

OFF LABEL (Not off limits)

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Optimizing Eye Care with Current Treatment Options

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“A lot of people go to college for seven years” “Yeah, they’re called doctors.”

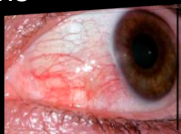
Introduction

- ✓ **FDA Process**
- ✓ **Off-label**
 - ✓ **Familiarize yourself** with the published literature and experience of colleagues
 - ✓ **Be reasonably confident** that patients will benefit
 - ✓ **Heed the drug's history** of adverse events, and advise and monitor patient's accordingly
 - ✓ **Document the decision-making** process and the informed-consent discussion that led to using a drug off-label
- ✓ **What legally can we do**

“Oh, and Senator, just one more thing. Love your suit!”

Dilating Medications

- ✓ **Epinephrine**
- ✓ **Indications:**
 - ✓ Dilate the pupil
 - ✓ Mydriasis
- ✓ **Off-Label**
 - ✓ Diagnose Episcleritis
 - ✓ Drop of epinephrine
 - ✓ Wait 5 minutes
 - ✓ Evaluate the superficial blood vessels
 - ✓ Getting the Red Out



Getting the Red Out then in....



Yes, I've heard. Kills men by the hundreds! And if he were here, he'd consume the English with fire balls from his eyes and bolts of lightning from his arse!

Antibiotic

- ✓ Fourth Generation Quinolones
 - ✓ Indications:
 - ✓ For the treatment of bacterial conjunctivitis caused by susceptible strains of gram + and some gram -
 - ✓ Vigamox (moxifloxacin)
 - ✓ Zymar (gatifloxacin)
 - ✓ Off-Label
 - ✓ Surgical Prophylaxis
 - ✓ Corneal Infections
 - ✓ Blepharitis

Antibiotic

✓ Tetracycline Derivatives

- ✓ Indications:
 - ✓ Tetracycline's primary use is for the treatment of acne vulgaris and rosacea.
- ✓ Off-Label
 - ✓ Meibomitis
 - ✓ Dry Eye
- ✓ Warnings
 - ✓ Stomach Aches
 - ✓ Yeast Infections
 - ✓ Diarrhea





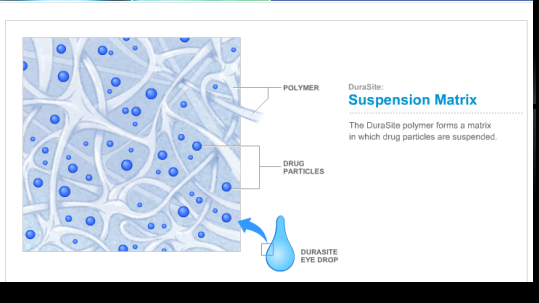
Antibiotic

✓ AzaSite (Inspire, N.C.)

- ✓ Azithromycin 1%
 - ✓ Macrolide
 - ✓ Bacteriostatic
 - ✓ Approved for Bacterial Conjunctivitis
- ✓ DuraSite
 - ✓ polymeric mucoadhesive matrix
- ✓ bid X 2 days, qd x 5 days



  **DuraSite Mechanism of Action**



DuraSite: Suspension Matrix

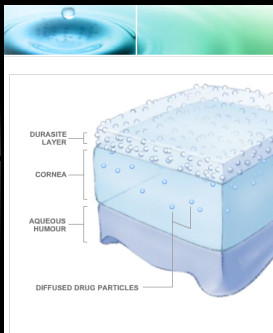
The DuraSite polymer forms a matrix in which drug particles are suspended.

POLYMER

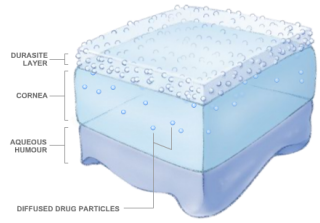
DRUG PARTICLES

DURASITE EYE DROP

DuraSite® Vehicle



DuraSite Mechanism of Action



DuraSite: Suspension Matrix

In the aqueous environment of the eye, these drugs are released from the polymer matrix and diffuse into the tear film where they wash over the cornea and conjunctiva.

AzaSite® Ocular Tissue Concentration Conclusions

- ✓ AzaSite® achieves significant drug concentrations in a variety of ocular tissues including:
 - ✓ Conjunctiva
 - ✓ Cornea
 - ✓ Eyelids
- ✓ AzaSite® levels remain high and sustained in ocular tissues over time
- ✓ DuraSite® adheres AzaSite® to the ocular surface aiding the delivery of superior concentrations to ocular tissue

Posterior Blepharitis

- ✓ Treatment Options
 - ✓ Lid disease
 - ✓ 1 gtt qhs
 - ✓ "Like ketchup"
 - ✓ FLIP-WHIP-DRIP
 - ✓ Remind patients that bottle is small
 - ✓ Rub in the remainder on the lid



“They call it a Royal with Cheese”



Allergy Medications

- ✓ Indications
 - ✓ Treatment of signs and symptoms of allergic conjunctivitis
 - ✓ Mast Cell Stabilizers
 - ✓ Anti-histamine
 - ✓ NSAID's
- ✓ Off-Label
 - ✓ Dry Eye Treatment
 - ✓ Red Eye Control
 - ✓ Pterygium

Glaucoma Medications



- ✓ Alphagan-P
 - ✓ Indications
 - ✓ The lowering of intraocular pressure in patients with open-angle glaucoma or ocular hypertension
 - ✓ Alpha adrenergic agonist
 - ✓ Off-label Use
 - ✓ Refractive Surgery
 - ✓ Treatment of glare and halos
 - ✓ Stabilizes pupil at 4mm
 - ✓ Use 1 drop q4-6h when needed (dusk)
 - ✓ Getting the Red out!



“The greatest trick the Devil ever pulled was convincing the world he didn't exist”

Restasis

- ✓ Indications
 - ✓ Approved by the FDA for the **treatment of dry eye**
 - ✓ Only prescription available for dry eye treatment
 - ✓ Safe and well tolerated
 - ✓ Level 2 DTS
 - ✓ Widely accepted on formularies
 - ✓ Very inexpensive for patients
 - ✓ Effective with in 1-3 weeks
 - ✓ Long lasting effects
 - ✓ Practice builder

Restasis

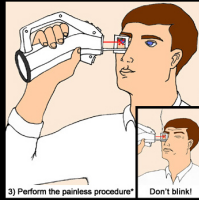
✓ Off-label Indications

✓ Post-LASIK Dryness

- ✓ Anti-inflammatory
- ✓ Increases Goblett cells
- ✓ Promotes regular surface for the cornea
- ✓ Encourages healing
- ✓ *Pre-treat ALL LASIK patients

✓ Cataract Surgery

- ✓ Refractive in nature
- ✓ Patient expectations
- ✓ Increase in inflammation with surgery



Restasis

✓ Off-label Indications

✓ Allergic conjunctivitis

- ✓ Eczema or atopic dermatitis
 - ✓ Severe conjunctival inflammation

✓ Atopic keratoconjunctivitis

✓ Vernal keratoconjunctivitis

- ✓ More common in males
- ✓ Typically steroids are used
 - ✓ Complications associated with steroids



Restasis

✓ Off-label Indications

✓ Corneal transplant (rejection prevention)

- ✓ T-lymphocytes mediator in rejection
- ✓ Cyclosporine potent T-cell inhibitor

✓ Post-corneal transplant glaucoma

- ✓ Steroids can induce IOP spikes

✓ Meibomian Gland Dysfunction

- ✓ N=33 study with Restasis and Placebo
 - ✓ Restasis group improved gland inclusions



Restasis

✓ Off-label Indications

- ✓ Thygeson's Keratitis
 - ✓ Young
 - ✓ Avoid complications of steroids
- ✓ Superior limbic keratoconjunctivitis
- ✓ Herpetic stromal keratitis



“My name is Maximus Decimus Meridius, commander of the Armies of the North, General of the Felix Legions, loyal servant to the true emperor, Marcus Aurelius. Father to a murdered son, husband to a murdered wife. And I will have my vengeance, in this life or the next.”


The Intraocular Lens

“I think I have the black lung..”

CrystaLens HD/AO

Bausch & Lomb
(eyeonics)

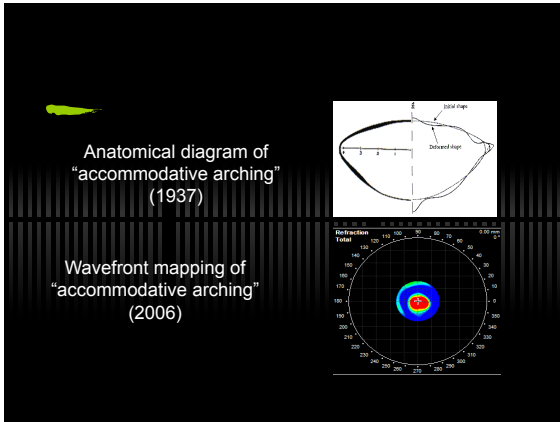
CURRENT DESIGN 5.0 HD

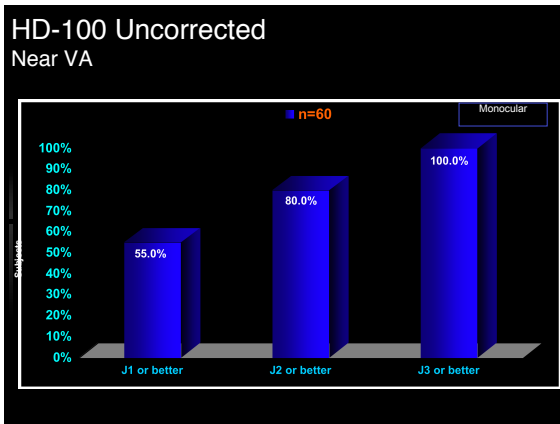


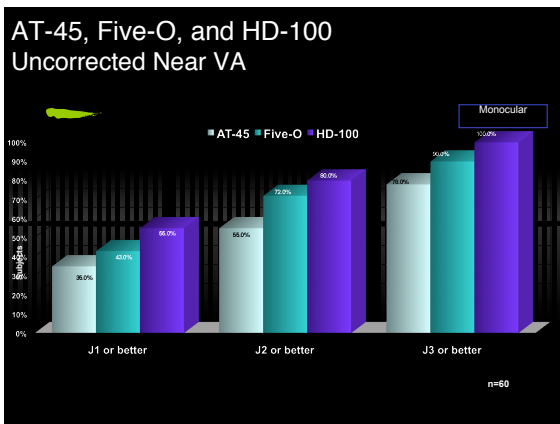
- ✓ Hinged optic to increase movement
- ✓ Larger 5 mm optic
- ✓ Haptics more square
- ✓ Arc length of haptics increased
- ✓ Lengthened haptics to maximize amplitude
- ✓ Surface reshaped with proprietary optical modification "HD"
- ✓ Suitable for in bag placement only

- ✓ Multipiece silicone posterior chamber IOL for the treatment of cataracts
- ✓ Built on the heritage of success of CrystaLens IOLs









Crystalens HD

Summary

- ✓ First and only FDA-approved accommodating IOL
- ✓ Mimics natural focusing action of the eye
- ✓ Provides single focal point
- ✓ Modified optic increases focal range
- ✓ Provides improved near vision versus previous generations, without compromise to intermediate or distance vision
- ✓ No compromise to contrast sensitivity

ReZoom

AMO

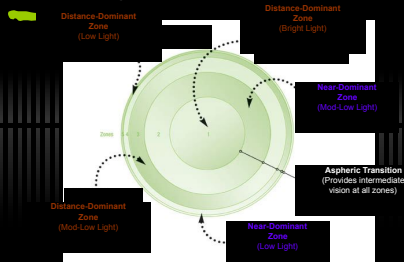
The ReZoom™ Multifocal IOL

- ✓ Hydrophobic acrylic material
- ✓ Balanced View Optics Technology
- ✓ OptiEdge triple edge design
- ✓ Three-piece design
- ✓ Capsule fits PMMA haptics
- ✓ 6.0 mm optic, 13 mm overall length
- ✓ Power Range: +6.0 – 30.0 D in half diopter increments

Balanced View Optics™ Technology

- ✓ Zones proportioned to provide good visual function across a range of distances in varying light conditions.
- ✓ Five concentric refractive zones create true multifocal vision
 - ✓ Zones 1, 3 and 5 are distance dominant
 - ✓ Zones 2 and 4 are near dominant
 - ✓ Aspheric transition between zones provides balanced intermediate vision

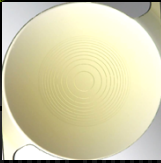
Balanced View Optics™ Technology



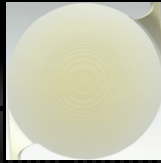
AcrySof® ReSTOR® Aspheric IOL

Alcon

AcrySof® IQ ReSTOR® IOL

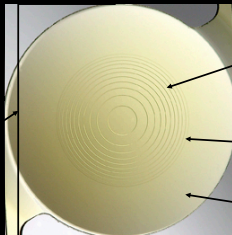


SN6AD3
 Add Power: +4.0 D
 Spectacle Plane: +3.2 D
 Range: +10.0 D to +34.0 D
 A-Constant: 118.9



SN6AD1
 Add Power: +3.0 D
 Spectacle Plane: +2.5 D
 Range: +10.0 D to +34.0 D
 A-Constant: 118.9

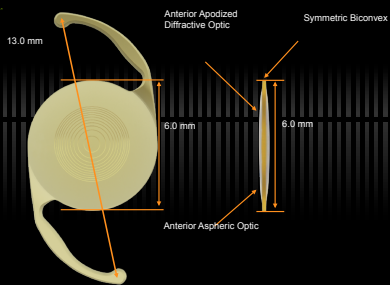
Anatomy of the Apodized Diffractive Technology



Model SN6AD3

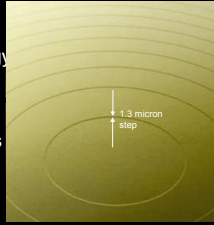
Central 3.6 mm apodized diffractive structure
 Step heights decrease peripherally from 1.3 – 0.2 microns
 A +4.0 D at lens plane equaling +3.2 at spectacle plane
 Outer refractive zone

Anatomy of the Apodized Diffractive Technology

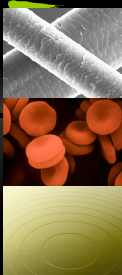


Apodization

- ✓ Gradual reduction or blending of the diffractive step heights.
- ✓ Optimally manages light energy delivered to the retina as it distributes the appropriate amount of light to near and distant focal points, regardless of the lighting situation.
- ✓ Designed to improve image quality



Technology of the AcrySof® ReSTOR® IOL in "Human" Terms

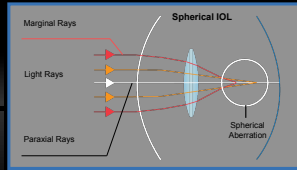


- ✓ Thickness of a Human Hair = 60 microns
- ✓ Thickness of a Red Blood Cell = 7 microns
- ✓ Step Height at periphery of the diffractive portion of the AcrySof® IQ ReSTOR® IOL = 0.2 microns

Design Objective

- ✓ Design considerations for the AcrySof® IQ ReSTOR® IOL:
 - ✓ Induce negative Spherical Aberrations with the lens to compensate for positive corneal Spherical Aberrations

The Problem – Spherical Optics



✓ Spherical aberration occurs when light rays are over-refracted at the periphery of a lens system, resulting in a region of defocused light which can decrease image quality.

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Lens Objectives

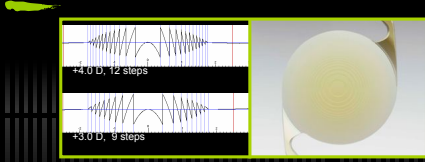
- ✓ Offer an additional choice of add power
- ✓ Maintain existing optical design characteristics and manufacturing processes

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SN6AD1 Design Characteristics

- ✓ Utilizes existing IQ ReSTOR® IOL +4.0 D platform with identical asphericity, energy distribution profile, and shape factor
- ✓ Modified add power from +4.0 D to +3.0 D
 - 9 diffractive steps vs. 12 diffractive steps
 - Slightly wider step spacing to modify the add power

Physical Comparison



- ✓ Both +4.0 D and +3.0 D have 3.6 mm Apodized Diffractive region
- ✓ +4.0 D central zone diameter = 0.74 mm
- ✓ +3.0 D central zone diameter = 0.86 mm

Tecnis

AMO

TECNIS® Multifocal IOL Specifications*

- ◆ Full diffractive posterior surface
 - Pupil-independent
- ◆ Wavefront-designed aspheric anterior surface
- ◆ Light distribution 50/50
- ◆ +5D to +34D in 0.5D increments
- ◆ Optical power add +4.0D
 - To optimize acuity at preferred reading distance of 33 cm
- ◆ Edge Design:
 - Acrylic: OptiEdge™ design
 - Silicone: Square edge

TECNIS® Acrylic MIOL ZMA09



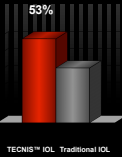
TECNIS® Silicone MIOL ZM300



*TECNIS Multifocal IOL under clinical investigation in the US.
ZMA09 available in markets outside the US.
Ophthalmic Consultants of Long Island

The TECNIS™ IOL - Clinical Results

A study showed the TECNIS™ lens provided up to 53% better contrast sensitivity under mesopic conditions compared to a spherical IOL.*

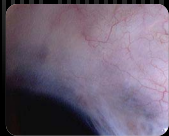
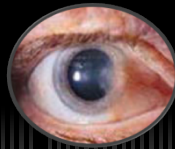


Packer M, et al. J Cataract Refract Surg. 2004;30:988-992.

“It’s K-Billy’s super sounds of the 70’s weekend”

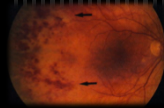
Mitomycin C (MMC)

- ✓ Indicated
 - ✓ Replaces a key component of the DNA replication process
 - ✓ Antimetabolite
 - ✓ Bladder Cancer; Pancreatic cancer; Breast cancer
- ✓ Off-Label
 - ✓ Pterygium Surgery
 - ✓ Filtering Glaucoma Surgery
 - ✓ PRK Refractive Surgery



Retinal Surgery

- ✓ No Vitreal Medication has been approved for the last 30 years
 - ✓ Until Macugen and Lucentis
 - ✓ Indicated for the treatment of AMD
- ✓ Off-Label
 - ✓ CMV Treatment
 - ✓ Gangcyclovir injections
 - ✓ Foscarnet

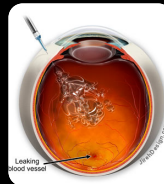


Retinal Surgery

- ✓ Triamcinolone (Kenalog)
 - ✓ Indicated for intramuscular use
 - ✓ Used by retinal surgeons injected into the retina
 - ✓ AMD
 - ✓ Diabetic macular edema
 - ✓ Retinal vein occlusion

Retinal Surgery

- ✓ Off-label
 - ✓ Avastin
 - ✓ Manufactured by Genentech
 - ✓ Indicated for the treatment
 - ✓ Colon Cancer
 - ✓ Rectal Cancer
 - ✓ Larger molecule of Lucentis
 - ✓ Monetary issues
 - ✓ Used by OMD's for the treatment of AMD



“Doodie!”



NSAID's

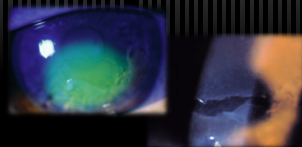
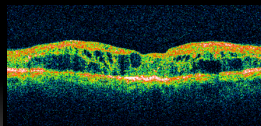
✓ Indications

- ✓ ACULAR® ophthalmic solution is indicated for the temporary relief of ocular itching due to seasonal allergic conjunctivitis. ACULAR® ophthalmic solution is also indicated for the treatment of postoperative inflammation in patients who have undergone cataract extraction.
- ✓ Xibrom is indicated for the treatment of postoperative inflammation and reduction of ocular pain in patients who have undergone cataract extraction.
- ✓ ACULAR LS® ophthalmic solution is indicated for the reduction of ocular pain and burning/stinging, following corneal refractive surgery

NSAID's

✓ Off-label

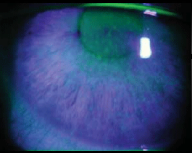
- ✓ Treatment of CME
 - ✓ W/Steroid
- ✓ Corneal Analgesic
 - ✓ Abrasion
 - ✓ Foreign body
 - ✓ Scratch



“No, baby, you’re money”

Contact Lenses

- ✓ Indicated for the correction of myopia and hyperopia
- ✓ Off-label
 - ✓ Bandage lens
 - ✓ PRK
 - ✓ Abrasion
 - ✓ Dry Eye
 - ✓ Useful for severe exposure
 - ✓ Patients with lid disease



Myokymia

- ✓ Spontaneous, fine fascicular contractions of muscle without muscular atrophy or weakness
- ✓ Most likely nerve fiber irritation
 - ✓ Stress
 - ✓ Fatigue
 - ✓ Caffeine
 - ✓ Alcohol

Myokymia

- ✓ Treatment
 - ✓ Self-limiting
 - ✓ Quinine
 - ✓ Tonic Water



How did you do?

- ✓ "A lot of people go to college for seven years" "Yeah, they're called doctors"
 - ✓ *Tommy Boy*
- ✓ "Oh, and Senator, just one more thing: love your suit!"
 - ✓ *Silence of the Lambs*
- ✓ Yes, I've heard. Kills men by the hundreds! And if he were here, he'd consume the English with fire balls from his eyes and bolts of lightning from his arse!
 - ✓ *Braveheart*
- ✓ "They call it a royal with cheese"
 - ✓ *Pulp Fiction*



How did you do?

- ✓ The greatest trick the devil ever pulled was convincing the world he didn't exist!
 - ✓ *Usual Suspects*
- ✓ My name is Maximus Decimus Meridius, commander of the Armies of the North, General of the Felix Legions, loyal servant to the true emperor, Marcus Aurelius. Father to a murdered son, husband to a murdered wife. And I will have my vengeance, in this life or the next.
 - ✓ *Gladiator*
- ✓ "It's K-Billy's Sound of the Seventies Weekend"
 - ✓ *Reservoir Dogs*
- ✓ "Doodie"
 - ✓ *Caddy Shack*
- ✓ "No, baby, you're money"
 - ✓ *Swingers*



Conclusion

- ✓ Know the medical indications of your prescription
- ✓ Keep looking for new technology
- ✓ Doctor your patients!
- ✓ Remember Standard of Care
 - ✓ What would a peer do in the same situation
- ✓ Watch more movies

“Pup and Taco”

Fletcher
(Thank You)

