Comprehensive Pharmacology Update

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www.eyeupdate.com

2009: A TPA Odyssey – Are We There Yet?
Vision Institute of Canada
Annual Fall Conference and Trade Show

Hilton Suites Hotel - Donald Cousens Conference Centre
Markham, Ontario
October 25, 2009

Dapiprazole Hydrochloride 0.5%
- Brand name: NU-REV
- Comparable to previously available Rev-Eyes
- Custom compounded and available through Vision Source & Focus Labs
  Fax: 501-753-6021
  Call: 866-752-6006
  http://vs-focus.com
- 5 ml bottle approximately $40

Antibacterial Medications
- Sulfa Preparations
- Erythromycin
- Bacitracin
- Bacitracin / Polymyxin B
- Bacitracin / Polymyxin B / Neomycin
- Chloramphenicol
- Gentamicin
- Tobramycin
- Trimethoprim / Polymyxin B
- Fluoroquinolones
- Azithromycin
- Oral antibiotics

Erythromycin
- Bacteriostatic
  - inhibits protein synthesis
- Broad Spectrum
  - mainly against gram positives
  - Staph. species often become resistant
- Not a drug of choice in treating active disease
- Nontoxic to corneal / conjunctival tissues
- Only available in ointment form
- Oral erythromycin
  - styes, hordeola, lid infections
- Pregnancy category B
Bacitracin
- Bactericidal - destroys cell walls
- Highly efficacious against gram positive bacteria
- Bacterial resistance is very rare
- Toxicity and allergic responses are very rare
- Available only in ointment form

Bacitracin and Polymyxin B
- Polymyxin B
  - Bactericidal - destroys cell membranes
  - Highly efficacious against gram negative bacteria
  - Resistance, toxicity, and allergic responses are very rare
  - Available only in ointment form
  - Pregnancy category B

Trimethoprim with Polymyxin B
- Polymyxin B has been discussed earlier
- Trimethoprim, a non-antibiotic antibacterial
  - Bacteriostatic and broad spectrum
  - Inhibits bacterial dihydrofolate reductase
  - Effective against most common ocular pathogens, except pseudomonas species
  - Excellent for bacterial infections in children
  - Haemophilus influenzae and streptococcus pneumoniae
- Available in solution only (Polytrim and generic)

Azithromycin 1% Ophthalmic Solution
- Topical eyedrop solution of azithromycin
- Only macrolide ophthalmic formulation
- Broad spectrum coverage, especially against gram positive pathogens
- Good tissue penetration; viscous vehicle
- Dosage: BID for 2 days then QD for 5 days
- Avoid use if patient is allergic to erythromycin
- Pregnancy category B; approved down to age 1
- Marketed as AzaSite 1% ophthalmic solution in a 2.5 ml opaque bottle by Inspire Pharmaceuticals
**Aminoglycosides**
- Bactericidal
- Inhibits protein synthesis
- Effective against most commonly encountered gram positive and gram negative bacteria
- Available in both solution and ointment form
  - Gentamicin - toxic/allergic reactions do occasionally occur
  - Tobramycin - resistance, toxic and allergic reactions rare (Category B)

**Fluoroquinolones**
- Potent, broad-spectrum bacterial antibiotics
- Inhibit bacterial DNA Gyrase and topoisomerase IV
- Cross-resistance between other antibiotics is rare
- Development of bacterial resistance is increasing with older fluoroquinolones
  - Ciloxan* (ciprofloxacin) and Ocuflox* (ofloxacin)
  - Ciprofloxacin and ofloxacin generically available
    - Quixin (levofloxacin 0.5%)
    - IQUIX* (levofloxacin 1.5%)
    - Zymar (gatifloxacin 0.3%)
    - Vigamox (moxifloxacin 0.5%)
    - Besivance (besifloxacin 0.6%)
- All are approved for pediatric use
- All are FDA category “C”
*Approved to treat microbial keratitis

**Levofloxacin 1.5% Ophthalmic Solution**
- First high concentration ophthalmic fluoroquinolone
- Ophthalmic version of oral Levaquin, the most highly prescribed oral fluoroquinolone
- FDA Indication: Bacterial keratitis
- Lower concentration Quixin approved for bacterial conjunctivitis
- Clinical usefulness: Any ocular bacterial infection
- Self-preserved in a 5 ml opaque bottle
- Marketed as IQUIX by Vistakon Pharmaceuticals

**The Newest Fluoroquinolone - Besifloxacin**
- New chemical entity: a chloro-fluoroquinolone
- NOT used systemically – only available in U.S.
- Relative resistance-proof: no oral counterpart
- FDA-approved medication: bacterial conjunctivitis
- FDA-approved treatment protocol: tid for 7 days
- Pediatric approval: ages 1 and older
- Preserved with 0.1% BAK; Durasite vehicle
- To be marketed as Besivance (0.6%) ophthalmic suspension by B&L Pharmaceuticals – 5 ml
Phase III Efficacy and Safety Study of Besifloxacin Ophthalmic Suspension 0.6% in the Treatment of Bacterial Conjunctivitis

“The broad spectrum of activity of besifloxacin ophthalmic suspension and its activity against resistant microorganisms could be an advantage with the emergence of resistance to the newer fluoroquinolones used to treat ophthalmic infections. Another potential benefit of besifloxacin ophthalmic suspension is that it is being developed exclusively for ocular use, and will not be used systemically, which in theory should reduce the potential for encountering resistant organisms resulting from prior systemic use.”

Tepedino, ME, et. al. Current Medical Research and Opinion, Vol. 25, No. 5, 2009

Antibiotics

Solutions: Tobramycin*
Fluoroquinolone**
Polytrim* or AzaSite (Peds)

Ointments: Polysporin*

*available in generic form
**ofloxacin and ciprofloxacin available generically

Perspective on the PDR

“Habits are hard to break. Reliance on the PDR is one. Discarding the previous year’s volume is another. Know the PDR for what it is: a limited resource for FDA – approved drug inserts written, chosen, and paid for by the drug manufacturers.”


Antibiotics - Systemic

- Penicillins
- Cephalosporins
- Tetracyclines
- Macrolides
- Fluoroquinolones

Resources:
- Drug Facts and Comparisons
- The Sanford Guide to Antimicrobial Therapy (www.sanfordguide.com)
- Tarascon Pocket Pharmacopoeia (www.tarascon.com)
- epocrates.com
Penicillins

- Dicloxacillin
- Augmentin

Dicloxacillin (Tegopen)

- Penicillinase-resistant PCN (since most all staph species produce penicillinase, wise choice for most lid infections)
- Useful in soft tissue staph infections, such as internal hordeola, preseptal cellulitis, etc.
- Usual dosage 250 mg qid x 1 wk
- If true allergy to PCN, then use oral fluoroquinolone as alternative
- Best taken on an empty stomach

Amoxicillin/ Clavulanic Acid (Augmentin)

- Clavulanic acid enables amoxicillin to be bactericidal against common gram positive pathogens
- Useful in treating soft tissue infections
- Cannot use if patient is allergic to penicillin
- Tx: 500, 875, or 1000 mg tablet q 12 hrs x 7-10 days
- Can be taken with meals
- More expensive than generic dicloxacillin or cephalexin

Methicillin Resistant Staphylococcus Aureus (MRSA)

- Infection caused by Staphylococcus aureus (“Staph”)
- Staph commonly carried on skin or in nose
- Skin infections (abscesses, boils) most common (25-30% colonized)
- MRSA is almost always spread by direct physical contact
- MRSA common in hospitals and healthcare facilities
- To prevent MRSA:
  - Keep infections clean and dry
  - Frequent hand washing
  - Avoid sharing personal items
MRSA Update

- 94,360 serious MRSA (invasive) in 2005
- 85% of invasive MRSA associated with healthcare
- Incidence highest in older persons (>65), blacks, and males
- www.cdc.gov/ncidod/dhqp/ar_mrsa_prevention.html
- In 1974, MRSA 2% of total staph infections; in 1995, MRSA 22%; in 2004 was 63%

Which Oral Drug is Best for MRSA Infection?

“For patients with known or suspected MRSA infection, the drug of choice is a combination of trimethoprim with sulfamethoxazole. This combination drug is available generically, and is written TMP-SMX-DS (the “DS” refers to double strength, which is the most commonly prescribed dosage). It is also known by two common brand names, Septra (Monarch Pharmaceuticals) and Bactrim ( Mutual Pharmaceutical). TMP-SMX-DS is the most effective drug we have against MRSA. The usual adult dosage is 160mg TMP with 800mg SMX b.i.d. x 1 week. Note that there is a sulfa drug component when contemplating allergy history.”

Source: Review of Optometry, June 15, 2008

Cephalexin (Keflex)

- Cephalexin - 1st generation cephalosporin
- Effective against most gram positive pathogens
- All cephalosporins share a 5-10% cross-sensitivity to PCN (true allergy to PCN, oral fluoroquinolone alternative)
- Usual dosage: 500 mg bid x 1 week
- Useful in soft tissue staph infections, such as internal hordeola, preseptal cellulitis, etc.

Penicillin Allergy and Cephalosporins

“This retrospective study of outpatients found a low absolute risk (1.1%), but a high relative risk (10-fold increase), of reacting to a cephalosporin after having reacted to a penicillin. However, the relative risk of reacting to a sulfonamide was similar, suggesting that a specific cross-reaction between penicillins and cephalosporins might not exist. The current approach of avoiding cephalosporins only in patients with severe allergic reactions to penicillins seems appropriate.”

Source: Journal Watch, June 1, 2006
The Tetracyclines

- Tetracycline, doxycycline, minocycline
- Doxycycline/minocycline most commonly used
- Advantages over tetracycline
  - Maintenance dose 20 - 100 mg daily
  - Can be taken without regard to meals
- Contraindicated in pregnancy, nursing mothers, under age 8; photosensitivity warning
- Indication in primary eye care
  - Meibomianitis (chronic inspissated glands)
  - Adult inclusion conjunctivitis (chlamydia)
  - Recurrent corneal erosion

Doxycycline

- Vibramycin original brand name
- Effective member of tetracycline family
- Advantages over tetracycline
  - Dosage 50 mg qd or bid
  - Can be taken without regard to meals
- Contraindicated in pregnancy, nursing mothers, under age 8; may cause photosensitivity
- Indication in primary eye care
  - Meibomianitis (chronic inspissated glands)
  - Adult inclusion conjunctivitis (chlamydia)
  - Recurrent corneal erosion
  - Inhibits matrix metalloproteinases

Oracea

- Doxycycline 30 mg immediate release and 10 mg delayed release beads (once daily 40 mg capsule)
- First and only oral therapy approved by FDA to treat rosacea
- Works by controlling inflammation
- Recommended to take in morning with a full glass of water
- Contraindications and side effects similar to tetracyclines (photosensitivity and yeast infections not observed in clinical trials).
- Marketed by Galderma

Medical Approach to RCE

- Small study – limited follow-up
- 100 mg doxycycline per day for 1 month and Lotemax q.i.d. for 1 month
- Results: Curative in almost all cases
- An alternative (or adjunctive) to ASP or conventional therapies
**Glucocorticosteroids and Doxycycline in RCE**

- The concentration and activity of metalloproteinase-9 are increased in patients with recurrent corneal erosion and ocular rosacea.
- Glucocorticosteroids have potent immunomodulatory effects, including downregulation of production of inflammatory cytokines such as interleukin 1 and tumor necrosis factor alpha, that stimulate metalloproteinase production.
- The rapid clinical response to doxycycline and corticosteroids in our patient group could be the direct result of direct inhibition of inflammation or inflammation-induced metalloproteinase activity.

*American Journal of Ophthalmology, July 2001*

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**Azithromycin (Zithromax)**

- Used for soft tissue infection (staph resistance)
- Drug of choice for chlamydial infections
- Erythromycin, clarithromycin (Biaxin), azithromycin (Zithromax) - macrolide antibiotics, of which erythromycin is prototype
- Dosage for chlamydial eye infection - four 250 mg capsules or two 500 mg capsules for one day or a single dose of a 1,000 mg suspension
- Z-max is a 2,000 mg oral suspension

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**Fluoroquinolones (Oral)**

- Broad spectrum; especially effective for G–organisms (not effective against chlamydia)
- Resistant bacteria continue to emerge
- Side effects: mild GI, mild HA, dizziness
- Use conservatively in pregnancy and children when benefits outweigh risks; photosensitivity warning
- Avoid Ofloxacin and Levofloxacin with theophylline
- Avoid fluoroquinolones with Coumadin
- Cipro now available once daily and available generically
- Levofloxacin (Levaquin) has replaced Cipro as “gold standard” in oral fluoroquinolone therapy

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**IMPORTANT DRUG WARNING**

- Fluoroquinolones, including AVELOX®/CIPRO®, are associated with an increased risk of tendinitis and tendon rupture in all ages. This risk is further increased in older patients usually over 60 years of age, in patients taking corticosteroid drugs, and in patients with kidney, heart or lung transplants.

*Reference: HCNN (electronic health alerts) 10-22-08*

- Fluoroquinolone therapy has been associated with possible tendinitis of the EOM’s, resulting in diplopia.

Oral Antibiotic Options

**Penicillin**
- Augmentin 875 mg (or 1000 mg) bid

**Cephalosporin**
- Keflex 500 mg (or 750 mg) bid

**Fluoroquinolone**
- Levaquin 500 mg (or 750 mg) qd

**Macrolide**
- Erythromycin (EES-400 mg qid)
- Azithromycin tri-pak (500 mg/d x 3d)

**Trimethoprim with sulfamethoxazole**
- Common (old) brand names Septra or Bactrim
- TMP-SMX-DS ("double strength")
- TMP-SMX-DS 160mg/800mg (take 2 bid x 1 week)
- A drug of choice for MRSA infections

Available Steroid Medications

- Hydrocortisone
- Medrysone
- Fluorometholone(s)
- Prednisolone
- Dexamethasone
- Rimexolone
- Loteprednol

Ester vs Ketone Corticosteroids

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Prednisolone

- Classic ketone-based corticosteroid
- Most anti-inflammatory action of the steroids
- Used for treating severe ocular conditions
- Percent concentration and frequency of administration allow therapy to match the clinical condition
- Available in suspension and solution
**Prednisolone Generic Suspension**

Because of reports of poor suspension quality, do not allow generic substitution here.

Pred Forte is recommended in severe cases of uveitis and severe episcleritis.

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**Dexamethasone**

- Classic ketone-based corticosteroid
- Concentration does not exceed .1% because of potency
- Has the greatest ocular hypertensive effect of the corticosteroids
- Therapeutic effectiveness less than prednisolone
- Rarely used as monotherapy
- Available in suspension and solution

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**Fluorometholone Alcohol**

- A progesterone-based steroid
- Useful in treating mild to moderate ocular conditions
- Has a reduced potential to increase IOP
- Available as FML 0.1% suspension and ointment (Allergan) and generic suspensions
- Also available as FML-Forte, a 0.25% solution (no increase in efficacy beyond the 0.1%. concentration)

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**Fluorometholone Acetate**

- A progesterone-based steroid
- Therapeutic profile not quite that of prednisolone acetate
- Has less tendency to increase IOP compared to prednisolone and, of course, dexamethasone
- Useful in treating moderate conditions
- Available as an ophthalmic suspension
- Known commonly as Flarex
**Difluprednate 0.05% Ophthalmic Emulsion**

- FDA approved September 2008 to treat inflammation and pain associated with ocular surgery
- Deacetylated in vivo to difluoroprednisolone
- Structurally similar to other corticosteroids
- Preserved with sorbic acid 0.1%
- Marketed as Durezol ophthalmic emulsion by Sirion Therapeutics in an opaque 5 ml bottle

**Prednisone Acetate 1% Ophthalmic Suspension**

- Historic “Gold Standard” ketone based: Pred Forte
- Prior generics of PA have been of poor quality
- Suspension particle “milling” process has been weak link
- New technology enables proper (<1 micron) particle size
- Omnipred 1% ophthalmic suspension now available in 5 mg and 10 ml by Alcon
- “...No difference in clinical effects between Omnipred and Pred Forte...”
  Reference: *Current Medical Research and Opinion, Vol. 23, No. 10, 2007*

**Loteprednol Etabonate**

- Only ester-based, site-specific steroid
- Works at target tissues, and then is quickly metabolized into inert compounds
- LE has high intrinsic activity when applied locally
- 0.5% loteprednol similar in therapeutic equivalence to 1% prednisolone acetate, yet causes little, if any, increase in IOP
- Available as 0.5% (Lotemax) and 0.2% (Alrex) ophthalmic suspensions

**Cyclosporin 0.05% Ophthalmic Emulsion**

- Topical immunomodulator with anti-inflammatory effects – exact mechanisms unknown
- Indication: “to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation”
- Available in 0.4 ml unit dose vials by Allergan. Supplied in 30-vial tray.
- Dosage: one drop to affected eye(s) b.i.d. Usually takes 1-6 months to reach full therapeutic effect
- Concurrent treatment with Lotemax bid for first 1-2 months may hasten results
Non-Ophthalmic Steroid Ointments/Creams

- Triamcinolone – high to medium potency steroid
- Available in cream, ointment and lotion (0.5%, 0.1%, 0.025%)

Reference: Drug Facts and Comparisons

Steroid Summary

Suspensions: Lotemax, Pred Forte
Ointment: FML
Cream: Triamcinolone .1% (for skin use only)

Systemic Prednisone

- Most common systemic corticosteroid rx’d
- Common initial dosage 40-60 mg
- Available generically and in Medrol DosePak
- Questions to ask before prescribing?
  - Diabetic?
  - Peptic Ulcer Disease?
  - Pregnant?

Antibacterial/Antifungal Combinations

- Prednisolone
- Dexamethasone
- Blephamide
- Isopto-Cetapred
- Vasocidin
- Metimyd
- Sulfrin
- Poly-Pred
- Pred-G
- Fluorometholone
- FML-S
- Loteprednol
- Zylet
- Hydrocortisone
- Cortisporin
**Tobramycin 0.3% and Dexamethasone 0.1%**
- Excellent coverage against most ocular pathogens with minimal concern of aminoglycoside toxicity
- Effective suppressor of inflammation
- Guard against prolonged use with dexamethasone (ketone based steroid)
- Marketed as TobraDex Suspension and Ointment by Alcon and generic suspension

**Tobramycin 0.3% and Loteprednol etabonate 0.5%**
- Excellent coverage against most ocular pathogens with minimal concern of aminoglycoside toxicity
- Safe, effective suppressor of inflammation
- Marketed as Zylet Ophthalmic Suspension by B&L Pharmaceuticals
- Available in 2.5, 5, and 10 ml bottles
- Lotemax and Zylet ointments are in development

**Neomycin, Polymyxin B, and 0.1% Dexamethasone**
- Excellent coverage against most bacteria
- Effective suppressor of inflammation
- Has been a time honored work horse in medical eye care
- Guard against aminoglycoside reactions and IOP increase
- Now a relatively obsolete combination
- Marketed as Maxitrol and generically

**Povidone - Iodine 5% ophthalmic solution**
- Broad spectrum microbicide
- Indicated for “irrigation of the ocular surface”
- “Off label” use: Tx adenoviral keratoconjunctivitis
  - Anesthetize with proparacaine
  - Instill 1 or 2 drops of NSAID
  - Instill several drops Betadine 5% in eye(s), close eye(s)
  - Swab or rub excess over eyelid margin
  - After 1 minute, irrigate with sterile saline
  - Instill 1 or 2 drops of NSAID
  - Rx steroid qid x 4 days
- No reports in clinical trials of adverse reactions.
- Avoid use if patient is allergic to iodine
- Marketed as Betadine 5% ophthalmic prep solution (30 ml opaque bottle) by Alcon surgical
- CPT 99070 supply code
**Treatment Options - Ocular Allergy**

- Artificial Tears
- Mild Vasoconstrictors
- Decongestant / Astringents
- Vasoconstrictor / Antihistamines
- Antihistamines
- Antihistamine / Mast Cell Stabilizers
- Mast Cell Stabilizers
- Non-steroidal Anti-inflammatories
- Mild Corticosteroids
- Systemic Antihistamines
- Potent Corticosteroids
- Homeopathic Formulations

**Antihistamine/ Mast Cell Stabilizer**

- Highly selective H1 receptor blockers with prolonged receptor binding
- Some mast cell stabilization
- Four are available
  - **Olopatadine** 0.1% (Patanol) bid (5 ml)
  - **Ketotifen** 0.2% (Pataday) qd (2.5 ml)
  - **Ketotifen** 0.025% (generic)
  - **Azelastine** 0.05% (Patanol) bid (5 ml)
  - **Azelastine** 0.05% (Opivar) bid (6 ml)
  - **Epinastine** 0.05% (Zaditor) bid (5 ml)
- All safe for pediatrics and adults

**Bepreve**

- Bepotastine besilate ophthalmic solution 1.5%
- Highly selective histamine receptor antagonist
- Works by stabilizing mast cells and suppressing eosinophil migration into inflamed tissues
- Approved to treat ocular itching due to allergic conjunctivitis
- Marketed by ISTA Pharmaceuticals

**Claritin Eye and Zyrtec Itchy Eye**

- **Ketotifen** 0.025% OTC
- Same active ingredient and safety profile as Zaditor, Alaway, Refresh Eye Itch Relief
- Twice daily dosing
- Claritin Eye marketed by Schering-Plough in 5 ml solution.
- Zyrtec Itchy Eye marketed by McNeil-PPC in 5 ml solution.
Patanase Nasal Spray

- Nasal spray 0.6%: 665 mcg of olopatadine hydrochloride in each 100 microliter spray (30.5 g bottle/240 sprays). 2 sprays per nostril twice daily
- Indicated for relief of seasonal allergic rhinitis in patients 12 years and older

Mast Cell Stabilizers

- Prevent the degranulation of mast cells
- Mast cells contain many mediators of inflammation
- Prophylactic, not actively therapeutic, in nature
- Possesses no anti-inflammatory properties
- Most effective in mild to moderate conditions; adjunctive Tx of choice in vernal conjunctivitis; role in GPC not fully understood; safe and effective

- 0.1% Pemirolast Potassium (Alamast) – Vistakon
- 2% Nedocromil Sodium (Alocril) - Allergan
- 0.1%Lodoxamide Tromethamine (Alomide) - Alcon;
- 4% Cromolyn Sodium (Crolom) -B+L; (Opticrom)-Allergan;

Loteprednol Etabonate

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- 0.5% loteprednol similar in therapeutic equivalence to 1% prednisolone acetate, yet causes little, if any, increase in IOP
- Available as 0.5% (Lotemax) and 0.2% (Alrex) ophthalmic suspensions

Systemic Antihistamines

OTC
- Chlorpheniramine (Chlor-Trimeton)
- Diphenhydramine (Benadryl)
- Loratadine (Claritin) - 10 mg qd

Rx
- Cetirizine (Zyrtec) - 5 or 10 mg qd
- Desloratadine (Clarinex) – 5 mg qd
- Fexofenadine (Allegra) - 60 mg bid; 180 mg qd
- Levocetirizine (Xyzal) – 5 mg qd
  - Metabolized by the liver
  - Excreted in bile and urine (1/2 dose if renal disease)
**XYZAL (levocetirizine dihydrochloride)**

- Approved for relief of symptoms associated with allergic rhinitis (seasonal and perennial) and the treatment of uncomplicated skin manifestations of chronic idiopathic urticaria in adults and in children 6 years of age and older.
- **Dosage:**
  - Adults and children 12 yrs of age and older: 5 mg tablet once daily in evening
  - Children 6-12 yrs of age: 2.5 mg (1/2 tab) once daily in evening
- **Clinical trials:**
  - Onset of action was seen at 60 min
  - Efficacy was demonstrated at the end of the 24-hour dosing interval
- Supplied in 5 mg tablets by Sanofi Aventis

*Reference: www.xyzal.com*

**Topical vs. Systemic Antihistamines**

- Systemics have more side effects (sedation, dizziness, tinnitus, nervousness, insomnia)
- Systemics may worsen the condition by causing dry eye
- Topicals appear to be more efficacious
- Topicals direct delivery to the desired site
- Topicals provide a higher concentration
- Topicals not prone to interact with alcohol or CNS depressants

**Veramyst (fluticasone furoate)**

- New treatment for seasonal and year-round allergy symptoms in patients 2 yrs and older.
- Helps reduce the nasal symptoms of allergic rhinitis.
- May also help red, itchy, and watery eyes in adults and teenagers with seasonal allergic rhinitis.
- Side effects: nose bleed or nasal sores, nasal fungal infection, glaucoma or cataracts may occur.
- For best results use once daily.
- Available in 10gm nasal spray (120 metered sprays, 27.5mcg per spray) by GlaxoSmithKline

*Reference: www.veramyst.com*

**Anti-Allergy**

**Acute** -
- Mild/Moderate - Antihistamine/mast cell stabilizer
- Moderate/Severe – Loteprednol (.2 or .5%)

**Chronic** - Antihistamine/mast cell stabilizer
**Anti-Viral Medicines**

**Topical**
- Trifluridine Viroptic

**Oral**
- Acyclovir Zovirax
- Valacyclovir Valtrex
- Famciclovir Famvir

- These are anti-herpetic drugs and are ineffective against the various adenoviral serotypes -

**Trifluorothymidine (Trifluridine)**
- A halogenated pyrimidine analog of thymidine
- Inhibits both virally-infected and non-infected cells
- Possesses good activity against both HSV-I and HSV-II
- Approved down to age 6
- Penetrates into epithelium, stroma, and aqueous
- Once dispensed by pharmacy, refrigeration not required
- Heals most herpetic ulcers in 5 to 8 days
- Use q 2h for first 4 to 5 days, then taper PRN
- Marketed as: Viroptic 1% (7.5 ml) by Monarch Pharmaceuticals and generic

**Acyclovir (ACV)**
- Analog of guanosine
- Specifically targets virally-infected cells
- Minimally toxic to uninfected cells
- **Best** to initiate therapy within 72 hours
- **Tx:** 800 mg by mouth 5 x D for 7 days for HZO; 400 mg 5 x D for 7 days for HSK
- Main side effect: occasional nausea
- Use with caution in kidney disease
- Available generically

**Valacyclovir**
- Prodrug of acyclovir - greater bioavailability
- Rapidly and completely converted to acyclovir after oral administration
- Can be taken without regard to meals
- Side effects: nausea / headache
- **Best** to initiate therapy within 72 hours
- **Dosage:** 1,000 mg caplet tid x 7 days for HZO; 500 mg tid x 7 days for HSK
- Use with caution in kidney disease
- Valtrex by GlaxoSmithKline
**Valacyclovir vs. Acyclovir for Recurrent HSV**

“One-year suppression therapy with oral valacyclovir (500-mg tablet daily) was shown to be as effective and as well-tolerated as acyclovir (400-mg tablet twice daily) in reducing the rate of recurrent ocular HSV disease.”


**Famciclovir**

- Prodrug of penciclovir, the active antiviral drug
- Intracellular half-life of 7-10 hours
- Active against HSV and VZV
- Best to initiate therapy within 72 hours
- Can be taken without regard to meals
- Side effects: minimal/rare - mostly nausea
- Dosage: 500mg q 8 hrs x 7 d for HZO; 250 mg q 8 hrs x 7 d for HSK
- Use with caution in kidney disease
- Marketed as Famvir by Novartis

**Zostavax**

- Vaccine for prevention of shingles in adults age 60 and older
- Marketed by Merck as Zostavax and is given as a single dose by injection
- Anyone who has been infected by chicken pox (more than 90% of adults in US) is at risk for developing shingles
- Contraindicated if hx of allergy to gelatin, neomycin; hx of acquired immunodeficiency states; pregnancy
- In landmark Shingles Prevention Study, Zostavax reduced risk of developing shingles by 51% (4 yrs of follow-up)
- Duration of protection after vaccination unknown

**Non-Steroidal Anti-Inflammatory Drugs**

- Inhibition of prostaglandin synthesis is the mechanism of action.
- They specifically inhibit the action of cyclooxygenase, an enzyme vital to prostaglandin synthesis.
- Prostaglandins are powerful mediators of inflammation.
  - *Acular LS* (Ketorolac Tromethamine 0.4%)-Allergan
  - *Voltaren* (Diclofenac sodium 0.1%) by Novartis
  - *Xibrom* (Bromfenac 0.09%) by ISTA
  - *Nevanac* (Nepafenac 0.1%) by Alcon
**Diclofenac sodium 0.1%**
- Diclofenac sodium 0.1% is a prostaglandin inhibitor used for post-op inflammation/CME
- Useful in decreasing corneal sensitivity associated with pain and photophobia
- Unlabeled indications: corneal abrasions, bullous keratopathy, non-specific corneal surface pain
- Voltaren solution by Novartis and generic

**Ketorolac Tromethamine 0.4%**
- Inhibits prostaglandin synthesis
- Indication: reduction of ocular pain and burning following corneal refractive surgery
- Also used for post-surgical inflammation, pain, photophobia and ocular allergies
- Acular LS 0.4% solution (Allergan)

**Ketorolac Tromethamine 0.45% solution (Acuvail)**
- Preservative-free formulation of ketorolac (NSAID)
- Indicated for treatment of pain and inflammation after cataract surgery
- Formulated at pH 6.8 and contains carboxymethylcellulose – enables drug to adhere to ocular surface and enhance patient comfort
- Approved by FDA for bid dosing beginning the day before cataract surgery and through the first 2 weeks of the post-operative period.
- Adverse events: 1-6% increased IOP, conjunctival hyperemia, corneal edema, ocular pain, headache, tearing, and burred vision.

**Bromfenac 0.09% solution**
- Topical NSAID indicated for treatment of post-op cataract inflammation
- Significant reduction of ocular inflammation with twice daily dosing (under studies for once daily dosing)
- Lower preservative concentration (BAK) than currently available NSAIDs
- Xibrom solution by ISTA
**Nepafenac 0.1% suspension**
- NSAID pro-drug
- Effective in controlling pain and post-operative inflammation associated with cataract surgery
- Dosing regimen of tid
- Nevanac suspension by Alcon

**COX-2 Inhibitors**
- Nonsteroidal anti-inflammatory drugs that work by inhibiting COX-2 (mediates pain and inflammation)
- Does not inhibit COX-1 (regulate cell function of GI tract and platelets)
- Relief of inflammation and pain of osteoarthritis and rheumatoid arthritis
  - Celebrex (celecoxib) - 100 or 200 mg bid

**Singulair (montelukast sodium)**
- Only seasonal allergy medication to block leukotrienes, an underlying cause of allergy symptoms
- Approved to help control asthma (not a steroid)
- Dosage: 10 mg tablet daily. Also available in chewable tablets (4, 5 mg) and oral granules (4 mg)
- Marketed by Merck
- **FDA WARNING (June 2009):** “Patients and healthcare professionals should be aware of potential neuropsychiatric events with these medications.”

**Oral Analgesics**
- OTC’s
- Non-narcotic Rx
- Narcotic Rx
Oral Analgesics

- **OTC’s**
  - Acetylsalicylic acid (ASA - aspirin) 325-500 mg
  - Acetyl-para-aminophenol (APAP-Tylenol) 325-500 mg
  - Ibuprofen (Advil, Nuprin) 200 mg
  - Naproxen (Aleve) 220 mg

Non-narcotic Rx Dosage

- Ibuprofen (Motrin) 200-800 mg
- Indomethacin (Indocin) 25-50 mg
- Naproxen (Anaprox, Naprosyn) 250, 375, 500 mg
- Tramadol HCl (Ultram) 50 mg

Controlled Substances

- **DEA Schedules**: Five schedules based on potential for abuse and physical/psychological dependence
  - **Schedule I**: High abuse potential (heroin, marijuana, LSD)
  - **Schedule II**: High abuse potential with severe dependence liability (narcotics, amphetamines)
  - **Schedule III**: Moderate dependence liability (certain narcotics, nonbarbiturate sedatives, etc)
  - **Schedule IV**: Less abuse potential than S3; limited dependence liability (nonnarcotic analgesics, antianxiety agents, etc)
  - **Schedule V**: Limited abuse potential (small amounts of narcotics in antitussives or antidiarrheals)

Oral Narcotic Analgesics

- **Pharmacology**: Centrally acting opioid receptor blockers
- Safe and effective for acute, short-term pain
- Four commonly used narcotics
  - Propoxyphene (mild to moderate pain) IV
  - Codeine (mild to moderate pain) III
  - Hydrocodone (moderate to severe pain) III
  - Oxycodone (severe pain) II
- Clinically used in combination with acetaminophen
- Generally Rx’ed as 1 tab po q4-6hrs PRN pain (disp #8)
- Onset 20 min., peak 1 hr, duration 4-6 hrs
**Controlled Substances**

- Prescriptions must include:
  - Name, date and address of patient
  - Name, address and DEA # of physician
  - Oral Rx’s promptly committed to writing
  - Can’t be dispensed or refilled more than 6 months after date issued or refilled more than 5 times
  - Written Rx signed by physician required for Schedule II (in emergency, signed Rx within 72 hrs)
  - Schedule II Rx’s cannot be refilled
  - *In many cases state laws are more restrictive than Federal laws

**FDA Action on Schedule IV Pain Medications Containing Propoxyphene**

- FDA Requirements for Manufacturers of propoxyphene-containing products
  - Strengthen boxed warning to emphasize overdose when using these products
  - Provide a medication guide (FDA-approved) to be given to patients with each Rx

- Safety Studies
  - FDA requiring new safety study assessing effects on the heart at higher than recommended doses
  - FDA to work with other agencies to conduct studies comparing safety of propoxyphene-containing products with other commonly used pain medications

- After further safety evaluations on propoxyphene, FDA will take necessary additional regulatory action

**Oral Analgesics**

**Schedule III**

- Narcotic Rx*  
  - Codeine: Tylenol #3 (APAP 300 mg + Codeine 30 mg)
  - Hydrocodone: Lortab, 5, 7.5 (APAP 500 mg + Hydrocodone 2.5, 5, 7.5 mg), Vicodin (APAP 500 mg + Hydrocodone 5 mg), Vicodin ES (APAP 500 mg + Hydrocodone 7.5 mg)

**Hydrocodone**

- Used for moderate degrees of pain (schedule III)
- Commonly combined with acetaminophen
- Commonly Rx’ed as: 500 mg acetaminophen with either 2.5, 5.0, 7.5 or 10 mg hydrocodone as Lortab 5/500 (for example), or 500 mg acetaminophen with 5 mg hydrocodone (Vicodin), 7.5/750 (Vicodin ES) or 10/660 (Vicodin HP)
- Dosage: 1 or 2 tabs po q4-6hrs PRN pain
### Oral Analgesics

**Schedule II**

- **Narcotic Rx**
  - Oxycodone
    - Percocet (APAP 326 mg + Oxycodone 5 mg)
    - Percodan (ASA 325 mg + Oxycodone 4.5 mg)
    - Tylox (APAP 500 mg + Oxycodone 5 mg)

* Addiction potential is not a concern when used for less than one week.

### Oxycodone

- Used for severe pain (schedule II)
- Commonly combined with acetaminophen
- Commonly Rx’ed as: 325 mg acetaminophen with 5 mg oxycodone (Percocet), or 500 mg acetaminophen with 5 mg oxycodone (Tylox)
- Dosage: 1 tab po q 6 hrs PRN pain
- Write the number to be dispensed, usually 4 to 8