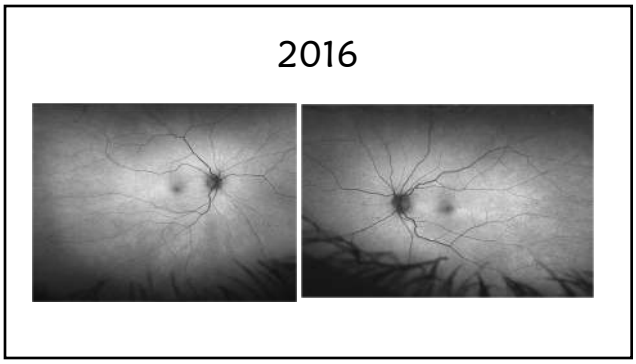

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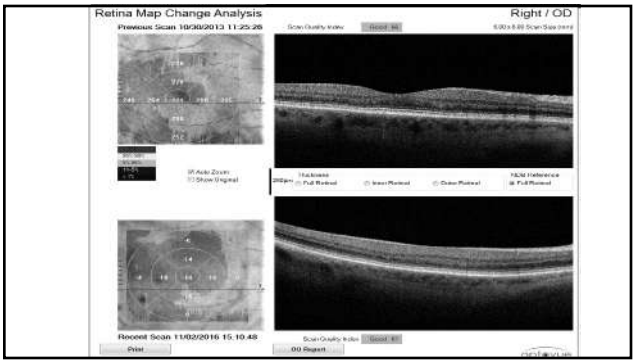

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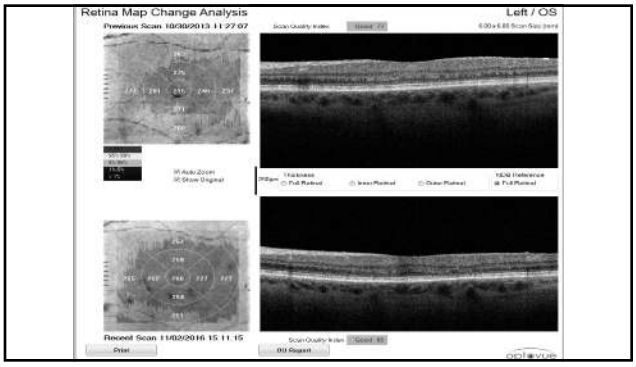

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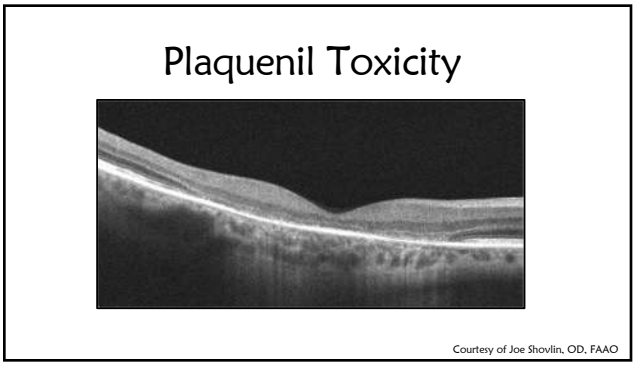

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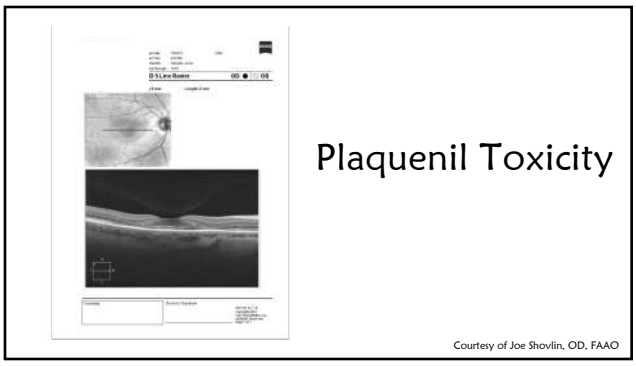

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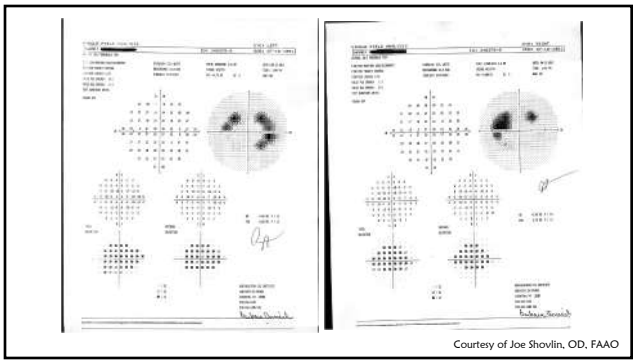
Courtesy of Joe Shovlin, OD, FAAO

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Question and Thank You!

Complications of Pharmaceuticals
Every Optometrist Should Know!

Greg Caldwell, OD, FAAO
PSS Eyecare
Saturday, September 6, 2025

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