

# “Oral and topical pain management in eye care”

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## Disclosures

- No financial disclosures

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## ORAL PAIN MEDICATIONS

- Manage underlying condition appropriately first from an ocular standpoint
- Topical/ocular pain control.....
- Cycloplegia (atropine, cyclopentolate, homatropine)
- NSAIDS
- Steroids
- Bandage CL
- Topical anesthetic in office only

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## PAIN MEDICATIONS

- If topical management is not enough, then consider oral pain relief
- Laws vary for OD's regarding use of controlled substances
- Two broad categories...
  - OTC pain relief, mostly NSAID's
  - Narcotic pain relief

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## COMPARISON OF ANALGESICS

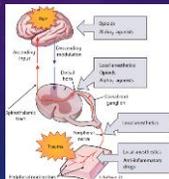


Image from [cvm.msu.edu/~Pain%20Management%20PDA.htm](http://cvm.msu.edu/~Pain%20Management%20PDA.htm)

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## NSAIDS

- OTC NSAID's are often enough to mitigate ocular pain
- Aspirin, Ibuprofen, APAP, naproxen
- Common Trade names aspirin, Advil, Tylenol, Aleve
- Aspirin 81mg, 325-500mg
- Advil 200mg
- Tylenol 325-500mg
- Aleve 220mg

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### RX NSAIDS

- Indomethacin (Indocin) 25, 50 mg
- Naproxen (Anaprox) 275, 550 mg
- Ibuprofen (Motrin) 200-800 mg
- Indomethacin very good for scleritis. TID dosing



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### COMMON NSAID CONCERNS

- GI upset (take with food or drink, don't lie down for 30 minutes)
- Bleeding
- Ulcers
- Caution also with renal disease, heart disease, liver disease (mostly APAP)
- Rx strength particularly problematic with heart disease

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### TRAMADOL (ULTRAM): USED TO BE NON-NARCOTIC, BUT NOW A CONTROLLED SUBSTANCE

- Immediate release (50-100 mg) and extended release (100-300 mg)/versions
- Maximum dose 300mg /day
- Dose q 6-8 h
- Schedule IV, so limited (but possible) abuse potential



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### NARCOTIC PAIN RELIEF

- As an OD, may or may not have authority to use (only Tramadol in Indiana for example)
- Standard warnings.....no alcohol, don't operate machinery



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### NARCOTIC SIDE EFFECTS

- Constipation very common, and can be severe
- Nausea and vomiting: often ceases after first few doses
- Sedation
- Lack of mental clarity
- Respiratory depression (most severe)

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### NARCOTIC PAIN RELIEF

- DEA Scheduled substances
- I-V
- Schedule one has high abuse potential, schedule five very limited abuse potential
- Two types of dependence....
- Psychological and physical
- Physical usually requires 2 weeks of use or more

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## OXYCODONE

- Schedule II :high abuse potential with severe dependence risk
- **Percocet**: 5mg with 325 mg of APAP
- **Percodan**:4.5mg with 325 of APAP
- **Tylox**: 5mg with 500mg of APAP

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## HYDROCODONE

- Schedule II
- **Lortab**: 2.5,5,7.5 mg with 500mg APAP
- **Vicodin**: 5mg with 500mg APAP
- **Vicodin ES**: 7.5MG with 500mg APAP
- **Norco**: 5,7.5,10 with 325 APAP
- **Zohydro ER**: 10,15,20,30,40,50

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## CODEINE

- Schedule III
- **Tylenol with Codeine**, all have 300mg of APAP
- Tylenol #2 : 15mg
- Tylenol #3 : 30mg
- Tylenol # 4 : 60 mg

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## ORAL STEROIDS

- When oral steroids are used appropriately for a relatively short time they are very, very safe
- After all, they are basically a natural substance already found in the body
- Be aware of body weight when dosing

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## WHO DOESN'T GET ORALS, OR GETS THEM VERY, VERY CAREFULLY

- Diabetics
- Patients with stomach problems / ulcers
- Patients with active infection
- Pregnant women



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## WHAT CAN THEY DO THAT'S BAD?

- Almost nothing in the short term! Most issues require long term use
- Increase Na<sup>+</sup>, decreased K<sup>+</sup> leading to fluid retention
- Hypertension
- Elevate blood glucose levels
- Stomach pain and ulcers (stomach upset with short term use)
- Insomnia, euphoria, psychosis (possible with short term use)
- Thin skin / bruising
- Osteoporosis
- Increased ICP
- PSC's (far more commonly than topicals)
- Increased IOP (far less commonly than topicals)

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## WHAT CAN THEY INTERACT WITH?

- Screw up glucose control
- ASA, Coumadin
- Digoxin
- Some antibiotics, anti-seizure meds, anti-TB meds (TB itself is a strong relative contraindication)



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## WHAT DO THEY DO THAT'S GOOD?

- Duh!.....they decrease inflammation and therefore inflammatory sequelae, such as pain

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## WHAT CAN WE USE ORAL STEROIDS FOR IN EYE CARE?

- Contact dermatitis / allergic response of the eye lids
- Reaction to insect bite or sting on the eye lids
- Recalcitrant CME
- Recalcitrant uveitis, especially bilateral or vitritis
- Choroiditis / retinitis
- Scleritis



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## USES OF ORALS IN EYE CARE

- Myasthenia Gravis
- Inflammatory orbital pseudotumor
- Thyroid eye disease / Grave's ophthalmopathy
- Optic neuritis (but not by themselves!)
- GCA
- DLK post LASIK (in conjunction with topicals)

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## OCULAR SIDE EFFECTS OF ORAL STEROIDS

- These are well known.....PSC's and increased IOP
- IOP increases are rare, but can occur with very long-term use
- PSC's are not rare!
- 10 mg per day or less for one year or less has almost no chance of PSC formation
- 16 mg per day or more over several years has a 75% chance of PSC formation
- Overall, general population has a .5% chance of PSC development while those on long term oral steroids have a 30% prevalence (across doses)

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## ORAL STEROIDS



- Oral steroids are generally prescribed in one of two ways.....
- 1) Medrol dose pack (methylpred)
- 2) Prednisone 10mg tablets

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## COMPARISONS

- When it comes to suppressing the HPA (hypothalamic-pituitary-adrenal) axis.....
- 25mg Cortisone = 20mg Hydrocortisone = 5mg Prednisone = 4mg Triamcinolone = 4mg Methylprednisone = .75mg Dexamethasone
- Potency essentially follows this order but in reverse
- Body produces an amount of cortisone that equals 5mg of prednisone per day

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## MEDROL DOSE PACK

- Available in different strengths
- Most commonly used is a package of 21, 4 mg tablets( 2 mg is available)
- Six are taken the first day, then one less each day thereafter (6-5-4-3-2-1 = 21 tablets)
- Self tapering and little to no suppression of the HPA axis
- In eye care, really only strong enough and long lasting enough for treatment of lid reactions

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## PREDNISONE

- Most common dosing is to give the desired amount in 10 mg tablets (need 40 mg, take 4 pills)
- Is available in 1, 2.5, 5, 10, 20, and 50 mg tablets
- Best choice for most of our desired uses in eye care
- Potent and flexible

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## DOSING

- Up to 60 mg, take entire dose in the morning
- Over this amount take ½ in morning, ½ in evening
- As previously mentioned, Medrol dose pack self tapers
- With prednisone, after relatively short course at full desired strength, taper by ten milligrams every other day

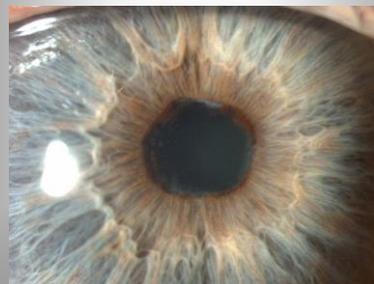
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## DOSING

- An alternative approach is to give twice the desired dose every other day then don't taper. Only for short term use, not long term
- Theory is that anti-inflammatory properties remain high but suppression of HPA axis is much, much less
- For long term use taper must be very slow
- As OD's we rarely would be involved in the long-term prescription of oral steroids

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## Topical Steroids



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## Quick review of topical steroids

- Several topical steroids available for ocular use
- Long track records for many of them with proven efficacy
- Differing levels of activity with differing side effect profiles
- Various clinical niches for different drugs
- Side effects well known.....PSC's (< orals), increased IOP (> orals), etc.

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## Prednisolone Acetate

- Most commonly used topical steroid
- Potent "gold standard" with good mix of effectivity and side effect profile
- .12% suspension (Pred mild)
- 1% suspension (Pred Forte, Omnipred). Econopred no longer exists: replaced by generic Omnipred with smaller molecule.

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## Prednisolone phosphate

- Goes on and off the market in generic form
- Rarely used
- Vasocidin drops in combo with Sulfacetamide
- Used in the SCUT trial

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## Durezol

- .05% Ophthalmic emulsion
- ½ dosing schedule compared to Pred Forte and others
- Generic available at around \$50-\$60
- Very effective against iritis, can be drug of choice
- VERY high propensity to elevate IOP

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## Loteprednol Etabonate



- Site-specific steroids often referred to as "soft steroids"
- .5% (**Lotemax**) and .2% (**Alex**)
- 1% **Inveltys**, .38% **Lotemax SM**, .25% **Eysuvis**

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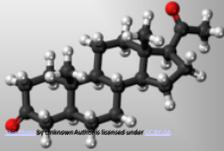
## Lotemax

- .5% Loteprednol suspension
- Almost as potent as Pred Forte but very little propensity to elevate IOP or cause PSC's
- In the eye, it binds to the target site and achieves therapeutic effect but then is quickly broken down
- Intrinsic esterases turn the drug into cortienic acid which is an inactive metabolite
- Available in ointment form which is preservative free and as a "gel" forming drop
- Generic of the .5% suspension had been made by Akorn (bankrupt)

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## Alrex

- .2% Loteprednol
- Similar to Lotemax but not potent enough to treat intraocular inflammation: surface only
- Cost issues: can cost more than Lotemax



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## Inveltys

- 1% Loteprednol
- Purchased by Alcon (Kala originally)
- Approved for post-op inflammation and pain
- Dosed BID

## Lotemax SM

- .38% Loteprednol
- SM for sub-micron technology: improved contact time, much improved AC penetration
- Approved for post-op inflammation and pain
- TID dosing

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## Eysuvis

- .25% Loteprednol
- Approved for 2-week course for dry eye therapy
- Purchased by Alcon from Kala

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## Dexamethasone

- Dexamethasone sodium phosphate or alcohol suspension
- .1% suspension (Maxidex)
- Potent, but tremendous ability to increase IOP
- Frequently used in combination with antibiotics (Tobradex, Maxitrol, Dexacidin)
- Tobradex ST : only .05% dexamethasone

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## Fluoromethalone

- Relatively weak, little risk of elevating IOP but limited clinical uses
- .1% ointment (FML)
- .1% suspension (FML and Eflone)
- .25% suspension (FML Forte)
- .1% acetate suspension (Flarex)

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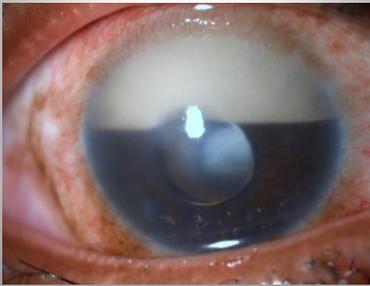
## Combinations

- Maxitrol, Dexacidin
- Pred-G
- Tobradex (has a generic) & Tobradex ST, Zylet
- Blephamide, Vasocidin
- FML-S



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## Topical NSAIDs



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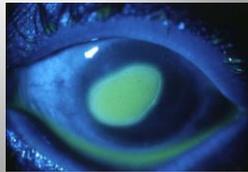
## Ketoralac

- **Acular LS** 0.4% (what does LS stand for?). QID
  - **Acuvail** preservative free, unit dose vials. BID
  - Original **Acular** is .5% and it has substantial issues with stinging
- Uses for topical NSAIDs include surface pain, post-operative pain / inflammation, CME
- Generic Acular and generic Acular LS: about \$35  
Acuvail about \$350

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## Diclofenac

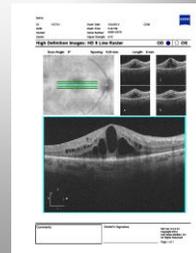
- Diclofenac .1% : branded Voltaren no longer available
- Generically available (earlier generic forms linked to corneal melting)
- QID dosing, cost can be as little as \$10-\$20



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## Nepafanac

- **Nevanac** .1% Nepafanac
- Prodrug
- TID dosing
- Excellent for CME
- Expensive
- **Ilevro** .3% Nepafanac
- QD dosing
- \$250 for 1.7 ml



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## Bromfenac

- Bromfenac .09% : **Bromday**
- Has a generic: good RX about \$60 for 1.7ml
- QD dosing
- Also **Prolensa** .07%. Decreased PH to increase corneal penetration (1.6 ml and 3ml)
- Also **Bromsite** .075%

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## Immune modulators

- **Restasis** .05% and generic
- Topical cyclosporin A: Inhibits T-cells
- Emulsion
- Also in multi-dose bottle
- Takes weeks to months for maximum effect
- BID dosing, .1% QD dosing version in Europe
- Possible suppressive use in HSK, HZV, and atopic disease



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## Xiidra

- Lifitegrast (Xiidra) 5%
  - Shire (Takeda)- now Novartis
  - FDA approval granted in July of 2016
  - BID dosing for dry eye
- Not exactly clear how it helps in dry eye, but most likely blocks T-cell adhesion, thus limiting T-cell mediated inflammation.
- Works quicker than Restasis, within about 2 weeks
- \$450.00 / 60 vial carton, can be up to \$600 +

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## Cequa

- Sun pharmaceuticals
  - FDA approval in August 2018
  - .09% cyclosporine A
  - BID dosing
  - Nanotechnology for delivery
- Available at special mail order pharmacy at reduced cost to commercially insured patients (no Medicare or Medicaid)
- Also available through traditional pharmacy channels

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## Verkazia

- .1% Cyclosporin emulsion by Santen
- FDA approved for Vernal conjunctivitis @ QID dosing
- Possible off label use for dry eye (similar to European Restasis), other atopic disease, etc.
- \$1500-\$2000!!!!!!!



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## Random topical steroid thoughts

- Genetic predisposition to being a steroid “pressure responder”. More common if family history of glaucoma
- Hispanics have an increased prevalence of PSC formation on steroids compared to other races
- Increased risk of ocular infection
- Can worsen Acanthamoeba keratitis, dendritic herpetic keratitis, and fungal keratitis

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The End

9/23/22

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