

**Ohio Department of Job and Family Services (ODJFS)
Drug Utilization Review (DUR) Board
Quarterly Meeting
February 25, 2009**

The quarterly meeting of the ODJFS DUR Board was called to order at 12:01 PM in room 1960 of the Riffe Building, 77 S. High St. Columbus, Ohio. Thomas Gretter, MD, Chair, presided. The following Board members were present:

David Brookover, RPh
Michael Farrell, MD
Kevin Mitchell, RPh
Lenard Presutti, DO
Donald Sullivan, RPh, PhD

Also present were Margaret Scott, RPh, DUR Administrator, Jill Griffith, RPh, DUR Director, and Pam Heaton RPh, PhD and Bob Cluxton, RPh, PhD, of the University of Cincinnati College of Pharmacy. Robert Kubasak, RPh, and J. Layne Moore, MD, were absent. Approximately 7 observers were present, most representing pharmaceutical manufacturers.

Reading, Correction & Approval of Previous Minutes:

The November 19th, 2008, DUR Board minutes were approved with no corrections. (1st K. Mitchell 2nd D. Sullivan).

DUR Committee Report:

J. Griffith gave the DUR Committee report.

In May and June 2008, the DUR Committee reviewed 847 profiles of patients prescribed regular release tablet formulations of other medications in addition to orally disintegrating tablet (ODT) formulations of Fazaclo[®], Zyprexa Zydis[®], Risperdal M tab[®], Abilify Discmelt[®] and the Remeron[®] and mirtazapine Soltab. 146 letters were mailed in December 2008. 61% (n=89) of physicians responded and 21% (n=31) provided comment. Comments included “My patient ‘cheeks’ his tablets, this formulation is best for him”; “My patient is a high risk patient and this formulation improves his compliance”. Comments were mainly positive and appreciative.

The December 2008 DUR Committee reviewed liquid antidepressant formulations prescribed for patients (> 6 years of age) noted to also be on oral, regular release tablet formulations of other medications. Drugs under review include: citalopram, fluoxetine, Lexapro[®], paroxetine and sertraline. 345 patient profiles were reviewed by the DUR committee and 66 letters were mailed in January, 2009. 59% (n=39) of physicians responded and 36% (n=24) provided comment. Most comments were the same and

related to ease of liquid administration for caregivers of patients with gastrostomy tubes / percutaneous endoscopic gastrostomy tubes (G-tubes/PEG tubes).

The January 2009 DUR Committee reviewed the profiles of patients on either Advair[®] (fluticasone/salmeterol) or Symbicort[®] (budesonide/formoterol) in addition to any other inhaled long acting beta agonist or inhaled corticosteroid, indicating duplicate therapy. 603 patient profiles were reviewed by the DUR Committee. The DUR Board approved the letter and response form as provided.

The February DUR Committee reviewed profiles of patients with medical claims including diagnosis codes for congestive heart failure (ICD-9 codes 428.0 through 428.9) and claims for any of the six thiazolidinedione (TZD) products: Avandia[®], Actos[®], ActoPlus Met[®], Avandamet[®], Avandaryl[®] or Duetact[®]. 254 patient profiles were reviewed by the DUR Committee. The DUR Board provided edits to the draft letter, one of which requires the physician to return the response form in 14 days rather than 30 days to compare response rates to previous mailings. Reference inclusion and a minor formatting change were also suggested. The draft response form was approved.

Health Plan Policy:

M. Scott announced that the Governor's budget (House Bill 1) proposes to carve pharmacy out of the managed care capitation rate. This will enable one list of covered drugs and prior authorization policy for all Medicaid consumers, regardless of enrollment in a managed care plan. The carve-out will also allow Ohio Medicaid to collect rebates for all drugs dispensed to Medicaid consumers. This is projected to save \$235 million in state fiscal year 2011. M. Scott is not sure how this will affect the DUR program, but it is likely that the DUR Board will be responsible for the full 1.7 million consumers covered by Medicaid.

M. Scott also noted that the Pharmacy & Therapeutics Committee had recommended that an age limit of 8 years be applied to Pulmicort Respules, due to its high market share (38%) among inhaled corticosteroids. The age limit is expected to be effective in June.

Unfinished Business:

T. Gretter introduced new member David Brookover, RPh. Mr. Brookover is a pharmacist for Kroger in Pickerington.

The Conflict of Interest Statement was signed by all Board members not present at the November 2008 meeting. J. Moore was absent from both the November and current meetings, so has not yet signed. D. Brookover signed the statement.

New Business:

J. Griffith provided a proposed review schedule for 2009:

March: Re-review 2008 pediatric insomnia, low molecular weight heparin, and doctor shopping reviews

April: New doctor shopping review

May: Overuse of albuterol inhalers
September: Ophthalmic and otic quinolones
October: Proton pump inhibitor duration of therapy

A discussion of appropriate use of ophthalmic quinolones followed. The University of Cincinnati's contract for the DUR program includes clinical information provided by faculty. P. Heaton provided a clinical review of quinolones used for conjunctivitis prepared by Dan Healy, Pharm.D., FCCP, FIDSA, Associate Professor of Pharmacy. A copy of the review is attached to the minutes. M. Farrell said that the total cost of the illness should be considered, including time lost from work or school. D. Sullivan expressed concern that the study design may not support the conclusion presented in the review. M. Scott said that she agreed with M. Farrell that getting patients back to school or work is important. T. Gretter suggested that this topic be revisited at the May meeting. P. Heaton will send the source articles. D. Sullivan asked for additional information about otic quinolones, and P. Heaton agreed to provide this as well.

J. Griffith asked if there are additional suggestions for review topics. B. Cluxton mentioned that California Medicaid is looking at drugs that have been heavily advertised direct to consumer. M. Scott mentioned that J. Griffith will attend the American Drug Utilization Review Symposium (ADURS) this weekend and will learn what other states are doing.

Announcements:

D. Sullivan discussed the definition of a generic drug in Ohio, as it applies to pharmacist substitution. Based on a conversation with William Winsley, Executive Director of the Ohio Board of Pharmacy, in order for a drug to be generically substituted the drugs must have the same amount of the active ingredient and have no question about bioavailability. As an example, a pharmacist can substitute any formulation of albuterol inhaler regardless of how the prescriber wrote the prescription. A hydrofluoroalkane (HFA) inhaler can be substituted for a chlorofluorocarbon (CFC) inhaler without a new order from the prescriber. Similarly, the different HFA albuterol products can be substituted. The substitution also does not need to be the same dosage form if there is no question of bioequivalence (e.g., a tablet can be substituted for a capsule). D. Sullivan has a write-up on this topic that he will send to M. Scott to be included in a future mailing to pharmacists.

The next DUR Board meeting will be Wednesday, May 20 at noon. The room has not been scheduled.

Adjournment:

T. Gretter adjourned the meeting at 12:42 PM.

Respectfully submitted:

Jill R.K. Griffith B.S., Pharm.D., DUR Program Director

Review prepared 2/25/09 by:

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Conjunctivitis is the most common encountered ocular malady in children and adults presenting with a red eye. There are both noninfectious (e.g., mechanical, chemical, allergic) and infectious causes (e.g., bacterial, viral, fungal). It is often difficult to distinguish on clinical grounds alone between causes; however, many are treated assuming a bacterial etiology if one cannot completely rule it out. Even among documented cases of bacterial conjunctivitis, most spontaneously resolve without antimicrobial administration within 7 to 14 days. Numerous studies and meta-analyses have not demonstrated major differences in overall outcomes between various antimicrobials and placebo. However, it should be noted that most studies have found a more rapid improvement in clinical symptoms and return to school or work with antimicrobial administration. Along with the theoretical advantage of preventing disease transmission to others, as well as preventing more severe sight-threatening infectious complications in some patients (eg, keratitis, scleritis), the accepted practice, especially in the United States, is to administer a short course of a topically-applied antimicrobial.

While almost any organism can cause bacterial conjunctivitis, the most common pathogens include *Staphylococcus aureus*, *Streptococcus pneumoniae* and *Haemophilus influenzae*. To a large extent, the etiology is based on age of the patient. For example, while the three aforementioned organisms are most commonly seen in children with bacterial conjunctivitis, *Chlamydia trachomatis* and *Neisseria gonorrhoeae* are more commonly involved in neonates and sexually-active adolescent or young adults.

There are numerous antimicrobial agents available for the management of bacterial conjunctivitis including bacitracin, neomycin, chloramphenicol, aminoglycosides (e.g., gentamicin, tobramycin), sulfacetamide, polymyxinB/trimethoprim, and various fluoroquinolones (e.g., ciprofloxacin, levofloxacin, ofloxacin, gatifloxacin and moxifloxacin). In general, all have been shown to be effective and safe for treatment of bacterial conjunctivitis. In addition, when one examines the national longitudinal surveillance database of common ocular isolates associated with bacterial conjunctivitis (Ocular TRUST, 1999-2006) in vitro susceptibility profiles slightly favor the newer fluoroquinolones; however, increasing rates of resistance is common to all of the agents. Very importantly, there does not appear to be a strong correlation between in vitro susceptibility and clinical response, in part because breakpoints denoting susceptibility are based on systemic, not ocular infections. In other words, topical

administration may result in very high concentrations of antibiotic at the site of infection, enough necessary for microbial eradication, but the isolate would be deemed “resistant” from in vitro antimicrobial testing based on systemic levels of the same antibiotic given intravenously or orally for non-ocular, systemic infections. As a result, slight differences among agents with respect to the percentage of isolates “susceptible” to a given antibiotic likely have very little bearing on predicting clinical outcome.

In addition to a slight in vitro advantage of the newer fluoroquinolones with respect to in vitro susceptibility, this class of compounds is also felt to be superior with respect ocular penetration as compared to older compounds. In fact, the combination of excellent in vitro susceptibility along with extensive ocular penetration compared to older agents (e.g., aminoglycosides, polymyxin B, trimethoprim, etc.) explains in part, the high rate of clinical efficacy seen for ocular infections involving bacteria. These notable characteristics are arguably most important for the more serious sight-threatening types of infections. With respect to the management of the less serious ocular infections such as bacterial conjunctivitis in which antimicrobial treatment hastens resolution compared to placebo, it appears that these advantages do not influence overall clinical outcome (e.g., eventual resolution of infection) compared to older agents such as polymyxin B/trimethoprim. That being said, two comparative trials involving various antimicrobials found the killing kinetics of moxifloxacin to be significantly more rapid compared to tobramycin, gentamicin, polymyxin B/trimethoprim and azithromycin for the three most common ocular isolates (e.g., *S. aureus*, *S. pneumoniae*, *H. influenzae*). These results are not surprising and theoretically may be desirable with respect to minimization of disease transmission while shortening the duration of symptoms, allowing for a more rapid return to school or work. A recently conducted multicenter randomized controlled clinical trial comparing a 7-day course of polymyxin B/trimethoprim (1 drop QID) versus moxifloxacin (1 drop TID) ophthalmic solutions in 56 patients (84 eyes, age < 18 years) with bacterial conjunctivitis found complete resolution of ocular signs/symptoms in 81% of the moxifloxacin-treated patients versus 44% of those receiving polymyxin B/trimethoprim at 48 hours. The authors felt that a more rapid resolution of the infection and clinical symptoms would be more cost effective when one considers factors in addition to drug costs such as the impact on disease transmission and lost funding from school absenteeism, and lost productivity from work. A recent cost-effectiveness analysis in abstract form (Waycaster. *Value in Health* 2008;11:A289) suggests lower overall treatment costs for moxifloxacin versus polymyxin B/trimethoprim for the treatment of bacterial conjunctivitis. However, these data are not yet available in a full published manuscript for critique.

In conclusion, fluoroquinolone ophthalmic solutions appear to possess several advantages with respect to in vitro susceptibility and ocular penetration kinetics allowing for more rapid resolution of bacterial conjunctivitis relative to older, less expensive agents. Whether these advantages truly result in a decrease in disease transmission or in more cost-effective management of uncomplicated cases of bacterial conjunctivitis has still not been completely elucidated.

General:

1. Hovding G. Acute bacterial conjunctivitis. *Acta Ophthalmol* 2008;86:5-17.
2. Tarabishy AB, Jeng BH. Bacterial conjunctivitis: a review for internists. *Cleveland Clinic J Med* 2008;75:507-512.
3. Mueller JB, McStay CM. Ocular infection and inflammation. *Emerg Med Clin N Amer* 2008;26:57-72.

Susceptibility Studies:

1. Everett SL, Kowalski RP, Karenchak LM, Landsittel D, Day R, Gordon YJ. An in vitro comparison of susceptibilities of bacterial isolates from patients with conjunctivitis and blepharitis to newer and established topical antibiotics. *Cornea* 1995;14:382-387.
2. Asbell PA, Colby KA, Deng S, et al. Ocular TRUST: nationwide antimicrobial susceptibility patterns in ocular isolates. *Am J Ophthalmol* 2008;145:951-958.

Penetration & Speed of Bacterial Killing:

1. Price FW, Dobbins K, Zeh W. Penetration of topically administered ofloxacin and trimethoprim into aqueous humor. *J Ocular Pharmacol Therap* 2002;18:445-453.
2. Lichtenstein SJ, Dorfman M, Kennedy R, Stroman D. Controlling contagious bacterial conjunctivitis. *J Pediatr Ophthalmol Strabismus* 2006;43:19-26.
3. Lichtenstein SJ, Wagner RS, Jamison T, Bell B, Stroman DW. Speed of bacterial kill with a fluoroquinolone compared with nonfluoroquinolones: clinical implications and a review of kinetics of kill studies. *Advances in Therapy*. 2007;24(5):1098-1112.

Clinical Trials:

1. Granet DB, Dorfman M, Stroman D, Cockrum P. A multicenter comparison of polymyxin B sulfate/trimethoprim ophthalmic solution and moxifloxacin in the speed of clinical efficacy for the treatment of bacterial conjunctivitis. *J Pediatr Ophthalmol Strabismus* 2008;45:340-349.
2. Larcombe J. Review: antibiotic therapy leads to slightly earlier recovery in acute bacterial conjunctivitis. *Evid Based med* 2006;11:180 (abstract).

Cost-Effectiveness:

1. Waycaster C. A cost-effectiveness analysis of two topical ophthalmic solutions indicated for the treatment of bacterial conjunctivitis *Value in Health* 2008;11:A289 (abstract).