Drug Utilization Review Board

Oklahoma Health Care Authority
4545 North Lincoln Boulevard, Suite 124
Oklahoma City, Oklahoma 73105
OHCA Board Room

Wednesday
October 14, 2009
6:00 p.m.

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

MEMORANDUM

TO: Drug Utilization Review Board Members

FROM: Shellie Keast, Pharm.D., M.S.

SUBJECT: **Packet Contents for Board Meeting – October 14, 2009**

DATE: October 7, 2009

NOTE: THE DUR BOARD WILL MEET AT 6:00 P.M.

THE NOVEMBER MEETING WILL BE HELD ON THURSDAY, NOVEMBER 12TH.

Enclosed are the following items related to the October meeting. Material is arranged in order of the Agenda.

Call to Order

Public Comment Forum

Action Item – Approval of DUR Board Meeting Minutes – See Appendix A.

Update on DUR / MCAU Program – See Appendix B.

Action Item – Vote to Prior Authorize Fibromyalgia Medications – See Appendix C.

Action Item – Vote to Prior Authorize Otic Anti-Infectives – See Appendix D.

Action Item – Vote to Prior Authorize New Narcotic Analgesic Medications – See Appendix E.

Action Item – Annual Review of Plavix® and 30 Day Notice to Prior Authorize Effient™ – See Appendix F.

Action Item – Annual Review of Topical Antiparasitics and 30 Day Notice to Prior Authorize Ulesfia™ – See Appendix G.

Action Item – Annual Review of Hypnotic Medications and 30 Day Notice to Prior Authorize Edluar™ and Intermezzo® – See Appendix H.

FDA and DEA Updates – See Appendix I.

Future Business

Adjournment

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Drug Utilization Review Board

(DUR Board)

Meeting – October 14, 2009 @ 6:00 p.m.

Oklahoma Health Care Authority
4545 N. Lincoln Suite 124
Oklahoma City, Oklahoma 73105
Oklahoma Health Care Authority Board Room

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

1. Call To Order

A. Roll Call – Dr. Graham

Items to be presented by Dr. Muchmore, Chairman:

2. Public Comment Forum

A. Acknowledgment of Speakers and Agenda Items

Items to be presented by Dr. Muchmore, Chairman:

3. Action Item – Approval of DUR Board Meeting Minutes – See Appendix A.

A. September 9, 2009 DUR Minutes – Vote
B. September 10, 2009 DUR Recommendation Memorandum
C. Correspondence

Items to be presented by Dr. Keast, Dr. Muchmore, Chairman:

4. Update on DUR / Medication Coverage Authorization Unit – See Appendix B.

A. Retrospective Drug Utilization Review for June 2009
B. Retrospective Drug Utilization Review Response for May 2009
C. Medication Coverage Activity Audit for September 2009
D. Help Desk Activity Audit for September 2009

Items to be presented by Dr. Patel, Dr. Muchmore, Chairman

5. Action Item - Vote to Prior Authorize Fibromyalgia Medications – See Appendix C.

A. COP Recommendations

Items to be presented by Dr. Chonlahan, Dr. Muchmore, Chairman

6. Action Item – Vote to Prior Authorize Otic Anti-Infectives – See Appendix D.

A. COP Recommendations

Items to be presented by Dr. Keast, Dr. Muchmore, Chairman

7. Action Item – Vote to Prior Authorize New Narcotic Analgesic Medications – See Appendix E.

A. COP Recommendations

Items to be presented by Dr. Keast, Dr. Muchmore, Chairman

8. Action Item – Annual Review of Plavix® and 30 Day Notice to Prior Authorize Effient™ – See Appendix F.

A. Current PA Criteria
B. Utilization Review
C. COP Recommendations

Items to be presented by Dr. Patel, Dr. Muchmore, Chairman

9. Action Item – Annual Review of Topical Antiparasitics and 30 Day Notice to Prior Authorize Ulesfia™ – See Appendix G.

A. Current PA Criteria
B. Utilization Review
C. COP Recommendations

Items to be presented by Dr. Le, Dr. Muchmore, Chairman

10. Action Item – Annual Review of Hypnotic Medications and 30 Day Notice to Prior Authorize Edluar™ and Intermezzo® – See Appendix H.

A. Current PA Criteria
B. Utilization Review
C. COP Recommendations

Items to be presented by Dr. Graham, Dr. Muchmore, Chairman

11. FDA and DEA Updates – See Appendix I.

12. Future Business

A. Please note that the November meeting will be held on Thursday, Nov. 12th.
B. Anxiolytic Criteria Review
C. Antiemetic Utilization Review
D. New Product Reviews
E. Annual Reviews

13. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES of MEETING of SEPTEMBER 9, 2009

BOARD MEMBERS:	PRESENT	ABSENT
Brent Bell, D.O., D.Ph.: Vice-Chairman	X	
Mark Feightner, Pharm.D.	X	
Anetta Harrell, Pharm.D.	X	
Evelyn Knisely, Pharm.D.	X	
Thomas Kuhls, M.D.	X	
John Muchmore, M.D., Ph.D.: Chairman	X	
Paul Louis Preslar, D.O., MBA	X	
James Rhymer, D.Ph.	X	
Bruna Varalli-Claypool, MHS, PA-C	X	
Eric Winegardener, D.Ph.		X

COLLEGE of PHARMACY STAFF:	PRESENT	ABSENT
Metha Chonlahan, D.Ph.; Clinical Pharmacist	X	
Karen Egesdal, D.Ph.; SMAC-ProDUR Coordinator/OHCA Liaison	X	
Ronald Graham, D.Ph.; Pharmacy Director	X	
Shellie Keast, Pharm.D, M.S..; DUR Manager	X	
Chris Le, Pharm.D.; Clinical Pharmacist/Coordinator	X	
Carol Moore, Pharm.D.; Clinical Pharmacist	X	
Neeraj Patel, Pharm.D.; Clinical Pharmacist	X	
Lester A. Reinke, Ph.D.; Associate Dean for Graduate Studies & Research	X	
Leslie Robinson, D.Ph.; PA Coordinator	X	
Visiting Pharmacy Student(s): Brian Monson, Jacquelyn Travers, Tammy Lambert	X	

OKLAHOMA HEALTH CARE AUTHORITY STAFF:	PRESENT	ABSENT
Mike Fogarty, J.D., M.S.W.; Chief Executive Officer		X
Nico Gomez; Director of Gov't and Public Affairs		X
Lynn Mitchell, M.D., M.P.H,; Director of Medicaid/Medical Services		X
Nancy Nesser, Pharm.D., J.D.; Pharmacy Director	X	
Howard Pallotta, J.D.; Director of Legal Services		X
Sylvia Lopez, MD, OHCA Physician Medical Consultant	X	
Lynn Rambo-Jones, J.D.; Deputy General Counsel III	X	
Rodney Ramsey; Drug Reference Coordinator	X	
Jill Ratterman, D.Ph.; Pharmacy Specialist	X	
Kerri Wade, Senior Pharmacy Financial Analyst	X	

OTHERS PRESENT:

Jeff Himmelberg, GlaxoSmithKline	Sam Smothers, MedImmune	John Seidenberger, Boehringer-Ingelheim
Patty Harwood, MedImmune	John Harris, Abbott Labs	Richard Ponder, Johnson & Johnson
Jim Graham, Ortho-McNeil Janssen	Brian Macomson, OMJSA	Jim Dunlap, Lilly USA
Lon Lowrey, Novartis	Laura Mitchell, Purdue Pharma	Kathy Rivas, PFE
Susan Stone, Allergan	Mike Presley, Forest	Ron Schnare, Shire
Kelly Rogers, Taro	Brian Shank, Pfizer	Brian Maves, Pfizer
Ean Miller, SWOSU COP	Lance Burcham, MedImmune	Donna Erwin, BMS
David Williams, Forest	Sherman Collins, Forest	Bonnie Bellah, OK Infant Alliance
Justin Caudle, J&J	David Graham, MedImmune	Charlene Kaiser, Amgen
Deitra Macey, PharmaDerm	Vince Morrison, Forest	Bruce Christian, Lilly
Kirsten Hua, Lilly	Mark DeClerk, Lilly	Rob Baxter, MedImmune
Albert Appiah, Pfizer	Tracy Copeland, Daiichi Sankyo	Pat Trahan, Taro

PRESENT FOR PUBLIC COMMENT:

Agenda Item No. 5	Richard Brittingham, M.D.; Comanche County Memorial Hospital
Agenda Item No. 5	Siavash Nael, M.D.; private practice
Agenda Item No. 5	Dr. Daniel Ting, Pfizer Inc.
Agenda Item No. 8	Brian Macomson, Pharm.D.; Johnson & Johnson
Agenda Item No. 9	Jeremy Franklin, M.D.; MedImmune
Agenda Item No. 9	Ed Co, M.D.; Integris Baptist
Agenda Item No. 9	Raja Nandyal, M.D., Neonatologist

AGENDA ITEM NO. 1: **CALL TO ORDER**

1A: Roll Call

Dr. Muchmore called the meeting to order. Roll call by Dr. Graham established a quorum.

ACTION: NONE REQUIRED

AGENDA ITEM NO. 2: **PUBLIC COMMENT FORUM**

Dr. Muchmore recognized the speakers for public comment:

Agenda Item No. 5: Richard Brittingham, M.D.; Comanche County Memorial Hospital
Siavash Nael, M.D.; private practice
Dr. Daniel Ting, Pfizer Inc.

Agenda Item No. 8: Brian Macomson, Pharm.D.; Johnson & Johnson

Agenda Item No. 9: Jeremy Franklin, M.D.; MedImmune
Ed Co, M.D.; Integris Baptist
Raja Nandyal, M.D., Neonatologist

ACTION: NONE REQUIRED

AGENDA ITEM NO. 3: **APPROVAL OF DUR BOARD MINUTES**

3A: August 12, 2009 DUR Minutes

Dr. Harrell moved to approve as submitted; seconded by Dr. Feightner.

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: **UPDATE ON DUR/MCAU PROGRAM**

4A: Retrospective Drug Utilization Review: May 2009

4B: Retrospective Drug Utilization Review Response: April 2009

4C: Medication Coverage Activity Audit: August 2009

4D: Help Desk Activity Audit: August 2009

Reports included in agenda packet; presented by Dr. Keast.

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: **30-DAY NOTICE TO PRIOR AUTHORIZE FIBROMYALGIA MEDICATIONS**

For Public Comment; Richard Brittingham, M.D.: Thank you ladies and gentlemen. My name is Richard Brittingham. I'm an internal medicine specialist. I practice internal medicine out of Comanche County Memorial Hospital in Lawton, Oklahoma. As such, I treat a lot of fibromyalgia, a lot of patients with chronic pain. What I want to share with you and I hope what will be read into your minutes is this letter that I received a couple of years ago from a fibromyalgia patient, and I'm going to quote it, at least the beginning of it: *"I'm so sorry I don't know which end is up anymore. My mind started to play tricks on me because of all this pain and I love all of you. Please forgive me. Love, Inga. P.S., I just can't stand the pain anymore. It's been going on too long."* This letter received in my hand from the Lawton Police Department. Unfortunately, it was a suicide letter. I've had a lot of difficulty managing fibromyalgia in the past, so have all the other clinicians that I know. I've had very little success with a lot of the traditional medications that we have used in the management of fibromyalgia and chronic pain. More recently now, with second generation and newer generation medications, we're starting to experience some success. I understand that with the Oklahoma Health Care Authority, there is a multi-tiered system which basically will deny my patients, many of whom are Oklahoma Health Care Authority patients, the opportunity to get relief from their suffering with the newer medications that are now available. So I would beseech this Board that when you make your deliberations tonight that you'll remember this letter in your minds as you vote for what drugs should be multi-tier and what drugs should be available to the general population. Thank you.

Dr. Kuhls: I have a question.

Dr. Brittingham: Sir.

Dr. Kuhls: What makes you think that the State of Oklahoma or the Oklahoma Health Care Authority would ever say that a drug could never be used on patient? 'Cause that's basically what you just said.

Dr. Brittingham: No, not at all. My claim is that I don't want to have to get another letter like this while I'm going through a multi-tiered system, sir.

For Public Comment; Siavash Nael, M.D.: Thank you very much. I am a psychiatrist by training and I've practiced psychiatry and pain management for the past 25 years. And for many reasons, I have been involved in chronic pain since 1982. It is a kind of déjà vu again, because I remember when Prozac came to the market, we did the same thing with Prozac and tricyclic. And same argument and is a very complicated problems and I understand discussion about the price control and medication availability. But eventually Prozac became almost gold standard. And after that, there were a lot of comparative studies between Prozac

and tricyclic which show actually both, all of them are effective. So I feel that again, you know, I have seen a lot of changes during my practice in pain management. From reading the history, as you know, Charles Darwin, and Alfred Noble, probably suffered from fibromyalgia. If they were here today, that they called them by neurasthenia and Charcot called them, again neurasthenia and hypochondriasis. Then the field developed to the point that up to a few years ago, we were following the principle of "*you don't believe it*", Yogi Berra said, "*then you will see it*". So almost the fact that this is something you manufacture in your mind. And then term like 'yuppie flus' and just 'wastebasket diagnoses. And unfortunately that was with medical community for a long time. Eventually fibromyalgia kind of worked, upgraded itself from, you know, cargo to coach class. So at this time, there are a lot of studies that's being performed and done for fibromyalgia and treatment. I have been involved in two clinical trials with fluoxetine and fibromyalgia and diabetic neuropathy and just going to start another one. So I have been very, very interested in following the development of new pharmaceutical medication. Again, it is very, very difficult because these are medications that are new and expensive. Takes about ten years for a medication to be presentably marketed and approved by FDA and goes through a lot of utilization review. I just basically, I'm summarizing. My slides cannot be shown. Summarizing the fact that there are, you know, for pain management, either we have analgesial, anagesial which is in fact peripherally like NSAID and also to some extent, opioid, or centrally again, opioid and tricyclic and anticonvulsant and things like that. We understand the NSAID mechanism of action and also opioid. There is no problem. And we treat them, almost successfully. The problem is that pain of fibromyalgia is a different kind of pain. I think that you all know that there are peripheral pain and then central pain, and they are sometime mixed; peripheral versus central. And peripheral pain again, can be managed. Central pain is the one that there is a very complex mechanism. Two major mechanisms that I can tell you at this time. One is the central mechanism of ionic transfer. There are voltage sensitive sodium channel and calcium channel that they are really, get stimulated by action potential and consequently, sodium influx into the cell which produce neurotransmitter glutamate and substance P, nitric acid. And so many other neurotransmitter that they are responsible for the pain reception. And there is a descending fibers that come from periaqueductal gray. I wish I could show it. Come actually down to the spinal cord and these are mainly are norepinephrine serotonergic neuron with they have inhibitory function of the pain. In other words if you have pain and its normal and neural transmitters inhibit the intensity of the pain. So these are two major theories and is basis for studies that is being done. First one is ligands that is voltage sensitive mechanism, gabapentin anticonvulsant and recently pregablin. But they do, they have affinity for these ligand and presynaptic membrane that decrease the flow of calcium. Therefore, prevent production of the glutamate ……..

Dr. Muchmore: We've reached the end of your allotted five minutes.

Dr. Nael: Just two more ……

Dr. Muchmore: Briefly.

Dr. Nael: You have also, I noticed that you have been, you have had the speakers about neurotransmitter, norepinephrine and serotonergic medications that affect the descending fiber. There are a lot more. I will be happy to answer any questions that you may have.

Dr. Muchmore: Any questions of Dr. Nael? Okay, our next speaker is Dr. Daniel Ting, with Pfizer, Inc.

For Public Comment, Dr. Daniel Ting: I appreciate the opportunity to address the Board. I want to kind of take you through a few bullet points. First, tapping onto what Dr. Brittingham mentioned, the fibromyalgia patient. The patient journey for a patient with fibromyalgia can last, most of these patients wander in the health care system from anywhere from two to ten years looking for accurate diagnoses and treatment. They often get into a cycle where they physician hop, they prescription hop, they routinely have failing treatments, and they switch or add therapies or diagnosis in search of accurately finding the relief of their symptoms. Because of that cycling in the health care system, oftentimes documentation is hard to track down. There's no one source. So these patients may have been on the recommended Tier-1 products at one time or another, or multiple times in that course; but because they physician hop and pharmacy hop, there's no one way of validating for a physician whether they've been on those therapies for the two or three week trials that's mandated by the Board. Okay, these patients are also high utilizers of health care. Not just pharmacy spend, but overall health care costs. Delaying treatment with FDA approved and indicated medications does nothing but delay the proper care of these patients and potentially shift perceived drug cost savings to more increased physician visits, testing, laboratory tests, and so on and so forth. Not only that, it creates an extra barrier for health care providers. Fibromyalgia patients are labor intense for physicians and by adding these barriers, that adds more to the process. A comment on the APS guidelines that were presented in 2005. Keep in mind, these guidelines were presented before any of the current FDA approved drugs were in place. The recommended antidepressants, tricyclics, some of the newer selective serotonin reuptake inhibitors, but they also in their guidelines, they state that "effective symptom relief but not complete elimination of pain" from these agents. It's part of my responsibility with Pfizer. I establish relationships with pain management thought leaders throughout my assigned geography. And I've asked them oftentimes, a lot of them are members of APS or have been past presidents of their state pain society, so I've asked them, what's with APS? Why haven't they updated their guidelines? And they look at me and say, well, you know, the guidelines are basically useless, fibromyalgia affects 2% to 5% of the population, so it's not a top priority for the organization. In fact, one of my pain management physicians stated that, and to quote, "*The truth of the matter is, APS has become relatively ostracized organization in the real pain community on the battlefront of people actually treating patients.*" [end of quote]. I'd also like to kind of review from the recommended Tier-1 agents, just looking at the products and their mechanism of action. Amitriptyline, as we all know, is a tricyclic antidepressant. It modulates reuptake of serotonin and norepinephrine in the descending pathway. It is not FDA approved for fibromyalgia. Cyclobenzaprine, a muscle relaxant. It's structurally related as a tricyclic antidepressant. It modulates serotonin and norepinephrine in the descending pathway of the central nervous system, and it is not FDA approved. Fluoxetine – it's an antidepressant which modulates serotonin reuptake in the descending pathway and is not approved for fibromyalgia. Tramadol – it's a pain medication indicated for mild to moderately severe chronic pain; mechanism of action, it's a new opiate receptor agonist, a weak one, with underlying serotonin and norepinephrine reuptake modulation.

Specialists who treat fibromyalgia use multimodal approach. Pharmacotherapy is but one mode of treatment for these patients. Practitioners choose agents based on patient presentation, symptoms and the mechanism of action of agents to be used with these patients. Having an armamentarium with different mechanisms of action is critical in treating fibromyalgia patients. I'd also like to explore the evidence for the Tier-1 products; tricyclics and the treatment of fibromyalgia, inclusive of Amitriptyline and Cyclobenzaprine. There are sixteen studies of which nine were placebo controlled trials. Seven lacked placebos controlled, so I won't discuss them. These had small sample sizes between 9 and 98. It may not be powered enough for an effect size. The largest effect was sleep quality, potentially due to their sedative properties. Doses were below that, normally using antidepressants. Most were very short term, four to six weeks. The FDA requires studies to be twelve weeks in fibromyalgia, to be able to notice a meaningful effect beyond the initial response. The longest duration study by Carette, et.al. in 1994 was a 26-week trial looking at Amitriptyline and Cyclobenzaprine, neither of which were better than placebo. Amitriptyline had a sample size of 98, Cyclobenzaprine had a sample size of 86. Fluoxetine in the treatment of fibromyalgia, three placebo controlled trials. Sample sizes ranged from 31 to 60 patients. The three trials, one 6-week, one 4-week and one 12-week. The outcome, reduction of pain in two out of the three trials. Tramadol in the treatment of fibromyalgia, three controlled trials. One was IV Tramadol, 100 mg, and it had a significant reduction of pain compared to placebo. The second study had a hundred patients in a randomized withdrawal trial, open label, three weeks, and then randomized to Tramadol or placebo for six weeks. Primary efficacy was time to exit from the study, significantly fewer patients on Tramadol discontinued the double blind phase. In the third study were 315 fibro patients, randomized double blind, withdrawal design, combination of Tramadol and acetaminophen were in these patients, and the pain and physical function was significantly improved in the Tramadol-acetaminophen group, compared to placebo.

Dr. Muchmore: We've gone quite a bit beyond your allotted five minutes.

Dr. Ting: Alright, I just want to wrap it up in saying that, you know, Lyrica, Pregabalin, was, we had four randomized trials in over 3,000 patients and received FDA approval in 2007, and I just appreciate the Board's time and ask that you consider these facts in your decision. Any questions?

Materials included in agenda packet; presented by Dr. Patel.

ACTION: NONE REQUIRED

AGENDA ITEM NO. 6: **30-DAY NOTICE TO PRIOR AUTHORIZE OTIC ANTI-INFECTIVES**

Materials included in agenda packet; presented by Dr. Chonlahan.

ACTION: NONE REQUIRED

AGENDA ITEM NO. 7: **ANNUAL REVIEW OF ANTI-ULCER PRODUCT BASED PRIOR AUTHORIZATION CATEGORY**

Materials included in agenda packet; presented by Dr. Le.

Dr. Kuhls moved to have three tiers, Tier 1 be competitive price generics, Tier 2 be pricey generics or supplemental rebated Tier 3's, and Tier 3 should be Tier 3's; and change pediatric criteria #2 to (a) GI bleed, and (b) Zollinger-Ellison or similar conditions; seconded by Dr. Feightner.

ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: **ANNUAL REVIEW OF NARCOTIC ANALGESIC PRODUCT BASED PRIOR AUTHORIZATION CATEGORY AND 30-DAY NOTICE TO PRIOR AUTHORIZE ONSOLIS™, NUCYNTA™, ZAMICET™, AND EMBEDA™**

For Public Comment, Dr. Brian Macomson: I'm here just if there are questions on Nucynta, no formal presentation.

Dr. Muchmore: Okay, does anybody have any questions of …… Macomson? Okay, there may be questions after we get through this.

Materials included in agenda packet; presented by Dr. Keast.

ACTION: NONE REQUIRED

AGENDA ITEM NO. 9: **ANNUAL REVIEW OF SYNAGIS PRIOR AUTHORIZATION**

For Public Comment; Jeremy Franklin, M.D.: Good evening. Thank you for letting me speak here. As he mentioned, my name is Dr. Jeremy Franklin. I am a pediatric infectious disease physician by training, board certified in general pediatrics as well as pediatric infectious disease. As he mentioned, currently I work as a medical contractor for MedImmune which makes Synagis. In my prior life, I was chief of pediatric infectious disease at Texas Tech. I also served on infection control as medical director and ran a Synagis clinic as medical director. I'm also Fellow of the American Academy of Pediatrics. So RSV is by far the leading cause of infant hospitalization in the US every single year, and as he mentioned, there is no vaccine, there is no treatment, there is only prevention with Synagis, which is a monoclonal antibody. As you all are aware, the new Red Book came out recently as well as the corresponding AAP policy statement. These have created quite a stir in the world of pediatrics. What I'm going to address are the changes primarily seen in the late pre-term group, as defined by 32-35 weeks gestational age. The

reason these have created such controversy is that there are rather significant changes being made based on level 3 evidence which is defined as expert opinion without significant clinical trial data to support these changes. And actually some of these changes are in direct opposition to published data, including the only level 1 evidence that is cited in the policy statement which are the two studies that led to approval of Synagis by the FDA. The first thing I want to talk about is the removal of the 35-weekers from consideration for prophylaxis. This decision was made based on expert opinion, again, with no clinical data to support that. In fact, there are lots of studies in the literature that show these children are just as at risk for severe RSV disease as the more premature infants. In addition, when you look at the IMpact trial which was the trial that led to approval of this medication by the FDA, it did include through 35 weeks completed gestational age. The second thing I'd like to mention is the fact that the new guidelines have lowered the age at onset of season from six months to three months of age for this late pre-term group. Again, the guidelines themselves admit that this is based on expert opinion without any definitive clinical data to support these changes. Again, the IMpact trial as well as eleven years of clinical experience have shown that infants above three months' of age continue to be hospitalized with RSV disease, and there are several studies that have demonstrated if you target three months as the cutoff, you're only going to prevent about a third of your RSV hospitalizations; whereas, if you use six months as the cutoff, you're going to target about two-thirds of your RSV hospitalizations. The last thing that I want to mention is the most important thing that we've got to consider, and that is the recommendation that in this late pre-term group, 32 to less than 35 weeks, these infants should only receive three doses of, a maximum of three doses of Synagis. So they should be prophylactic up to 90 days of age and not thereafter, regardless of where the season is at that time. Again, there is absolutely no published literature that would support such a truncated dosing regimen. In fact there is no data to support any dosing regimen that doesn't include dosing throughout the entire RSV season. Also, you've got to consider the pharmacokinetics of Synagis. It has a half-life of approximately 20 days, so to maintain protective antibody levels throughout the season; you have to dose on a monthly basis. So I'll summarize by saying that in these three key areas for the late pre-term infants, these recommendations represent a very significant departure from the clinical evidence, from the FDA-approved dosing regimen, and from a decade of clinical experience. I would ask that the committee consider all of the relevant literature, including PK data and that you continue to support evidence based medicine, and what has actually been the standard of care for many years now. I would also as a pediatrician, ask you to continue to protect these very vulnerable infants that cannot protect themselves, cannot speak for themselves, by continuing to provide prophylaxis for infants 32 through 35 completed weeks of gestation, less than six months of age at the start of season, and to continue the dosing throughout the entire RSV season. That's all I have and I'll take questions if there are any.

Dr. Lopez: I have a question. Dr. Franklin, have you spoken to Dr. Meissner or anybody else on the committee that made these recommendations?

Dr. Franklin: I have not personally talked with Dr. Meissner. I have spoken with physicians that were involved in the discussions and again, a lot of these recommendations are based on expert opinion and it is not by any means a unanimous expert opinion. So there was division within the committee itself. I know there have been people in our company who have talked with Dr. Meissner.

Dr. Lopez: But the consensus of the committee was to make these new recommendations?

Dr. Franklin: That was the consensus of the committee, but again, definitely not a unanimous decision.

Dr. Lopez: Would you consider these infectious disease doctors expert in their field?

Dr. Franklin: It's very interesting because not everyone who's on the COID committee is an expert in RSV and there were numerous internationally known experts in RSV who were not consulted, and through personal conversations with them, they don't agree with all the recommendations that were made by the COID. So again, expert opinion, but not necessarily all the experts on the field were in agreement.

Dr. Lopez: But they're infectious disease doctors, are they not?

Dr. Franklin: They are ma'am, as am I.

For Public; Ed Co, M.D.: Good evening. Thank you for giving me the opportunity. Let me tell you my credentials. I'm a neonatologist at the Integris Baptist Medical Center. I'm also the chairman of their department of pediatrics at Integris Southwest Medical Center. And I'm also a member of the leadership team of the Oklahoma Infant Alliance which is working on trying to decrease the complications of late pre-term babies, and I'm also the founders of two non-profit network which is supporting families with special needs which is the Oklahoma Family Network and another education network which is the (unintelligible) network, which is working on trying to improve the care of our neonates in the NICU. In one of the programs that we have established in our quality initiatives is the Synagis program. We have a successful Synagis program that we have developed since three to four years ago, and this started because we have been part of having our babies come back, you know. We know how much those babies spend in the NICU, how much the cost, and for them to come back and get readmitted to the peds ICU or the pediatric floor, that's very costly. And we developed this program not only to give the Synagis program, but also prevention program where we teach the family education how to wash their hands and everything and provide them education materials. And this program, since we initiated it in 2006 and 2007, our readmission of babies that we discharged, we have 42 of them come back to the hospital, readmitted. In 2007, 2008 we have, because of the program, we have decreased that to 19 patients which is down to 10%. And then last year, our program was so successful we were able to cut down our readmission babies to 10 patients which is barely 4%. So we have been very successful with this program and we feel that, I'm here today, not as just a physician, but as a patient advocate. Somebody has to speak up for these babies. We spend a lot of time with these babies and we want them to have a healthy life and that the new recommendation by the AAP guidelines that has recently been issued, I think, doesn't have a lot of evidence based medicine in it. We don't know the reason why they decide to do that, but I'm sure that one of the main reasons could be cost containment and no, Synagis is not a cheap drug. But I think what we have shown is that the drug may be expensive at the initial phase, at the beginning stage, but in the long run we are able to save a lot of money if these babies don't come back and get readmitted to the peds ICU. And one of the, and also

one of the things that our new President has been talking is preventive medicine. And in the June issue of TIME magazine says it's all about prevention. And if we are going to prevent RSV, the first step toward containing healthcare costs is to avoid getting sick. And I think that Synagis has proven that it's a very powerful drug, it's very helpful, and we've been successful. But we could, if we implement what they recommended, we could be victims of our own success. Thank you.

Dr. Kuhls: Dr. Co and I have already talked about this subject a little bit. Dr. Co called me, but the basic bottom line question is, do you have faith in the American Academy of Pediatrics and the committee on infectious diseases and the Red Book committee?

Dr. Co: I think I have faith in the, you know, the committee that, there was recommendations in all the fields, but I think for this specific, I think I do not necessarily agree with this. I think, I don't see really any evidence that shows that whatever they have decided has evidence based, you know. If you look at, I think if you look at the recommendations, they don't show any references, so I don't know where they get this information, why they decided, you know. So that's a big question mark. So I don't know. And I, the only thing I can think of is really, it's probably the cost maybe, that may be the major issue. But I think if you ……..

Dr. Kuhls: Well I'm sure that it was one issue. Probably the second issue was somehow looking at data of when do babies get rehospitalized after an NICU stay in 32 to 35 weekers, and that's within the three months, and that's where they came up with those three doses, right?

Dr. Co: Yeah.

Dr. Kuhls: Which they have at least that data. But you're right. There's problems in looking at that data, looking at three versus six doses, right?

Dr. Co: Yes.

Dr. Kuhls: The problem I have with all this is that if we don't look at guidelines by expert committees, and we determine that we just don't like what national guidelines by experts looking at all the data are, we might as well not have any guidelines or data at all from the AAP. That's the fundamental problem I'm having with that. Did you understand?

Dr. Co: Yes I understand that totally, yeah. But I said the only, you know, reason, I can't find any real evidence there that suggests that why they came up with this recommendation and I think ……..

Dr. Kuhls: And I think your Synagis program at Baptist is working great, but maybe it's going to work just as well with the new guidelines because you're doing a good job and making sure that every baby gets the number of doses that they're supposed to have and it's a great program to do that, but that change in the recommendations may not change the efficacy or probably won't, based on national guidelines now that are going to change the effectiveness of your program.

Dr. Co: What I can tell you is when we did the Synagis program, we based guideline based on the IMpact trial and we followed that to the letter. And that's how we became so successful. And if, I'm afraid that if we follow these new guidelines, you have, first of all, you have the group, we would miss one gestational age group, which is the 35, 34 to 35, 35 to 36 weeks. That one week. That's about, I would say that's about over a hundred babies.

Dr. Kuhls: And how many of those babies got rehospitalized?

Dr. Co: I don't have this, you know, because I, we did ……

Dr. Kuhls: But that's the number that you really want to know, because if you drop 35 to 36 weeks, right, that's the one they're dropping, so you really want to know what that rehospitalization rate is in your program.

Dr. Co: Yeah, I will go back and look at that specifically for that rate, but you know, but I can't tell you right now. I need to go back to that data and I can provide you with that information. And then the other thing that the main problem is, instead of having the full dose, a baby that is discharged from NICU who is a late weeker could get one dose of the Synagis if he's born at our office, you know, and get one dose and that's it. And then the peak season for RSV is around January, February. They're going to miss that, they aren't going to catch it, you know. So that's the reason why I felt that ……..

Dr. Kuhls: That's because, that's because the committee determined that you get rehospitalized within three months of NICU stay in that age group, so that's why they picked the one dose. And I understand the problem. I have problems with going against national guidelines by an expert, the expert committee.

Dr. Co: Yeah, I am just like you. I would follow those guidelines but in this situation I feel that this went against what I felt was a successful, you know, drug ……

Dr. Kuhls: Program, and you were doing success, right?

Dr. Co: Yes, so that's why ……..

Dr. Muchmore: You know, I'm all in favor of interested organizations like my group of endocrinologists putting out guidelines, but they sure aren't infallible and sometimes they turn out to be ill advised and have to be retracted. And I agree with most of the guidelines of my organizations, but there are some that I think were poorly advised and will be retracted on further evidence. So we have to be aware of that possibility.

Dr. Kuhls: Oh, I agree.

Dr. Co: Thank you.

Dr. Muchmore: Thank you, Dr. Co. Dr. Raja Nandyal?

For Public Comment; Raja Nandyal, M.D.: Thanks for giving me this privilege. I'm Dr. Raja Nandyal. I'm one of the neonatologists at OU Children's Hospital. I'm speaking here as a patient advocate rather than a person who is running the follow-up clinic at OU Children's Hospital. I'm a neonatologist with about 23 years of experience which encompassed taking care of children during the pre-Synagis, pre-Respigam era, took care of the patients before the Synagis came and we used to see several of our NICU graduates die during winter from RSV infection and as Dr. Muchmore mentioned earlier, now it is we don't see a lot of these hospitalizations from RSV infections, and one thing I want to request to the Board is to consider leaving it to the physicians' discretion. I'll give an example to support my point. Last week, in fact before I came here, like under ten days back, I was somewhat ambiguous whether to come or not, you know. But when I saw this patient who came to a follow-up

clinic last Thursday. This was a 14-month old boy, born at 37 weeks, who had diaphragmatic hernia and hypoplastic left lung from the diaphragmatic hernia, had (unintelligible) and had you know, (unintelligible) and had pulmonary hypertension and was in the hospital for about 3 ½ months with repeated lung infections (unintelligible) problems, and I'm sure the cost exceeded, I don't know the exact amount. I did not ask them. I'm guessing close to $2 million or more, hospitalization. And after he went home, he received Synagis during the last season and was hospitalized again twice for pneumonia. One of them was from RSV, but fortunately it was a milder case. Now his weight is equal to an 8-month old kid and he is very bright, he is not delayed. His cognitive age is 16 months. His chronological age is about 14 ½ months. And has mild motor delay. He's not on oxygen, not on any diuretics. According to current AAP guidelines, he does not qualify for Synagis. And I did recommend to the pediatrician in my letter to use Synagis, but my concern is then what if the Synagis is given by the pediatrician, if it's not paid, what will happen. And there are, again quoting Dr. Muchmore, again earlier he mentioned, not all guidelines are 100% right. Guidelines that based on the committee's opinion. As a good physician, we have to use our discretion. We cannot follow everything that's written in a book 100%. If I do that, in other words, I can be 100% right if I follow the book, but I may lose a kid. And my concern is we spent, I mean, just imagine the parents' anguish, you know to see the kid dying from RSV when the kid spent so much time in the hospital. So many things were done, still made it. And I felt like, is it right to lose a kid who is almost like a, who has spent so much time in the hospital and if you look at the cost, it's like close to $2 million to save $10,000. Is it right to do that? They'd say no. I was looking at it and I went through the current criteria, then I realized I agree with Dr. Franklin the evidence which is there is only more like a 3B evidence. It's not a solid, it's an expert's opinion and obviously there is a need to save money. Probably that's why he came, but I felt like it's not right to lose this kid this season because of money. And I, my request is, please leave it to the physicians discretion. The physicians and the panel, I'm sure you agree sometimes, you know. There comes a situation where you don't follow the Academy of whatever specialty you have. As a neonatologist, sometimes I disagree with the Academy of Neonatal medicine and a sectional recommendation. In that area, I'm an expert. I know. But here I'm a neonatologist, not a pediatric infectious disease specialist, but I follow, I run the follow-up clinic. I'm looking at the total situation. My request is to please consider leaving it to the physicians' discretion.

Dr. Kuhls: Doctor, I want to let you know, like Dr. Franklin, I'm a board certified pediatrician. I'm a board certified pediatric infectious disease expert. I have taken part in trials for RSV therapy and what you're telling me now is that we should change our current criteria for Synagis, is that correct? That we should eradicate all the current criteria that we have now and basically just leave it up to a doctor's discretion, especially neonatologists who picks one dose and then sends the kid home from the hospital. Is that correct?

Dr. Nandyal: No, I'm not saying that we should forget the criteria. What I'm saying is ……

Dr. Kuhls: You just said that it should be the doctor's discretion that a 37 weeker …….

Dr. Nandyal: Based on the current criteria, it's not following the, you know, the kid does not quote/unquote meet the criteria to have severe lung problem in the past. Not oxygen dependent, not chronic lung disease. And so in a situation like that, that's not following the criteria but ……..

Dr. Kuhls: But your example of your patient doesn't fit the current guidelines. So what you're telling me is, we need to get rid of the current guidelines. Let's not even talk about the new guidelines, okay? That's something totally different. What you're saying in your argument is that the current criteria for PA's, not only here, but pretty much across the country, you should get rid of, because really a 37-weeker, that patient should get it and we should just look at doctor's discretion.

Dr. Nandyal: I'm not saying that. But we need to have some discretion for physicians' expertise and experience, based, individualized to the patient's care. We cannot apply a blanket of certain recommendations to all, to entire population. We have to use our discretion.

Dr. Kuhls: So you're not happy, you're not happy with even the, all the previous guidelines by the American Academy of Pediatrics in terms of Synagis.

Dr. Nandyal: The previous guidelines did say something like within the last 24, four months. If you look at it as a separate criteria which the current one does not mention that, there's a 24-month period is there.

Dr. Kuhls: No, I'm talking, well I'm talking about 37-weekers.

Dr. Nandyal: Not 37-weekers. This baby had BPD initially ……

Dr. Kuhls: No, I understand. Chronic lung disease, got Synagis. But then got past it, wasn't on any medication, so it doesn't fit the current guidelines, so you're really against the current guidelines, too, not just the new recommendation by the American Academy of Pediatrics.

Dr. Nandyal: No, I would not say that, no.

Dr. Preslar: I think he's just saying in this particular case, and I tend to agree that the doctor needs to have flexibility in a particular case to say that. And in the Academy of Family Physicians, we, one of the things we have and we're one of the top research, resource networks in the country through OKPRN and the major emphasis and the reason we've gotten grants from NIH and distributed data back to docs is because it's been evidence based research. And so I don't think we should look past that.

Dr. Kuhls: But the point is the evidence based research, and I will tell you that Dr. Franklin can talk if he wants to. Are you happy with the current criteria?

Dr. Franklin: I agree with Dr. Nandyal, that there should always be room for the physician to advocate for their patient and their individual situation. The benefit of the 2006 guidelines compared to the 2009 guidelines is that there is a lot more of 2006 that seems to be grounded in clinical data. You can go to the literature, you can pull it that this supports this, whereas with the 2009 guidelines, the major changes that I outlined in my presentation are based on level 3 evidence, which is expert opinions.

Dr. Kuhls: Oh I understand that. I understand your argument totally. But that's not what we're talking …… we're talking about the 2006 guidelines are based pretty heavily on evidence based medicine. What he's arguing for is even going against evidence based medicine in many ways.

Dr. Nandyal: No, I didn't say that. I think you are misinterpreting what I said.
Dr. Preslar: I don't think that's what he said.
Dr. Kuhls: Well if you take a 37-weeker who is not on diuretics, who's not getting steroids, who's done well, who's a 14-month child now, right? Even with the current recommendations ……
Dr. Nandyal: But was hospitalized twice during this last season with pneumonia – you know the lung segments ……
Dr. Kuhls: Even with the current recommendations, that's what I'm saying, will still have problems getting that accepted. But you're not arguing for the new recommendations, you're arguing even against the 2006 recommendations. That's my whole point.
Dr. Preslar: Well what if you make an error on the 37 and you give it to them? I mean, like you spent, like you said, $10,000, but you have a potential for saving about $2 million.
Dr. Kuhls: Well, we'll talk about that. We'll talk about that, 'cause that has to come into plan and to argument. But the point is, I think we need to point out that the 2006 recommendations, they're very little controversy about the 2006 recommendations. The real changes are the 2000, to the 2009 recommendations, three dose …… all the stuff Dr. Franklin said. I understand Dr. Franklin totally.
Dr. Muchmore: As far as physician discretion, the physician can always apply for a prior authorization, say "this is an unusual case".
Dr. Kuhls: Well, we need to talk about that when we get to the discussion and stuff, because I, I agree with you totally, with that. And we'll get there. But I think we have to be careful in are we arguing against the 2006 recommendations or are we arguing against the 2009 recommendations, because there's a total difference.
Dr. Nandyal: 2006 recommendations do have some quotient for including patients like this. I did review that and the current recommendations do not mention that. I did review that, you know, clear. I can show the evidence afterward.
Dr. Kuhls: Would you like to speak to that Dr. Franklin? What's, where is that, what is that?
Dr. Franklin: I don't know the patient, I mean ……
Dr. Kuhls: No, but I mean where did going from the 2006 to 2009 change that patient that he talked about? Ralph? Lance? Sam?
(responses – unable to hear)
Dr. Kuhls: Well, we'll talk about going from 2006 to 2009, but the patient that we discussed between 2006 and 2009 recommendations, it has been changed since. That's all I'm saying.
(unknown audience member): I think in the 2006 guidelines there were, a little more ambiguity or vagueness in that chronic lung disease category, so I would, a lot of physicians still put children with chronic lung disease in that (unintelligible). 2009 maybe just ……
Dr. Kuhls: I'm not, I'm not so sure about that. I'm not so sure about that.
Dr. Kuhls: Okay, but I think that's an important distinction when we start talking about this because we need to discuss if we're making changes from 2006 to 2009, or we're changing 2006 recommendations.
Dr. Muchmore: Okay. Thank you. Any other comments on these?
Dr. Nesser: Dr. Lopez, did you have any comments?
Dr. Lopez: No, not really. What, what did come up and is the exception. And we certainly don't want in any way want to forget about those medically fragile infants, I'm a neonatologist also. So I am very sensitive to the time and effort that's spent on these babies and you don't ever want to lose a single one to RSV or anything. So we will at the Health Care Authority take into consideration any infant that a primary care doctor feels is that exception to the rule. We will do it on an individual case.
Dr. Muchmore: And in this case, we should take it very, very seriously because the consequences are just plain awful.
Dr. Kuhls: Well, the problem is, is that when you look at the IMpact trial, hospitalization rate is reduced 55%, but you would think that mortality rate changes, but in reality, the mortality rate does not change. There's no evidence that Synagis lowers mortality rate, which is kind of amazing to me. But that's what the IMpact trial said.
Dr. Franklin: The Impact trial wasn't designed to measure mortality.
Dr. Kuhls: Right.
Dr. Franklin: Yeah, I think the important thing to remember is that to be able to do a clinical study that would actually demonstrate a decrease in mortality because of the small amount of mortality associated with RSV overall, you would have to do a clinical trial in a prospective manner with hundreds of thousands of patients, which will never be done.
Dr. Kuhls: That's right. Which means that we're talking about if there are differences, there's relatively small differences.
Dr. Muchmore: But just the difference of whether they end up on a vent or not is a big difference.
Dr. Kuhls: That's right. There's no doubt that Synagis is a great drug.
Dr. Muchmore: We used to have them hanging out the doors of the PICU before palivizumab.
Dr. Kuhls: Before the …… I agree totally. It's a very, very important drug.
Dr. Muchmore: The one comment I'd like to make about this is I think that you need to consider, one, the guidelines may not hold 'til the next year, but the one place where you're going to get the gotchas, where you're going to get the people in the public saying "what were those clowns thinking of?", is when you give a baby who's three months for the November injection, you let him have an injection in November and December and January, and then you cut it off right at the height of the RSV season. That sounds to me ill advised. And I, even if an expert panel recommended it, just sociologically, that's a bad time to be cutting off the injections.
Dr. Kuhls: It is …… are you going to present this first and then we'll talk about it?
Dr. Moore: I'm just waiting.
Dr. Kuhls: There is a reason why that committee came up with that,
(unknown): What is it?

Dr. Kuhls: It's based on looking at rehospitalization rates at when a baby leaves the NICU. Okay? And we're not talking about 28-weekers or less. We're not talking about 32-weekers and less. We're talking about 32 to 35 weekers. We're not talking about little babies. The babies that used to hang out in the ICU that Dr. Muchmore talks about are the 28-weekers, 26-weekers, 25-weekers. That's not what all this is about. They still get the full doses through the full season, well, let's say less than 28 weeks for sure. But we're talking in a group of babies that are 32 weeks to 35 weeks. Many of those babies never were on the ventilator, period. And when you look at that subgroup, when babies are rehospitalized, it's shortly after they left the NICU. They leave the NICU two weeks, four weeks, nine weeks, they get sick. Those are the babies that come in. In those older preemies, those are the babies that, once they get old enough, they do very well. And that's, and I think what Dr. Lopez tried to say is, yeah, there are chronic illness babies that have been on the ventilator and stop that will fall out and those babies may still need Synagis, but in that small subgroup of 32 to 35 weekers, three doses are when you have the greatest risk of being rehospitalized. That's where that data came from.
Dr. Muchmore: And that makes sense, because you're going to have a lot less risk in that group than say, the 28-weekers.
Dr. Kuhls: Exactly. And the 28-weekers, the recommendation from 2006 to 2009 did not change. Okay? That recommendation for 28-weekers, they all go through the whole season, get the whole dose, that didn't change. 32 weeks and less, there's a little few extra criteria, but the recommendations for 32 weeks and less didn't change. The whole change and what this is argued about is the 32 to 35 week group.
Dr. Muchmore: Right.
Dr. Kuhls: They're older, do better babies, okay?
Dr. Lopez: We don't have the degree of chronic lung disease nowadays. With changes in ventilation strategies and Survanta that we used to even ten, fifteen years ago. These infants for the most part are relatively healthy when they go home and many of them are medication free.
Dr. Muchmore: And that's cool.
Dr. Lopez: Yeah, it's great for the neonatalogists.
Dr. Muchmore: I just, what I have envisioned in my mind is Oklahoma Health Care Authority cut off my palivizumab injections as of February and my baby was hospitalized with RSV in February or March.
Dr. Kuhls: I have some concerns that you have a 32-week baby who was on the ventilator for a week, who's sick, who then goes home and gets two doses in October-November, November-December and then when peak season hits, January and February, I have concerns that they got their two doses or three doses and then they're left. I have the same concern ……..
Dr. Muchmore: Especially for the 32-weeker as opposed to the 34-week and six days.
Dr. Kuhls: Well, though there wasn't previous …… 32-weekers are the thing the recommendations haven't changed.
Dr. Muchmore: Yeah.
Dr. Kuhls: It's this older group that is sort of the gray group of some really healthy babies, some really sick babies, and people are trying to make thing. So I think we're talking, I think you need to present the data, but I think I understand MedImmune's arguments totally. I understand the, my group that I look to, the committee on infectious diseases and the Red Book committee and the AAP of their new recommendations, and I hope after the presentation, that I can kind of make everybody sort of happy but we need the presentation first.
Dr. Muchmore: Okay.
Dr. Kuhls: The arguments are very, the arguments here are very real, okay? But we're talking about a small group of babies that are really sick …… the babies that are born 32 to 35 weeks that are born in March or April, they're going to get one or two doses anyways and stop. The babies that are born earlier in the year, they're not going to get any based on the current recommendations. So we're really talking about babies born six months of the year, six months of the year that might be getting fewer doses. We're talking about relatively few numbers, even though this argument seems really, really big. The changes in recommendation are not for a huge number of babies.
Dr. Preslar: Well let's start the show.
Dr. Muchmore: Dr. Franklin's been wanting to make a comment for some time.
Dr. Franklin: I just wanted to discuss some data and remarks to these comments, if I may. The first thing is, really, Dr. Boyce from Tennessee in 2000 published data looking at RSV related hospitalization rates for premature infants. If you take out chronic lung disease and just look at prematurity, there is essentially no difference in hospitalization rates for a 36-weeker compared to a 28-weeker; so this whole notion of these are well babies is really not true. Also if you look at this from a, from a pathology standpoint, Dr. Langston's paper, again these babies, even up to 35 weeks, don't have normal lungs and their lungs don't recover within three months. Some of the data from Dr. Friedrich and Dr. Hoo shows that these, these decreases in lung function persist six, seven, ten years out. So they don't become magically well babies within three months. The other thing is, is there's been some study recently looking at age of hospitalization, first RSV hospitalization. One was Dr. McCormick from 2002 that showed that the mean, I'm sorry, median age of RSV hospitalization for first hospitalization, roughly five months of age. Dr. Resch, 2005, did a similar study that showed the mean age of hospitalization again roughly five months of age.
Dr. Kuhls: Those are all 32 to 35 weekers?
Dr. Franklin: Yeah, and it doesn't make a difference if you cut it at 32 weeks or you cut it at 35 weeks. The average age is still about five months. And then the last one I'll just mention is Dr. Rossi from 2007, looked at odds ratios for RSV related hospitalization and then three to five months, that odds ratio was still 4-point something or other, with statistical significance. So keep those facts in mind also, please.
Dr. Lopez: And Dr. Franklin, ventilation strategy in 2009 …….
Dr. Franklin: Sorry, I couldn't hear ……..
Dr. Lopez: Ventilation strategies in 2009 are very different from 2000.
Dr. Franklin: Not all these babies were ventilated, though, ma'am.

Dr. Lopez: But the ones that were.
Dr. Kuhls: Well, let's get this show on the road.
Dr. Muchmore: Okay.
Materials included in agenda packet; presented by Dr. Moore.
MOTION NO. 1: Dr. Feightner moved that infants 32 to 34 weeks are not limited to the three months' of the three doses, that they receive the full five or six doses if indicated. Second by Dr. Preslar.
ACTION: MOTION CARRIED
MOTION NO. 2: Dr. Bell moved to start dosing October 15th with a six dose injections. Second by Dr. Preslar.
ACTION: MOTION CARRIED
MOTION NO. 3: Dr. Feightner moved to accept the guidelines as modified. Second by Ms. Varalli-Claypool.
ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: **FDA & DEA UPDATES**
Materials included in agenda packet; presented by Dr. Graham.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 11: **FUTURE BUSINESS**
Materials included in agenda packet; submitted by Dr. Graham.
11A: Pediculicides Annual Review
11B: Anxiolytic Criteria Review
11C: New Product Reviews
11D: Annual Reviews
ACTION: NONE REQUIRED

AGENDA ITEM NO. 12: **ADJOURNMENT**
The meeting was adjourned at 10:18 p.m.

The University of Oklahoma
Health Sciences Center
COLLEGE OF PHARMACY
PHARMACY MANAGEMENT CONSULTANTS

Memorandum

Date: September 10, 2009

To: Nancy Nesser, Pharm.D., J.D.
Pharmacy Director
Oklahoma Health Care Authority

From: Shellie Keast, Pharm.D., M.S.
Drug Utilization Review Manager
Pharmacy Management Consultants

Subject: DUR Board Recommendations from Meeting of September 9, 2009

Recommendation 1: Annual Review of Anti-Ulcer Product Based Prior Authorization Category

MOTION CARRIED by unanimous approval.

The College recommends the following tier structure with placement of generic formulation products according to the SMAC applied.

Special Prior Authorizations of Miscellaneous Products
- ranitidine (Zantac® Effervescent Tabs) – must have reason why member cannot take other dosage forms.
- famotidine (Pepcid® Suspension) – reserved for members less than 1 month old.

Tier 1	Tier 2	Tier 3
omeprazole (Prilosec® 10mg & 20mg caps)	pantoprazole (Protonix® Tabs)	omeprazole (Prilosec ®40mg caps & Susp)*
	Supplemental Rebated Tier 3	omeprazole/antacid (Zegerid® Caps & Pkts)*†
		esomeprazole (Nexium® Caps and I.V.)*
		lansoprazole (Prevacid® Caps and ODT)*
		dexlansoprazole (Kapidex® caps)
		pantoprazole (Protonix® Susp & I.V.)*
		rabeprazole sodium (Aciphex® Tabs)

Mandatory Generic Plan Applies
*Special Formulations including ODTs, Granules, Suspension, and Solution for I.V. require special reason for use.
†Not Covered Effective 10/1/2009—No Federal Drug Rebate Agreement

Criteria for Approval of a Tier-2 medication:

1. A 14-day trial of omeprazole dosed up to 40mg per day (two 20mg caps) that has resulted in inadequate relief of symptoms or intolerable adverse effects.
2. Contraindication to all available Tier 1 medications.
3. An indication not covered by lower tiered medications.

Criteria for Approval of a Tier-3 medication:

1. A 14-day trial all available Tier 2 medications that has resulted in inadequate relief of symptoms or intolerable adverse effects.
2. Contraindication to all available Tier 2 medications.
3. An indication not covered by lower tiered medications.

Criteria for Approval of Age Appropriate PPIs for Pediatric Members under the age of 19:

1. A recent 14-day trial of an H_2 receptor antagonist that has resulted in inadequate relief of symptoms or intolerable adverse effects.
2. Recurrent or severe disease such as:
    a. GI bleed
    b. Zollinger-Ellison or similar disease

Recommendation 2: Annual Review of Narcotic Product Based Prior Authorization

No Action Required

The College of Pharmacy does not have any recommendations for this category.

The University of Oklahoma
Health Sciences Center
COLLEGE OF PHARMACY
PHARMACY MANAGEMENT CONSULTANTS

Recommendation 3: Annual Review of Synagis®

The College of Pharmacy recommended the following changes to the approval criteria for Synagis® based on the new AAP guidelines:

A. Member Selection. Members must be included in one of the following age groups at the beginning of the RSV season:*

1) Infants and children less than 24 months old with Chronic Lung Disease (CLD) (formerly bronchopulmonary dysplasia) who have required medical treatment (O2, bronchodilator, corticosteroid, or diuretic therapy) for CLD in the 6 months prior to RSV season.
2) Infants up to 24 months old with moderate to severe pulmonary hypertension, cyanotic heart disease, or those on medications to control congestive heart failure.
3) Infants less than 12 months of age, born at 28 weeks gestation or earlier
4) Infants less than 6 months of age, born at 29-31 weeks gestation.
5) Infants less than 12 months of age, born before 35 weeks gestation, with congenital abnormalities of the airway
6) Infants less than 12 months of age, born before 35 weeks gestation, with severe neuromuscular disease
7) Infants, up to 3 months old at the start of RSV season, born at 32-34 weeks gestation, who have one of the following risk factors: (up to three doses only)
    a. Child care attendance
    b. Siblings younger than 5 years of age

* Treatment should continue through the entire RSV season as indicated, except #7 (only up to 3 months of age).

B. Length of treatment. Synagis® is approved for use only during RSV season, which is generally November 15 through April 30, as determined by Oklahoma State Dept. of Health. Approval dates will be November 1 through March 31, 2009

C. Units authorized. The maximum duration of therapy is five (5) doses, with a dose to be administered no more often than every 30 days. Infants born at 32-34 weeks gestation will receive a maximum of three doses; prophylaxis to be administered only up to 3 months of age. Members given doses more frequently than every 30 days will not

be authorized for additional doses. Doses administered prior to the member's discharge from a hospital will be counted as one of the approved total.

D. Dose-pooling. To avoid unnecessary risk to the patient, multiple patients are not to be treated from a single vial. Failure to follow this recommendation will result in referral of the provider to the Quality Assurance Committee of the Oklahoma Health Care Authority.

The Drug Utilization Review Board made the following changes:

1. The Drug Utilization Review Board rejected item A7 and recommended not limiting the infants who are 3 months old at the start of the RSV season and meet the other requirements for receipt of Synagis® to 3 doses only.

MOTION CARRIED by majority approval.

2. The Drug Utilization Review Board recommends keeping the current definitions for the start of the Synagis® season. Petitions will be accepted October 1st and approval dates will be October 15th thru March 31st. The total number of doses for all approved members will be a total of 6 doses or until the end of the season (March 31st).

MOTION CARRIED by majority approval.

3. The Drug Utilization Review Board recommended approval of all other changes proposed by the College of Pharmacy.

MOTION CARRIED by unanimous approval.

The final approval criteria are outlined below:

A. Member Selection. Members must be included in one of the following age groups at the beginning of the RSV season:

1) Infants and children less than 24 months old with Chronic Lung Disease (CLD) (formerly bronchopulmonary dysplasia) who have required medical treatment (O2, bronchodilator, corticosteroid, or diuretic therapy) for CLD in the 6 months prior to RSV season.
2) Infants up to 24 months old with moderate to severe pulmonary hypertension, cyanotic heart disease, or those on medications to control congestive heart failure.

3) Infants less than 12 months of age, born at 28 weeks gestation or earlier
4) Infants less than 6 months of age, born at 29-31 weeks gestation.
5) Infants less than 12 months of age, born before 35 weeks gestation, with congenital abnormalities of the airway
6) Infants less than 12 months of age, born before 35 weeks gestation, with severe neuromuscular disease
7) Infants, up to 3 months old at the start of RSV season, born at 32-34 weeks gestation, who have one of the following risk factors:
    a. Child care attendance
    b. Siblings younger than 5 years of age

B. Length of treatment. Synagis® is approved for use only during RSV season, which is generally November 15 through April 30, as determined by Oklahoma State Dept. of Health. Approval dates will be October 15 through March 31.

C. Units authorized. The maximum duration of therapy is six (6) doses, with a dose to be administered no more often than every 30 days. Members given doses more frequently than every 30 days will not be authorized for additional doses. Doses administered prior to the member's discharge from a hospital will be counted as one of the approved total.

D. Dose-pooling. To avoid unnecessary risk to the patient, multiple patients are not to be treated from a single vial. Failure to follow this recommendation will result in referral of the provider to the Quality Assurance Committee of the Oklahoma Health Care Authority.

OFFICE OF ATTORNEY GENERAL
STATE OF OKLAHOMA

September 2, 2009

Drug Utilization Review Board
Oklahoma Health Care Authority
ATTN: Nancy Nesser, PharmD
4545 N. Lincoln Boulevard, Suite 124
Oklahoma City, Oklahoma 73105

Re: Comments Regarding Proposed Prior Authorization Requirements for Fibromyalgia Medication

Dear Dr. Nesser:

I write to urge caution regarding the Drug Utilization Review Board's proposed prior authorization policy that would require patients to try and fail with a number of off-label treatments before receiving medicines approved by the FDA for fibromyalgia.

Conditioning patients' coverage for FDA-approved treatments upon off-label treatments substitutes the judgment of third-parties for that of the FDA and doctors. Such a requirement also undermines the doctor-patient relationship by mandating broadly applicable medical decisions in cases best left to physicians considering the needs of specific patients.

Oklahoma has opposed efforts by drug makers and insurance companies to promote or require medicines for off-label use. Notably, the State negotiated a 2006 settlement with Schering-Plough over off-label marketing of the brain cancer drug Temodar and a 2004 settlement with Warner-Lambert based on its off-label marketing of Neurontin. Further, earlier this year Oklahoma recommended that the Centers for Medicare and Medicaid Services prohibit health insurers from requiring off-label treatments for patients covered under Medicare Part D as a prerequisite for receiving coverage for treatments approved by the FDA.

"Off-label" use is far different from requiring generics that are less expensive and equally efficacious. The same harms that have resulted from off-label marketing by pharmaceutical companies and off-label step therapy requirements by private insurers could apply here. For these reasons, the proposed prior authorization requirements should be approached with great caution.

313 N.E. 21ST STREET • OKLAHOMA CITY, OK 73105 • (405) 521-3921 • FAX: (405) 521-6246

Thank you.

Sincerely,

W.A. DREW EDMONDSON
ATTORNEY GENERAL

WAE:seh

cc: Mike Fogarty
CEO, Oklahoma Health Care Authority

Appendix B

Retrospective Drug Utilization Review Report

Claims Reviewed for July 2009

Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
Total # of messages returned by system when no limits were applied	43,857	56,177	1,020,515	28,815
Limits which were applied	Established, Major, Males and Females, Age 0-18	Males and Females, Narcotics, Age 26-27	Contraindicated, Epilepsy, Males and Females, Age 19-50	High dose and Duration , Tetracyclics, Age 0-150
Total # of messages after limits were applied	17	165	101	20
Total # of members reviewed after limits were applied	17	134	64	20

LETTERS			
Prescribers		**Pharmacies**	
Sent	**Responded**	**Sent**	**Responded**
121		0	

Retrospective Drug Utilization Review Report

Claims Reviewed for May 2009

Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
Limits which were applied	Established, Major, Males and Females, Age 66-150	Narcotics, Males and Females, Age 23-25	Contraindicated, Epilepsy, Males and Females, Age 0-18	High Dose and Duration, Fibric Acid Derivatives, Males and Females, Age 0-150

Response Summary (Prescriber)
Letters Sent: 67
Response Forms Returned: 32

The response forms returned yielded the following results:

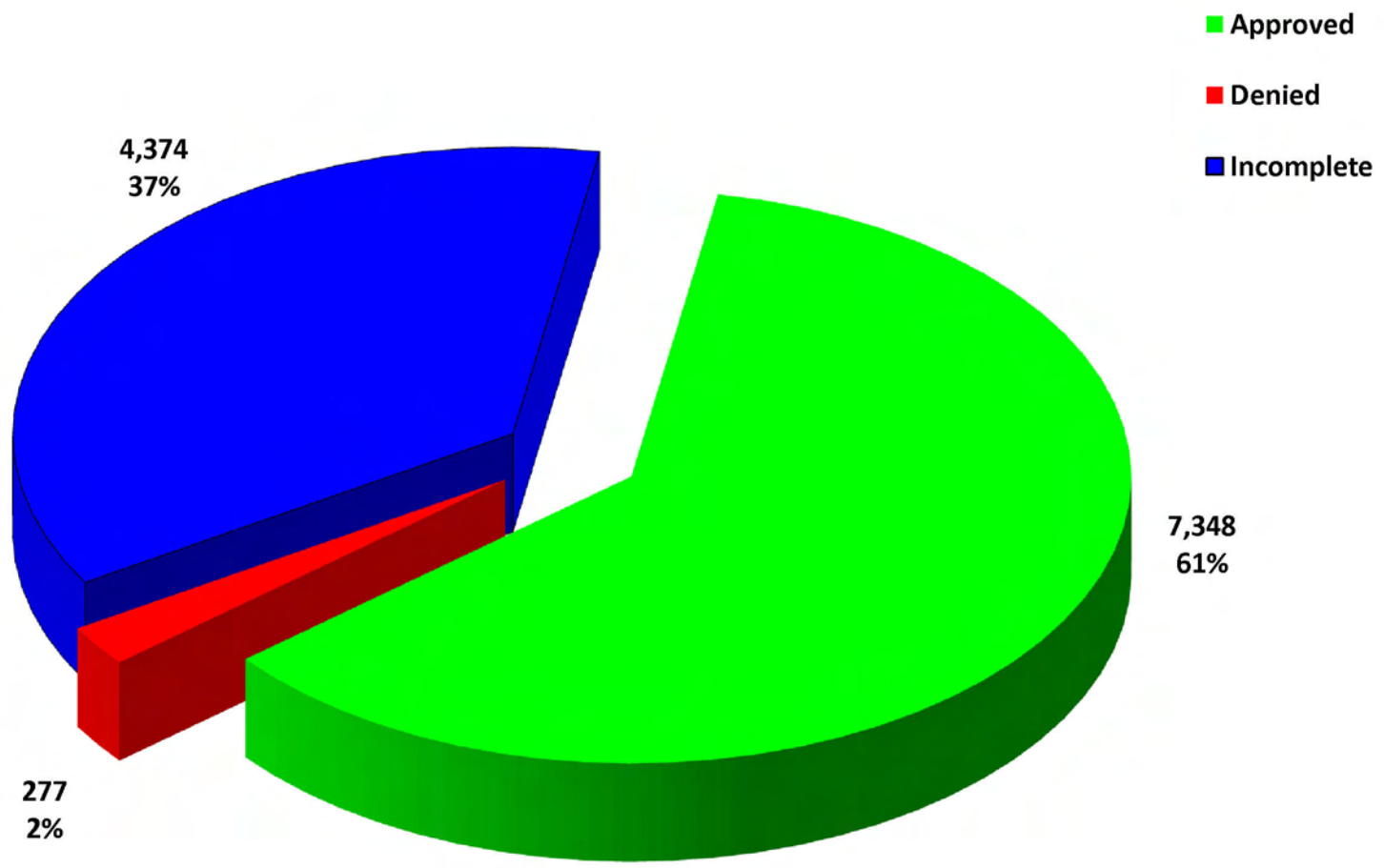
2 (6%)	*Record Error—Not my patient.*
1 (3%)	*No longer my patient.*
2 (6%)	*Medication has been changed prior to date of review letter.*
12 (38%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
8 (25%)	*I am aware of this situation and will plan to continue monitoring therapy.*
7 (22%)	*Other*

Response Summary (Pharmacy)
Letters Sent: 4
Response Forms Returned: 1

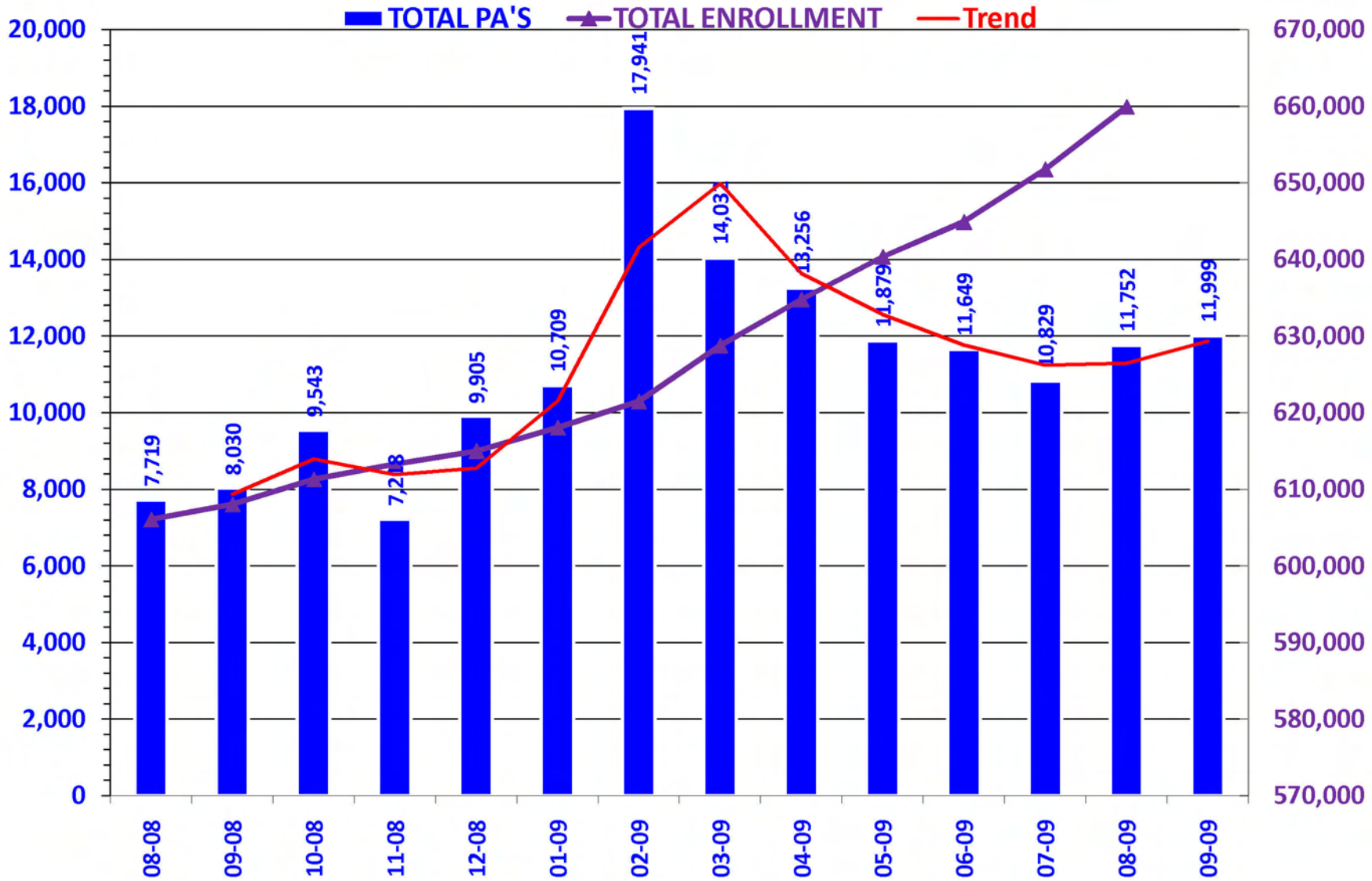
The response forms returned yielded the following results:

0 (0%)	*Record Error—Not my patient.*
0 (0%)	*No longer my patient.*
0 (0%)	*Medication has been changed prior to date of review letter.*
1 (100%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
0 (0%)	*I am aware of this situation and will plan to continue monitoring therapy.*
0 (0%)	*Other*

PRIOR AUTHORIZATION ACTIVITY REPORT: September 2009



PRIOR AUTHORIZATION REPORT:
September 2008 – September 2009



Prior Authorization Activity

9/1/2009 to 9/30/2009

	Average Length of	Approved	Denied	Incomplete	Total
Advair/Symbicort	352	142	0	98	240
Amitiza	164	4	0	10	14
Antidepressant	334	176	6	401	583
Antihistamine	300	181	0	242	423
Antihypertensives	348	53	1	93	147
Benzodiazepines	96	3,697	16	711	4,424
Bladder Control	280	3	1	12	16
Brovana (Arformoterol)	284	3	0	1	4
Byetta	356	4	0	1	5
Elidel/Protopic	81	17	0	25	42
ESA	66	178	0	32	210
Fibric Acid Derivatives	0	0	0	4	4
Fortamet/Glumetza	0	0	0	3	3
Forteo	0	0	0	2	2
Glaucoma	221	2	0	14	16
Growth Hormones	171	41	1	5	47
HFA Rescue Inhalers	180	86	1	71	158
Insomnia	142	35	4	113	152
Misc Analgesics	179	7	25	27	59
Muscle Relaxant	62	55	72	77	204
Nasal Allergy	212	4	46	120	170
NSAIDS	329	32	7	75	114
Nucynta	0	0	1	4	5
Ocular Allergy	228	4	1	14	19
Ocular Antibiotics	16	4	0	15	19
Opioid Analgesic	123	94	3	128	225
Other	140	163	30	296	489
Pediculicides	18	21	9	65	95
Plavix	356	114	0	63	177
Proton Pump Inhibitors	129	73	7	328	408
Singulair	258	434	2	531	967
Smoking Cessation	73	23	1	59	83
Statins	336	13	1	37	51
Stimulant	233	695	8	367	1,070
Symlin	359	1	0	3	4
Synagis	0	0	2	23	25
Topical Antibiotics	13	3	0	50	53
Topical Antifungals	106	4	0	17	21
Ultram ER and ODT	130	2	2	1	5
Xolair	359	2	0	1	3
Xopenex Nebs	197	19	0	28	47
Zetia (Ezetimibe)	361	7	0	8	15
Emergency PAs		3	0	0	3
Total		**6,399**	**247**	**4,175**	**10,821**

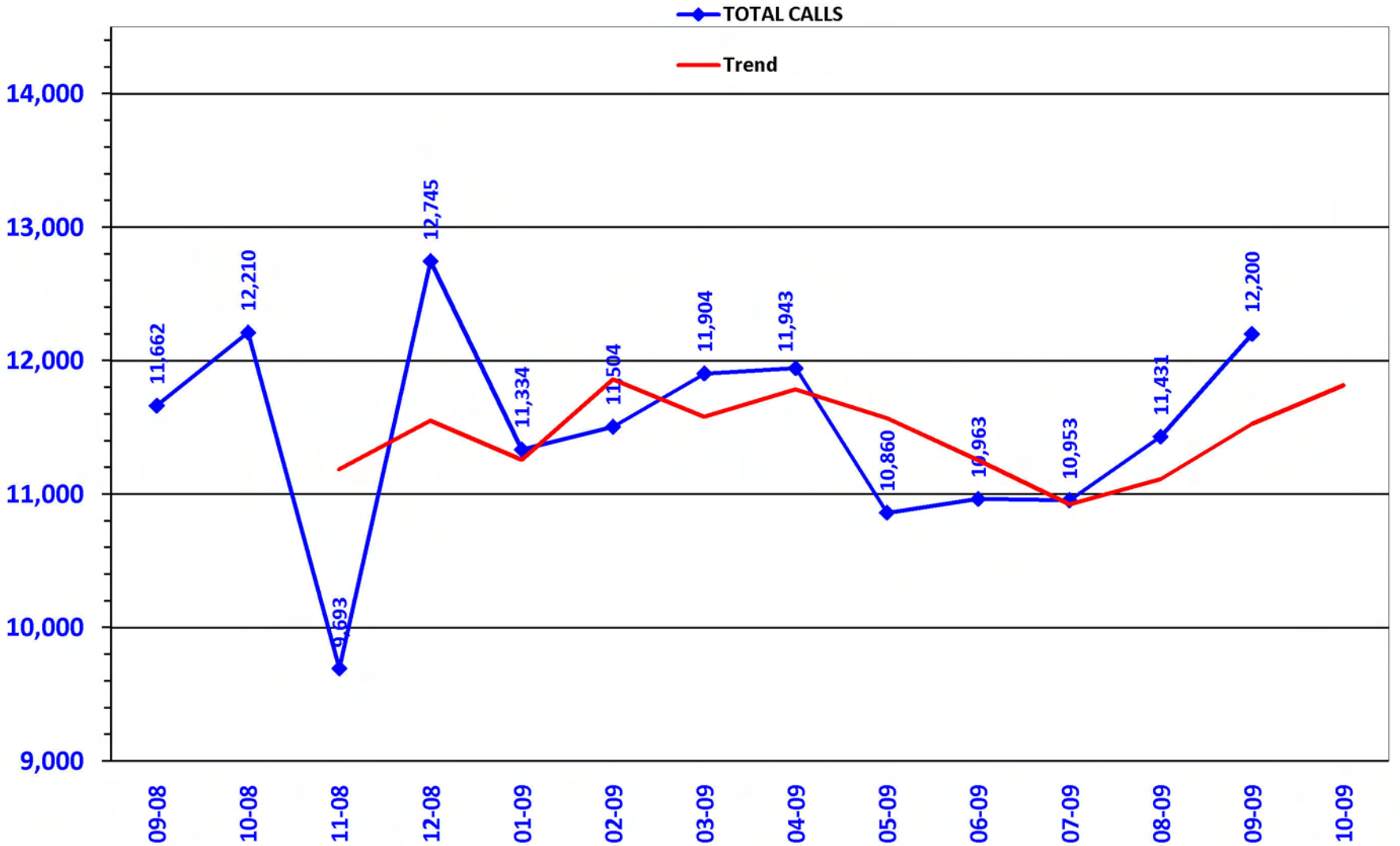
Overrides					
Brand	185	73	0	14	87
Dosage Change	14	378	12	22	412
High Dose	0	0	0	1	1
IHS - Brand	91	38	0	0	38
Ingredient Duplication	13	8	0	3	11
Lost/Broken Rx	13	78	4	5	87
Nursing Home Issue	13	74	0	6	80
Other	21	22	0	4	26
Quantity vs. Days Supply	202	268	13	138	419
Stolen	3	1	0	0	1
Overrides Total		**940**	**29**	**193**	**1,162**
Regular PAs + Overrides Total		**7,339**	**276**	**4,368**	**11,983**

Denial Reasons	
Lack required information to process request.	2,131
Unable to verify required trials.	1,832
Does not meet established criteria.	260
Not an FDA approved indication/diagnosis.	108
Requested dose exceeds maximum recommended FDA dose.	96
Member has active PA for requested medication.	82
Considered duplicate therapy. Member has a prior authorization for similar medication.	69
Medication not covered as pharmacy benefit.	26
Drug Not Deemed Medically Necessary	6

Duplicate Requests: 933

Changes to existing PAs: 891

CALL VOLUME MONTHLY REPORT:
September 2008 – September 2009



Appendix C

Vote to Prior Authorize Fibromyalgia Medications

Oklahoma Health Care Authority, October 2009

This category was introduced for possible inclusion in the Product Based Prior Authorization program in July 2009. See the July DUR, August DUR and September DUR packets for a more complete discussion of the category. This notice and statement is presented to meet the statutory requirements of 63 O.S. Sec. 5030.5.

Recommendations:

The College of Pharmacy recommends placing Fibromyalgia products into the Product Based Prior Authorization Program. The following Tier 1 drug list has been reviewed and determined to be acceptable for use as initial therapy for the majority of members. The College of Pharmacy recommends this list to the Drug Utilization Review Board based on cost and clinical effectiveness for approval before referral to the Oklahoma Health Care Authority.

Tier 1	Tier 2	Tier 3*
Amitriptyline Cyclobenzaprine Fluoxetine Tramadol	Supplemental Rebated Tier 3	Lyrica® (Pregabalin) Cymbalta® (Duloxetine HCl) Savella™ (Milnacipran)

*May be rebated to Tier 2 status only.

Approval Criteria:

1. Recent trials (within the last six months) of two Tier 1 medications and all available Tier 2 medications at least 3 weeks in duration that did not provide adequate response, or resulted in intolerable adverse effects, or
2. Contraindication(s) to all available lower tiered medications,
3. Current stabilization on a Tier 2 or 3 medications (samples will not be accepted if member has not had appropriate lower tiered trials).
4. Clinical Exceptions include:
    a. Diagnosis of seizures, diabetic neuropathy, or neuropathy for Lyrica®(Pregabalin)
    b. Diagnosis of diabetic neuropathy for Cymbalta® (Duloxetine HCl)

A Fibromyalgia information leaflet will be mailed to the members with a petition submitted for this category.

Appendix D

Vote to Prior Authorize
Otic Anti-Infective Medications

Oklahoma Health Care Authority, October 2009

This category was introduced for possible inclusion in the Product Based Prior Authorization program in July 2009. See the July DUR, August DUR and September DUR packets for a more complete discussion of the category. This notice and statement is presented to meet the statutory requirements of 63 O.S. Sec. 5030.5.

Recommendations:

The College of Pharmacy recommends establishing a PBPA category for otic antibiotics to ensure appropriate use in accordance with current treatment guidelines. The following Tier 1 drug list has been approved and determined to be acceptable for use as initial therapy for the majority of members. The College of Pharmacy recommends this list to the Drug Utilization Review Board based on cost and clinical effectiveness for approval before referral to the Oklahoma Health Care Authority. No supplemental rebate will be offered for this category.

Otic Antibiotics		
Tier 1	**Tier 2**	**Special PA***
Ofloxacin **(Floxin Otic)**	Ofloxacin **(Floxin Otic) Droperette**	Acetic Acid, Antipyrine, Benzocaine, Glycerin **(Auralgan)**
Acetic acid **(Vosol, Acetasol)**	Ciprofloxacin, Dex or HC **(Ciprodex, Cipro HC, Cetraxal Drop.)**	Acetic Acid, HC **(Acetasol HC, Vosol HC)**
Neomycin, Polymixin B, HC **(Cortisporin, Cortomycin, Pediotic)**	Neomycin,Polymixin B, HC, thonzonium **(Cortisporin TC)**	
Chloroxylenol/Pramoxine **(Pramotic)**	Neomycin,Colistin, HC **(Coly-Mycin, and Coly Mycin-ES)**	
	Chloroxylenol/Pramoxine/Zinc **(Zinotic, Zinotic ES, Chlorpram Z)**	
	Chloroxylenol, benzocaine, and HC **(Trioxin)**	

***Special Prior Authorization criteria previously approved by DUR Board.**

Prior Authorization Criteria

1. Member must have adequate 14-day trial of at least two Tier 1 medications, or
2. Approval may be granted if there is a unique FDA approved indication not covered by Tier 1 products or infection by organism not known to be covered by all Tier 1 agents.
3. A ciprofloxacin combination product may be approved when a steroid containing product is required for severe otitis externa and the tympanic membrance is not intact.

A specialized form will be included with the faxed back response for petitions submitted for this category.

Appendix E

Vote to Prior Authorize
Onsolis™, Nucynta™, Zamicet™, and Embeda™

OKLAHOMA HEALTH CARE AUTHORITY

OCTOBER 2009

RECOMENDATIONS

The College of Pharmacy recommends placement of the following products in the current Tier structure:

- **Onsolis™-** to be placed in the Oncology Only section with a quantity limit of 4 units per day.
- **Nucynta™-**to be placed in Tier 2 of the short-acting products Tier structure, with a quantity limit of 6 tablets per day. One Tier 1 trial must be tramadol.
- **Embeda™-**to be placed in Tier 3 of the long-acting products Tier structure, with a quantity limit of 2 capsules per day.
- **Zamicet™-**to be placed in Tier 2 of the short-acting products with a quantity limit based on a maximum of 3,250 mg of APAP per day.

Narcotic Analgesics

Tier-1 products are covered with no prior authorization necessary.

Tier-2 authorization requires:
- documented 30 day trial/titration period with at least two Tier-1 medications within the last 90 days, or
- clinically appropriate pain therapy requiring time-released medication for long-acting products

Tier-3 authorization requires:
- documented 30 day trial with at least two Tier-2 medications within the last 90 days, or
- documented allergy or contraindication to all Tier-2 medications

- Members with an oncology-related diagnosis are exempt from the prior authorization process, although quantity and dosage limits still apply. Actiq®, Fentora®, and Onsolis® are approved only for oncology-related diagnoses.
- Only one long-acting and one short-acting agent can be used concurrently

Tier-1	Tier-2	Tier-3	Oncology Only
All immediate release narcotics not listed in a higher tier	**Long Acting**		
	fentanyl patch (Duragesic®)	morphine sulfate (Avinza®)	
	morphine ER	morphine sulfate (Kadian®)	
	oxymorphone (Opana® ER)	oxycodone (OxyContin®)	
		tramadol ER (Ultram ER®, Ryzolt®)	
		morphine and naltrexone (Embeda™)	
	Short Acting		
	hydrocodone (Xodol®)		fentanyl (Actiq®)
	hydrocodone (Zamicet™)		fentanyl (Fentora®)
	Tapentadol (Nucynta™)		Fentanyl (Onsolis™)

Blue Color indicates supplemental rebate participation

Appendix F

ANNUAL REVIEW OF PLAVIX® AND 30 DAY NOTICE TO PA EFFIENT™

OKLAHOMA HEALTH CARE AUTHORITY
OCTOBER 2009

CURRENT PRIOR AUTHORIZATION CRITERIA

PLAVIX® 75 MG

1. Plavix® therapy will be approved for members who:
    a. meet approved diagnostic criteria, and
    b. have failed aspirin therapy (due to either side effects or event recurrence), or have a documented aspirin allergy, or use Plavix® concomitantly with aspirin.
2. The approved diagnoses are as follows:
    a. Recent stroke
    b. Recent myocardial infarction
    c. Established peripheral artery disease
    d. Acute coronary syndrome (unstable angina/non-Q-wave MI)
    e. Percutaneous coronary intervention with stent placement (aspirin trial not required)
    f. Transient ischemic attacks
3. Length of approval: 1 year.

PLAVIX® 300 MG

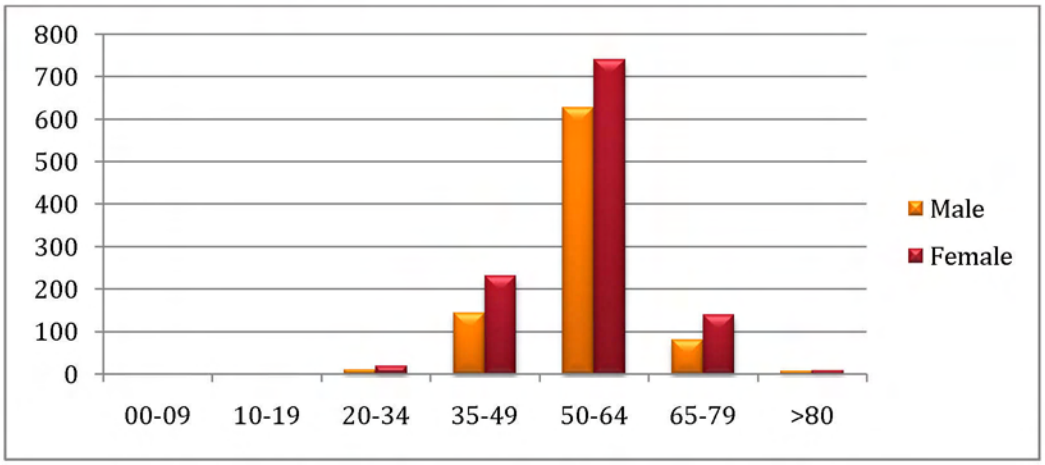
1. FDA approved diagnosis of non-ST-segment elevated acute coronary syndrome or ST segment elevated acute myocardial infarction.
2. Approval will be for only one dose of 300mg.

TRENDS IN UTILIZATION

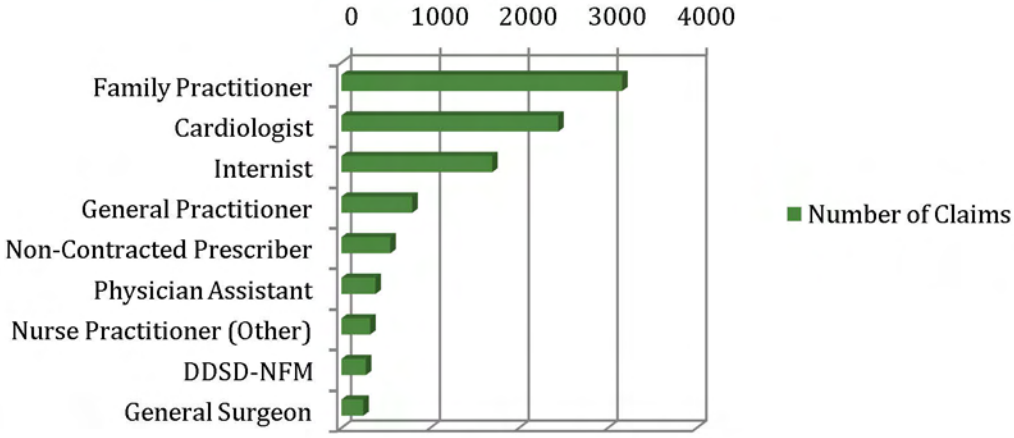
FISCAL YEAR UTILIZATION COMPARISON

Fiscal Year	Total Members	Total Claims	Paid Amount	Paid per Claim	Per-Diem Cost	Total Units	Total Days
2008	1,875	9,717	$1,702,047.42	$175.16	$4.46	381,479	381,808
2009	2,026	10,578	$2,029,367.63	$191.85	$4.87	416,373	416,657
% Change	**8.1%**	**8.9%**	**19.2%**	**9.5%**	**9.2%**	**9.1%**	**9.1%**
Change	**151**	**861**	**$327,320.21**	**$16.69**	**$0.41**	**34,894**	**34,849**

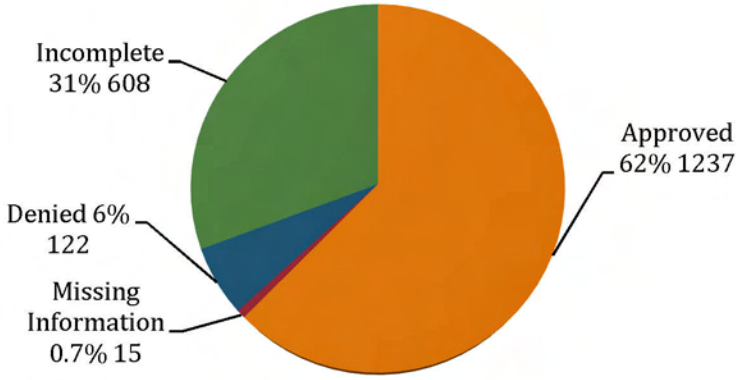
MEMBER DEMOGRAPHICS FOR FISCAL YEAR 2009



PRESCRIBERS OF PLAVIX®



PRIOR AUTHORIZATION OF PLAVIX®



MARKET CHANGES

Prasugrel (Effient™) was approved by the FDA on July 10, 2009. It is indicated for UA/NSTEMI and STEMI patients who are to be managed with percutaneous coronary intervention (PCI), primary or delayed. However, in patients who required emergency CABG surgery after treatment with prasugrel, the bleeding risk was increased.[1] Prasugrel is contraindicated in patients with a history of TIA or stroke.[1] Prasugrel does not require renal or hepatic dosing adjustments, but use in populations with severe impairment has not been studied. It is metabolized by CYP 3A4, 2B6, 2C9 and 2C19, but drug interactions are not expected to be significant.[1]

Patients weighing less than 60kg had 30-40% higher AUC of the active metabolite of prasugrel, so a dose of 5mg daily is recommended in these patients. Safety and efficacy of this dose have not been established.[1] Prasugrel is pregnancy category B.[1]

In the Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition (TRITON-TIMI 38), patients with ACS (UA, NSTEMI, or STEMI) who were to receive a PCI were randomized to 60 mg of prasugrel followed by 10 mg daily or 300 mg loading dose of clopidogrel followed by 75 mg daily. Prasugrel significantly reduced death from the combined endpoint of CV death, nonfatal MI, or nonfatal stroke compared to clopidogrel.[1] For UA/NSTEMI patients, the relative risk reduction (RRR) was 18.0%, with a 95% confidence interval of 7.3% to 27.4%. In STEMI patients, the RRR was 20.7%, 95% CI of 3.2% to 35.1%.[1] Most of the risk reduction came from a decrease in nonfatal myocardial infarctions (RRRs of 23.9 (12.7, 33.7) and 25.4 (5.2, 41.2) for UA/NSTEMI and STEMI patients respectively).[1] Differences in CV death and non-fatal stroke were not significant.[1]

PATIENTS WITH OUTCOME EVENTS IN TRITON-TIMI 38*

	Prasugrel (%)	Clopidogrel (%)	Relative Risk Reduction % (95% CI)	p-value
UA/NSTEMI	**N=5,044**	**N=5,030**		
Composite Endpoint	9.3	11.2	18.0 (7.3, 27.4)	0.002
CV Death	1.8	1.8	2.1 (-30.9, 26.8)	0.885
Nonfatal MI	7.1	9.2	23.9 (12.7, 33.7)	<0.001
Nonfatal Stroke	0.8	0.8	2.1 (-51.3, 36.7)	0.922
STEMI	**N=1,769**	**N=1,765**		
Composite Endpoint	9.8	12.2	20.7 (3.2, 35.1)	0.019
CV Death	2.4	3.3	26.2 (-9.4, 50.3)	0.129
Nonfatal MI	6.7	8.8	25.4 (5.2, 41.2)	0.016
Nonfatal Stroke	1.2	1.1	-9.7 (-104.0, 41.0)	0.77

*Adapted from Prasugrel (Effient™) product labeling. Eli Lilly and company. Approved 7/10/2009. Available from: http://www.accessdata.fda.gov/drugsatfda_docs/label/2009/022307s000lbl.pdf

Patients receiving prasugrel had a significantly higher rate of life-threatening bleeding than patients receiving clopidogrel in the TIMI study. The hazard ratio for fatal bleeds with prasugrel was 4.19 (CI 1.58-11.11).[2]

BLEEDING EVENTS IN TRITON-TIMI 38*

	Prasugrel (%)	Clopidogrel (%)	p-value
Non-CABG-Related	**(N=6,741)**	**(N=6,716)**	
Major or Minor Bleeding	4.5	3.4	0.002
Major Bleeding	2.2	1.7	0.029
Life-Threatening	1.3	0.8	0.015
Minor Bleeding	2.4	1.9	0.022
CABG-Related	**(N=213)**	**(N=224)**	
Major or Minor Bleeding	14.1	4.5	0.005
Major Bleeding	11.3	3.6	0.002
Life-Threatening	0.9	0	0.146
Minor Bleeding	2.8	0.9	0.134

*Adapted from Prasugrel (Effient™) product labeling. Eli Lilly and company. Approved 7/10/2009. Available from: http://www.accessdata.fda.gov/drugsatfda_docs/label/2009/022307s000lbl.pdf

13 patients in the prasugrel group discontinued the study due to colonic neoplasms, compared to 4 patients in the clopidogrel group (P=0.03).[2] While this difference is statistically significant, it remains to be seen whether this relationship will be confirmed in postmarketing surveillance.[1]

The FDA summarized the overall risk-benefit profile of prasugrel:

"For each 1,000 patients treated with prasugrel instead of clopidogrel, there were the following:

24 cardiovascular end points prevented:

- 21 nonfatal myocardial infarctions
- 3 cardiovascular deaths
- 0 strokes

10 excess TIMI major or minor bleeding events would occur, comprising the following:

- 2 fatal bleeding events
- 3 nonfatal TIMI major bleeding events (intracranial hemorrhage or a hemoglobin (Hb) decrease greater than 5 gm per dL)
- 5 TIMI minor bleeds (Hb decrease between 3 gm and 5 gm per dL)"[3]

RECOMMENDATIONS

The College of Pharmacy recommends placing a prior authorization on both Plavix® and Effient™ after 90 days of therapy. The following change is recommended to the current approval criteria for Plavix® and would apply after the first 90 days of therapy:

1. Plavix® therapy will be approved for members who:
    a. meet approved diagnostic criteria, and
    b. ~~have failed aspirin therapy (due to either side effects or event recurrence), or have a documented aspirin allergy, or use Plavix® concomitantly with aspirin.~~
2. The approved diagnoses are as follows:
    a. Recent stroke
    b. Recent myocardial infarction
    c. Established peripheral artery disease
    d. Acute coronary syndrome (unstable angina/non-Q-wave MI)
    e. Percutaneous coronary intervention with stent placement ~~(aspirin trial not required)~~
    f. Transient ischemic attacks
3. Length of approval: 1 year.

The approval criteria for Effient™ would be as follows:

1. Effient™ therapy will be approved for members who meet approved diagnostic criteria,
2. The approved diagnoses are UA/NSTEMI and STEMI patients who are to be managed with percutaneous coronary intervention (PCI), primary or delayed.
3. Length of approval: 1 year.
4. Effient™ will not be approved for members with the following situations:
    a. CABG surgery
    b. Members with a history of TIA or stroke
    c. Members greater than 75 years of age

After the end of 15 months, prescribers should provide supporting information for the continuation of these products.

REFERENCES:

1. Prasugrel (Effient™) product labeling. Eli Lilly and company. Approved 7/10/2009. Available from: http://www.accessdata.fda.gov/drugsatfda_docs/label/2009/022307s000lbl.pdf
2. Wiviott SD, Braunwald E, McCabe CH, Montalescot G, Ruzyllo W, Gottlieb S, et al. Prasugrel versus clopidogrel in patients with acute coronary syndromes. N Engl J Med. 2007;357:2001-15. Available from: http://nejm.highwire.org/cgi/content/full/357/20/2001#T3
3. Schafer JA, Kjesbo NK, Gleason P. Critical review of prasugrel for formulary decision makers. *JMCP.* 2009; 15(4):335-343.

Appendix G

Annual Review of Topical Anti-Parasitics - Fiscal Year 2009
30 Day Notice to Prior Authorize Ulesfia™

Oklahoma Health Care Authority
October 2009

Current Prior Authorization Criteria

Currently, the following OTC products are covered:

NDC Code	NDC Desc	Package Size	Drug Form	Description
00472-5242-67	PERMETHRIN	59	ML	PERMETHRIN TOPICAL 1% LIQUID
00472-5242-69	PERMETHRIN	118	ML	PERMETHRIN TOPICAL 1% LIQUID
15127-0243-31	LICE TREATMENT	120	ML	PERMETHRIN TOPICAL 1% LIQUID
49348-0143-30	LICE CREAM RINSE	120	ML	PERMETHRIN TOPICAL 1% LIQUID
49348-0434-37	LICE KILLING	240	ML	PERMETHRIN TOPICAL 1% LIQUID
49348-0460-30	LICE TREATMENT	60	ML	PERMETHRIN TOPICAL 1% LIQUID
49348-0460-34	LICE TREATMENT	60	ML	PERMETHRIN TOPICAL 1% LIQUID

Prescription-Only Topical Anti-Parasitics Will Require Prior Authorization

Malathion lotion (Ovide®)
- Available only after first-line treatment with an OTC product has failed (PA removed 1/1/2009 due to Supplemental Rebate)
- Member must be at least 6 years old
- Quantity limit of 60ml for 7 day supply; may be repeated once if needed for current infestation after 7 days from original fill date

Crotamiton lotion (Eurax®) (not FDA approved in pediatric patients)
- Available only after treatment with OTC product has failed
- Quantity limit of 60 grams or milliliters for 30 day supply

Lindane lotion & shampoo
- Available only after first-line treatment with an OTC product has failed
- Member must be at least 13 years old or weigh at least 110 pounds
- Quantity limit of 60ml for 7 day supply
- One 7 day supply per 30 days maximum

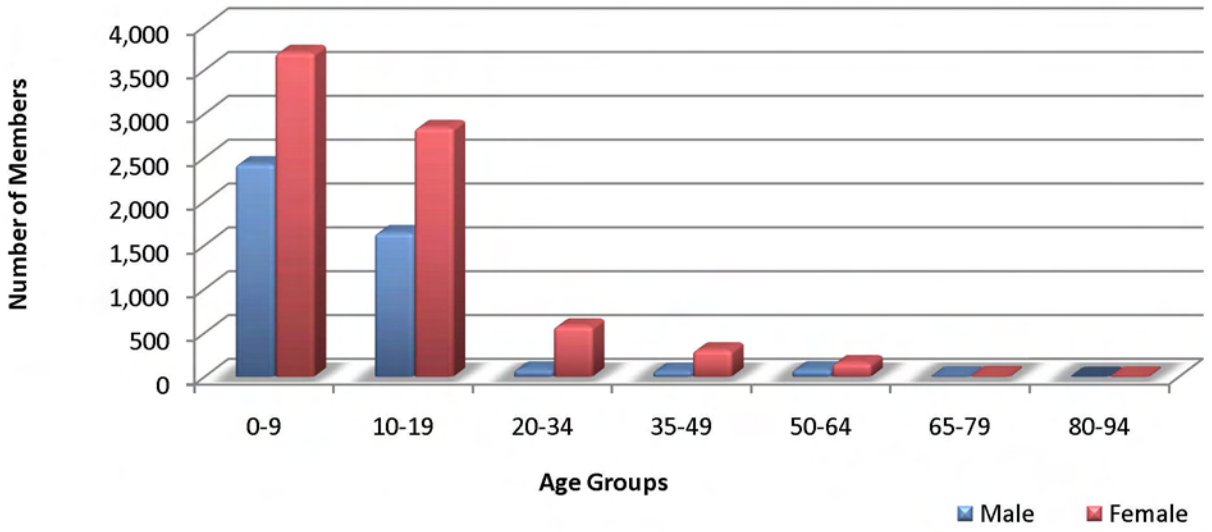
Clinical exception if known resistance to OTC Permethrin and Pyrethrin.

Utilization of Topical Anti-Parasitics

Comparison of Fiscal Years

Fiscal Year	Members	Claims	Paid Amount	Paid/Claim	Perdiem	Units	Days
2008	13,178	19,826	$1,432,723.74	$72.26	$7.08	1,310,198	202,345
2009	11,908	17,460	$403,833.03	$23.13	$2.49	1,169,800	161,926
Percent Change	-9.6%	-11.9%	-71.8%	-68.0%	-64.8%	-10.7%	-20.0%
Change	-1,270	-2,366	-$1,028,890.71	-$49.13	-$4.59	-140,398	-40,419

Demographics of Members Utilizing Topical Anti-Parasitics: FY 2009



Prescribers of Topical Anti-Parasitics: FY 2009

Specialty	Claims
General Pediatrician	4,515
Family Practitioner	4,269
Physician Assistant	2,038
Nurse Practitioner (Other)	1,782
General Practitioner	1,343
Prescriber Only	916
Unknown	881
Emergency Medicine Practitioner	372
Internist	354
DDSD-NFM	220
General Surgeon	185

Prior Authorization of Topical Anti-Parasitics

There were a total of 1,340 petitions submitted for this PBPA category during fiscal year 2009. The following chart shows the status of the submitted petitions.

Status of Petitions for Topical Anti-Parasitics: FY 2009

Status	Total PA Count
Approved	566
Denied	435
Incomplete	339

Market News and Update

- March 2009-**Malathion Lotion 0.5%** (generic for Ovide®) approved by FDA

- April 2009-**Ulesfia™ (benzyl alcohol) Lotion** approved by the FDA for the treatment of head lice infestation in patients 6 months of age and older.
  Mechanism: Benzyl alcohol inhibits lice from closing their respiratory spiracles, which results in obstruction of the spiracles by the vehicle and subsequent asphyxiation of the lice. Benzyl alcohol does not have ovocidal activity.
  Topical dosage-The amount of lotion that should be used for each treatment is determined by the length of hair to be treated (See table below). Repeat treatment in 7 days.

Hair Length		Amount of Ulesfia™ Lotion per Treatment
Short	0-2 inches	4-6 oz (½-¾ bottle)
	2-4 inches	6-8 oz (¾-1 bottle)
Medium	4-8 inches	8-12 oz (1-1½ bottles)
	8-16 inches	12-24 oz (1½-3 bottles)
Long	16-22 inches	24-32 oz (3-4 bottles)
	Over 22 inches	32-48 oz (4-6 bottles)

Pricing- EAC is approximately $26.85/bottle
AWP is approximately $30.51/bottle

Conclusion and Recommendations

The College of Pharmacy recommends continuing the current criteria with the following addition:

Ulesfia™ (benzyl alcohol) Lotion

- Available only after first-line treatment with an OTC product has failed
- Member must be at least 6 months old
- Quantity Limit of 4 bottles per 14 days

Utilization Details of Topical Anti-Parasitics: Fiscal Year 2009

Chemical Name	Brand Name	Claims	Units	Days	Members	Paid Amount	Units/ Day	Claims/ Member	Perdiem	% Paid
Permethrin	PERMETHRIN CRE 5%	9,097	561,804	89,030	7,153	$134,907.80	6.31	1.27	$1.52	33.41%
Permethrin	PERMETHRIN LOT 1%	5,487	397,678	45,143	3,632	$65,535.73	8.81	1.51	$1.45	16.23%
Malathion	OVIDE LOT 0.5%	1,166	68,878	11,240	907	$155,901.88	6.13	1.29	$13.87	38.61%
Permethrin	SM LICE LOT TREATMNT	676	43,987	6,404	529	$8,544.02	6.87	1.28	$1.33	2.12%
Permethrin	ACTICIN CRE 5%	311	20,430	3,110	250	$4,814.53	6.57	1.24	$1.55	1.19%
Pyrethrins/Butoxide	LICE KILLING SHA	201	35,757	1,635	148	$2,411.12	21.87	1.36	$1.47	0.60%
Permethrin	LICE TREATME LIQ 1%	199	18,191	1,658	142	$2,468.90	10.97	1.40	$1.49	0.61%
Lindane	LINDANE SHA 1%	128	7,529	1,026	109	$14,306.54	7.34	1.17	$13.94	3.54%
Malathion	MALATHION LOT 0.5%	52	3,068	650	50	$7,517.99	4.72	1.04	$11.57	1.86%
Permethrin	V-R LICE RIN LIQ 1%	45	4,553	540	38	$528.43	8.43	1.18	$0.98	0.13%
Lindane	LINDANE LOT 1%	39	2,816	332	31	$5,370.95	8.48	1.26	$16.18	1.33%
Crotamiton	EURAX CRE 10%	38	2,942	765	28	$920.56	3.85	1.36	$1.20	0.23%
Crotamiton	EURAX LOT 10%	21	2,168	393	20	$604.58	5.52	1.05	$1.54	0.15%
	Totals	**17,460**	**1,169,801**	**161,926**	**11,908***	**$403,833.03**	**7.22**	**1.47**	**$2.49**	**100.00**

***Total number of unduplicated members**

Utilization Details of Topical Anti-Parasitics: Fiscal Year 2008

Chemical Name	Brand Name	Claims	Units	Days	Members	Paid Amount	Units/ Day	Claims/ Member	Perdiem	% Paid
Permethrin	PERMETHRIN CRE 5%	7,705	515,679	62,083	5,983	$142,353.64	8.31	1.29	$2.29	9.94%
Lindane	LINDANE SHA 1%	5,114	333,414	60,347	3,409	$624,446.33	5.52	1.50	$10.35	43.58%
Malathion	OVIDE LOT 0.5%	4,599	283,503	51,025	3,115	$543,733.39	5.56	1.48	$10.66	37.95%
Permethrin	PERMETHRIN LOT 1%	765	53,535	5,685	591	$8,688.52	9.42	1.29	$1.53	0.61%
Lindane	LINDANE LOT 1%	746	54,113	9,111	605	$97,791.53	5.94	1.23	$10.73	6.83%
Permethrin	ACTICIN CRE 5%	427	30,000	3,766	367	$8,085.39	7.97	1.16	$2.15	0.56%
Crotamiton	EURAX CRE 10%	154	9,963	4,331	120	$2,709.50	2.3	1.28	$0.63	0.19%
Crotamiton	EURAX LOT 10%	117	9,545	4,520	84	$2,536.09	2.11	1.39	$0.56	0.18%
Permethrin	SM LICE LOT TREATMNT	107	7,053	854	92	$1,272.34	8.26	1.16	$1.49	0.09%
Permethrin	LICE TREATME LIQ 1%	42	3,764	288	36	$505.10	13.07	1.17	$1.75	0.04%
Pyrethrins-Piperonyl Butoxide	LICE KILLING SHA	41	8,729	273	41	$535.15	31.97	1.00	$1.96	0.04%
Permethrin Creme	V-R LICE RIN LIQ 1%	9	899	62	7	$66.76	14.5	1.29	$1.08	0.00%
	Totals	**19,826**	**1,310,197**	**202,345**	**13,178***	**$1,432,723.74**	**6.48**	**1.50**	**$7.08**	**100.00**

***Total number of unduplicated members**

Ulesfia™ Product Details

Indication
Ulesfia™ Lotion is a pediculicide indicated for the topical treatment of head lice infestation in patients 6 months of age and older.

Dosage Forms
Ulesfia™ Lotion, 5% in 8 oz. bottles

Contraindications
Ulesfia™ Lotion has no contraindications listed within the FDA-approved manufacturer's labeling

Pregnancy Risk Factor B

Precautions

- **Neonatal Toxicity**-Intravenous administration of products containing benzyl alcohol has been associated with neonatal gasping syndrome consisting of severe metabolic acidosis, gasping respirations, progressive hypotension, seizures, central nervous system depression, intraventricular hemorrhage, and death in preterm, low birth weight infants. Neonates (i.e. patients less than 1 month of age or preterm infants with a corrected age of less than 44 weeks) could be at risk for gasping syndrome if treated with Ulesfia™ Lotion
- **Eye Irritation**-Avoid eye exposure. Ulesfia™ Lotion may cause eye irritation. If Ulesfia™ Lotion comes in contact with the eyes, flush them immediately with water. If irritation persists, consult a physician.
- **Contact Dermatitis** Ulesfia™ Lotion may cause allergic or irritant dermatitis.
- **Use in Children**-Ulesfia™ Lotion should only be used on children (6 month s of age and older) under the direct supervision of an adult. Keep out of reach of children.

Drug Interactions
There are no known drug interactions for Ulesfia™ Lotion.

Common Adverse Effect

- Pruritus
- Erythema
- Irritation
- Anesthesia
- Hypoesthesia
- Pain

Less Common Adverse effects

- Dandruff
- Exfoliation
- Dermatitis
- Paraesthia
- Dryness
- Rash
- Excoriation
- Thermal Burn

Patient Information

- This medication is to be used as directed by the physician. Use only on scalp and scalp hair. Avoid contact with eyes. As with any topical medication, patients should wash hands after application.
- Instruct patients on proper use of Ulesfia™ Lotion, including the amount to apply, how long to leave it on the hair, and the importance of a second treatment 1 week (7 days) after the initial application

REFERENCE

1. Ulesfia(TM) (benzyl alcohol) Product Information. Purdue. January 16, 2009.
2. Benzyl Alcohol Product Information. Lexi-Comp, Inc. (Lexi-Drugs) Lexi-Comp, Inc. Accessed October 2, 2009.

Appendix H

Annual Review of Hypnotic Medications - Fiscal Year 2009

Oklahoma Health Care Authority

October 2009

Current Prior Authorization Criteria

Current Prior Authorization of Hypnotic Medications

1. In order to receive a Tier 2 product (or a Tier 3 product if no Tier 2 products exists) a minimum trial of 30 days with at least two Tier 1 products (including zolpidem) should be attempted. Also, clinical documentation of attempts to correct any primary cause for insomnia should be provided.
2. In order to receive a Tier 3 product, all available Tier 2 products should be attempted for a minimum of 30 days each. All other Tier 2 criteria should also be met.
3. FDA approved diagnosis (Ambien CR® only covered for sleep maintenance insomnia).
4. No concurrent anxiolytic benzodiazepine therapy greater than TID dosing and no concurrent ADHD medications.
5. Approvals granted for 6 months.

All members under the age of 18 will require a petition for use of hypnotic medications.
Quantity limit of #30 per 30 apply for all medications in this category.

Tier 1*	Tier 2	Tier 3
Estazolam **(ProSom®)** Temazepam **(Restoril®) 15 and 30mg** Flurazepam **(Dalmane®)** Triazolam **(Halcion®** zolpidem **(Ambien®)** Zaleplon **(Sonata®)**		Eszopiclone **(Lunesta®)** Temazepam **(Restoril®) 7.5 and 22.5 mg** Ramelteon **(Rozerem®)** Zolpidem **(Ambien CR®)** Zolpidem† Oral Spray **(Zolpimist™)**

***Mandatory Generic Plan Applies.**
†Requires special reason for use.

During fiscal year 2009, the patent for Sonata® expired. Zaleplon was made available in generic formulation and a SMAC pricing was subsequently applied, after which time, that product was moved to Tier 1.

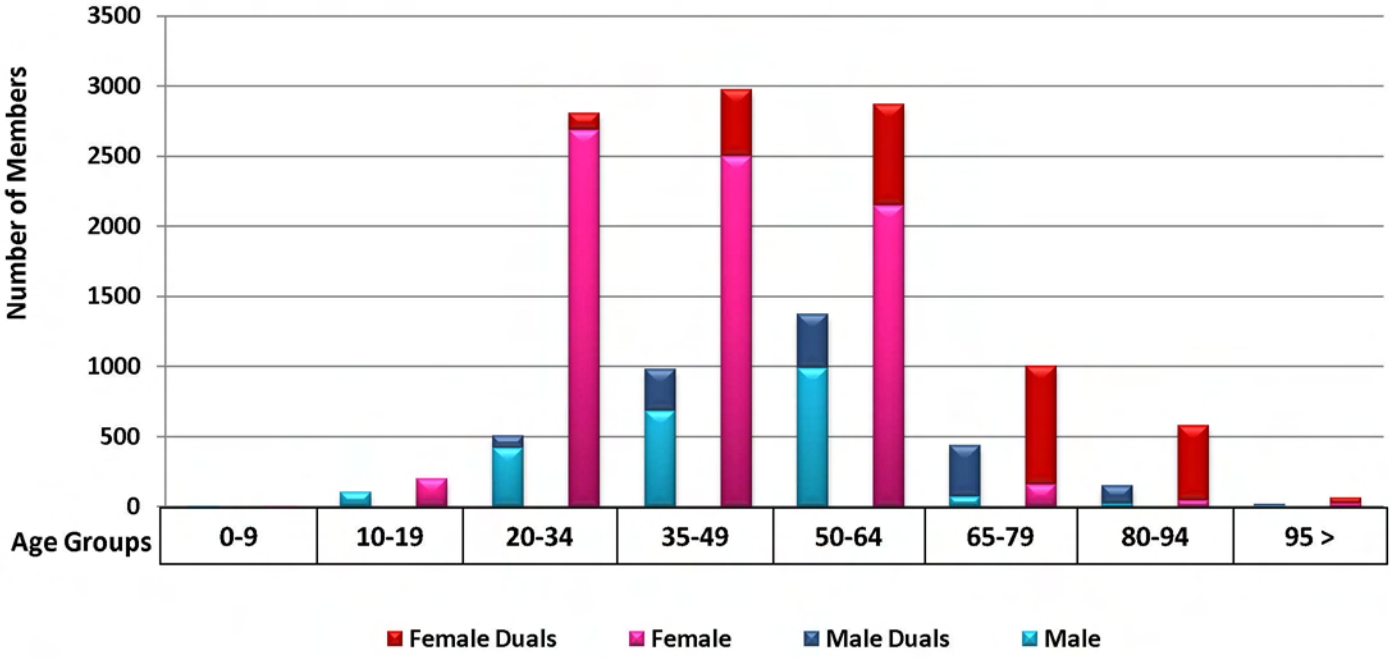
Utilization of Medication or Class

Comparison of Fiscal Years

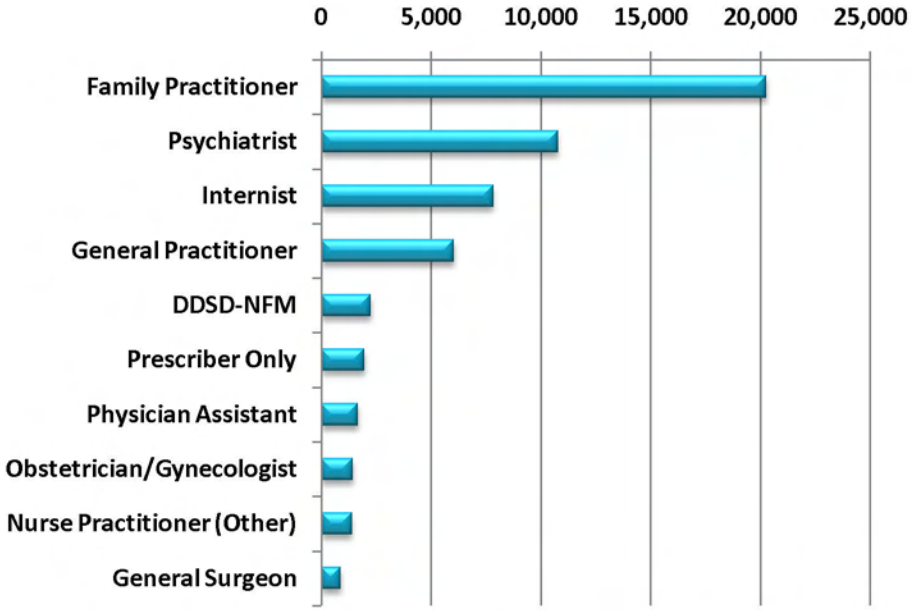
Fiscal Year	Members	Claims	Paid Amount	Paid/Claim	Perdiem	Units	Days
2008	13,583	55,106	$1,824,671.72	$33.11	$1.14	1,614,289	1,606,899
2009	14,107	59,590	$1,683,539.97	$28.25	$0.98	1,735,785	1,711,142
Percent Change	3.90%	8.10%	-7.70%	-14.70%	-14.00%	7.50%	6.50%
Change	524	4,484	-$141,131.75	-$4.86	-$0.16	121,496	104,243

Of the 14,107 members utilizing this category in fiscal year 2009, approximately 3,998 members were categorized as Medicare dual eligible members. Approximately 29% of the claims (17,443) and 18% of the cost ($294,882.20) were incurred by this group of members.

Demographics of Members Utilizing Hypnotic Medications: FY 2009



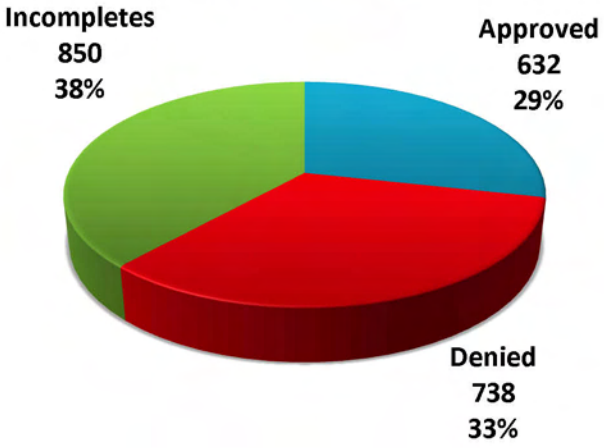
Prescribers of Hypnotic Medications by Number of Claims: FY 2009



Prior Authorization of Hypnotic Medications

There were a total of 2,220 petitions submitted for the Hypnotic Medications category during fiscal year 2009. For this category there is a computerized step edit implemented at the point of sale to detect two Tier 1 agents. If Tier 1 agents are detected the claim is allowed to run without a prior authorization. All members under the age of 18 are required to submit a petition. The following chart shows the status of the submitted petitions.

Status of Petitions for Hypnotic Medications: FY 2009



Market News and Update

Anticipated Patent Expirations

- Lunesta-2012
- Rozerem-2017
- Ambien CR-2019

Edluar™ (Zolpidem Sublingual Tablets)

- In March of 2009 the US Food and Drug Administration (FDA) approved Edluar™ 5 mg and 10 mg sublingual tablets for the short-term treatment of insomnia characterized by difficulties with sleep initiation. Edluar™ is a sublingual formulation of zolpidem and is categorized as schedule IV. Edluar™ is not approved for use in pediatric patients.

Intermezzo® (Zolpidem Sublingual Tablets)

- Transcept Pharmaceuticals, Inc. has filed an NDA for their version of zolpidem sublingual tablets and is expecting a decision from the FDA on or before October 31st, 2009.

Recommendations

The College of Pharmacy recommends the placement of Edluar™ and Intermezzo® in Tier 3 of the Hypnotics Medications PBPA Category. The petition must also include specific reason why member cannot take zolpidem tablets and all other available Tier 1 hypnotic medications.

Utilization Details of Hypnotic Medications: Fiscal Year 2009

Medication	Claims	Members	Units	Days	Paid Amount	Claims/ Member	Perdiem	% Paid
ZOLPIDEM TAB 10MG	20,917	6,340	596,998	598,755	$124,986.80	3.3	$0.21	7.42%
TEMAZEPAM CAP 30MG	13,692	3,140	407,460	403,819	$112,004.76	4.36	$0.28	6.65%
TEMAZEPAM CAP 15MG	9,562	2,865	289,553	274,610	$72,067.12	3.34	$0.26	4.28%
AMBIEN CR TAB 12.5MG	4,690	1,093	135,988	135,768	$627,526.56	4.29	$4.62	37.27%
ZOLPIDEM TAB 5MG	3,993	1,712	107,294	106,925	$24,615.81	2.33	$0.23	1.46%
LUNESTA TAB 3MG	1,775	403	52,735	52,605	$266,494.39	4.4	$5.07	15.83%
TRIAZOLAM TAB 0.25MG	1,113	335	32,642	27,846	$11,370.44	3.32	$0.41	0.68%
ROZEREM TAB 8MG	962	235	28,381	28,374	$104,827.97	4.09	$3.69	6.23%
LUNESTA TAB 2MG	552	165	16,158	16,192	$83,197.56	3.35	$5.14	4.94%
FLURAZEPAM CAP 30MG	463	128	13,982	13,682	$3,053.10	3.62	$0.22	0.18%
RESTORIL CAP 7.5MG	396	102	11,237	11,234	$95,894.72	3.88	$8.54	5.70%
TEMAZEPAM CAP 7.5MG	395	124	11,012	11,214	$91,741.21	3.19	$8.18	5.45%
AMBIEN CR TAB 6.25MG	360	147	10,009	9,777	$43,800.43	2.45	$4.48	2.60%
ESTAZOLAM TAB 2MG	179	38	5,376	4,896	$2,469.52	4.71	$0.50	0.15%
ZALEPLON CAP 10MG	147	70	4,457	4,232	$2,409.90	2.1	$0.57	0.14%
FLURAZEPAM CAP 15MG	116	43	3,847	3,363	$759.86	2.7	$0.23	0.05%
TRIAZOLAM TAB 0.125MG	93	34	2,555	2,433	$922.44	2.74	$0.38	0.05%
LUNESTA TAB 1MG	63	22	1,680	1,845	$8,694.23	2.86	$4.71	0.52%
ESTAZOLAM TAB 1MG	56	14	1,645	1,636	$691.32	4	$0.42	0.04%
ZALEPLON CAP 5MG	29	16	1,246	826	$585.42	1.81	$0.71	0.03%
HALCION TAB 0.25MG	13	1	780	390	$1,417.47	13	$3.63	0.08%
AMBIEN TAB 10MG	12	2	360	360	$1,740.53	6	$4.83	0.10%
TEMAZEPAM CAP 22.5MG	6	2	180	180	$1,423.93	3	$7.91	0.08%
RESTORIL CAP 22.5MG	2	2	60	60	$485.63	1	$8.09	0.03%
TRIAZOLAM 0.25MG TAB	2	1	60	60	$19.22	2	$0.32	0.00%
SONATA CAP 10MG	2	2	90	60	$339.63	1	$5.66	0.02%
Totals	**59,590**	**14,107***	**1,735,785**	**1,711,142**	**$1,683,539.97**	**4.22**	**$0.98**	**100%**

*Total number of unduplicated members

Edluar™ Product Information

Indication
Edluar™ is indicated for the short-term treatment of insomnia characterized by difficulties with sleep initiation.

Dosage Forms
- 5mg and 10mg sublingual tablets
- Not scored

Contraindications
Edluar™ is contraindicated in patients with any known hypersensitivity to zolpidem tartrate or any of the inactive ingredients.

Pregnancy Risk Factor C

Precautions
- **Co-morbid Diagnoses**: Sleep disturbances may manifest as a physical/psychiatric disorder; the failure of insomnia to remit after 7 to 10 days of treatment may indicate the presence of a primary psychiatric and/or medical illness that should be evaluated. Worsening of insomnia or the emergence of new thinking or behavior abnormalities may be the consequence of an unrecognized psychiatric or physical disorder
- **Severe anaphylactic and anaphylactoid reactions:** Rare cases of angioedema involving the tongue, glottis or larynx have been reported in patients after taking the first or subsequent doses; Some patients have had additional symptoms such as dyspnea, throat closing or nausea and vomiting that suggest anaphylaxis
- **Abnormal thinking and behavioral changes**: Visual and auditory hallucinations have been reported as well as behavioral changes such as bizarre behavior, agitation and depersonalization; "sleep-driving", preparing and eating food, making phone calls, or having sex; worsening of depression, including suicidal thoughts and actions in those primarily depressed
- **Withdrawal symptoms:** Mild dysphoria, insomnia, abdominal and muscle cramps, nausea/vomiting, sweating, tremors, convulsions
- **CNS depressant effects:** Due to the rapid onset of action, Edluar™ should be ingested immediately prior to going to bed. Caution against engaging in hazardous occupations, operating machinery, or driving a motor vehicle after ingesting the drug. Should not be taken with alcohol due to additive effects. Possible combined effects with other CNS-depressants
- **Respiratory Depression:** Caution in patients with compromised respiratory function-sleep apnea syndrome or myasthenia gravis
- **Elderly and/or Debilitated:** Impaired motor and/or cognitive performance or sensitivity
- **Hepatic Impairment:** Prolonged elimination therefore, treatment should be initiated with 5 mg in patients with hepatic compromise, and they should be closely monitored
- **Renal Impairment:** No dosage adjustment of Edluar™ in renally impaired patients is required; however, these patients should be closely monitored
- **Patients with Depression:** Administer with caution to patients exhibiting signs or symptoms of depression; suicidal tendencies are more common in this group; the least amount of drug should be prescribed at any one time
- **Pediatrics:** Edluar™ is not recommended for use in children; safety and effectiveness of Edluar have not been established in patients below the age of 18

Common Adverse Effects

- Drowsiness
- Dizziness
- Diarrhea
- Headache
- "Drugged" Feeling

Less Common Adverse Effects

- Chest Pain
- Rash
- Dry mouth
- Fatigue
- Anorexia
- Abnormal Dreams
- Sleep Disorder

Drug Interactions

Any drug with **CNS-depressant effects** could potentially enhance the CNS-depressant effects of zolpidem. **Imipramine** in combination with zolpidem produced an additive effect of decreased alertness. Similarly, **chlorpromazine** in combination with zolpidem produced an additive effect of decreased alertness and psychomotor performance. These drugs did not show any significant pharmacokinetic interaction. A study involving haloperidol and zolpidem revealed no effect of haloperidol on the pharmacokinetics or pharmacodynamics of zolpidem. Some compounds known to inhibit CYP3A may increase exposure to zolpidem. Consideration should be given to using a lower dose of zolpidem when **ketoconazole** and zolpidem are given together. Patients should be advised that use of Edluar™ with ketoconazole may enhance the sedative effects.

Patient Information

- After taking Edluar™, you may get up out of bed while not being fully awake and do an activity that you do not know you are doing. The next morning, you may not remember that you did anything during the night. You have a higher chance for doing these activities if you drink alcohol or take other medicines that make you sleepy with Edluar. Reported activities include:
    - driving a car ("sleep-driving")
    - making and eating food
    - talking on the phone
    - having sex
    - sleep-walking
- Take Edluar™ right before going to bed as prescribed and only if you can get a full night (7-8 hours) of sleep
- Do not take Edluar™ with alcohol or other medications that can make you sleepy or if you have had an allergic reaction to zolpidem
- Use caution in driving, operating machinery, or doing other dangerous activities until you know how Edluar™ affects you. Edluar™ may impair your mental and physical abilities to perform these tasks.
- Serious side effects that could occur and if they do, you should contact your Doctor, include:
    - Abnormal thoughts and behavior
    - Anxiety
    - Getting out of bed while not being fully awake and do an activity that you do not know you are doing
    - Memory loss

- Store Edluar™ between 68° and 77°F and protect from light and moisture.
- Keep Edluar™ and all medicines out of reach of children.

REFERENCE

Edluar™ (zolpidem tartrate sublingual tablets) Product Information. Purdue Pharmaceuticals. May 2009.

Appendix I

Results from the 2008 National Survey on Drug Use and Health: National Findings

Source of Prescription Drugs

- Past year nonmedical users of prescription-type psychotherapeutic drugs are asked how they obtained the drugs they recently used non-medically. Rates averaged for 2007 and 2008 show that over half of the nonmedical users of prescription-type pain relievers, tranquilizers, stimulants, and sedatives aged 12 or older said they got the drugs they used most recently "from a friend or relative for free." In a follow-up question, the majority of these respondents indicated that their friend or relative had obtained the drugs from one doctor.

- Among persons aged 12 or older in 2007-2008 who used pain relievers non-medically in the past 12 months, 55.9 percent got the pain relievers they most recently used from a friend or relative for free. Another 8.9 percent bought them from a friend or relative, and 5.4 percent took them from a friend or relative without asking. Nearly one fifth (18.0 percent) indicated that they got the drugs they most recently used through a prescription from one doctor. About 1 in 20 users (4.3 percent) got pain relievers from a drug dealer or other stranger, and 0.4 percent bought them on the Internet. These percentages are similar to those reported in 2006-2007.

- In 81.7 percent of the instances in 2007-2008 where nonmedical users of prescription pain relievers aged 12 or older obtained the drugs from a friend or relative for free, the individuals indicated that their friend or relative had obtained the drugs from just one doctor. Only 1.6 percent reported that the friend or relative had bought the drugs from a drug dealer or other stranger.

- In 2007-2008, 42.8 percent of past year methamphetamine users aged 12 or older reported that they obtained the methamphetamine they used most recently from a friend or relative for free, lower than the 49.7 percent reported in 2006-2007. In contrast, the percentage of past year methamphetamine users who bought it from a friend or relative increased from 25.1 percent in 2006-2007 to 30.1 percent in 2007-2008. About one in five users (21.7 percent) in 2007-2008 bought the methamphetamine they used most recently from a drug dealer or other stranger, which was comparable with the rate for 2006-2007 (20.5 percent).

Safety

Heparin: Change in Reference Standard

Audience: Pharmacists, physicians, hospital risk managers and consumers

[Posted - 10/01/2009] FDA notified healthcare professionals and patients of a change to heparin, effective October 1, 2009, which will include a new reference standard and test method used to determine the potency of the drug and able to detect impurities that may be present in heparin. The change, which will also harmonize the USP unit dose with the WHO International Standard unit dose, will result in approximately a 10% reduction in the potency of the heparin marketed in the United States.

This may have clinical significance in some situations, such as when heparin is administered as a bolus intravenous dose and an immediate anticoagulant effect is clinically important. Healthcare providers should be aware of the decrease in heparin potency as they monitor the anticoagulant effect of the drug; more heparin may be required to achieve and maintain the desired level of anticoagulation in some patients.

There will be simultaneous availability of heparin manufactured to meet the "old" and "new" USP monograph, with potential differences in potency. Products using the new "USP unit" potency definition are anticipated to be available on or after October 8. FDA is working with the manufacturers of heparin to ensure that an appropriate identifier is placed on heparin made under the new USP monograph. Most manufacturers will place an "N" next to the lot number. FDA is also working with the heparin manufacturers to study the impact of this variation in potency and will make the results available when the studies have concluded.

[10/01/2009 - Public Health Alert - FDA]

[10/01/2009 - Information for Consumers - FDA]

Safety

Tamiflu (oseltamivir) for Oral Suspension: Potential Medication Errors

Audience: Pharmacists, pediatrics healthcare professionals

[UPDATED 10/05/2009] New information added to web site.

[UPDATED 09/25/2009] New links added to provide information on emergency use in infants less than 1 year of age and directions to pharmacists on emergency compounding of oral suspension from capsules.

[Posted 09/24/2009] FDA issued a Public Health Alert to notify prescribers and pharmacists about potential dosing errors with Tamiflu (oseltamivir) for Oral Suspension. U.S. health care providers usually write prescriptions for liquid medicines in milliliters (mL) or teaspoons, while Tamiflu is dosed in milligrams (mg). The dosing dispenser packaged with Tamiflu has markings only in 30, 45 and 60 mg. The Agency has received reports of errors where dosing instructions for the patient do not match the dosing dispenser. Health care providers should write doses in mg if the dosing dispenser with the drug is in mg. Pharmacists should ensure that the units of measure on the prescription instructions match the dosing device provided with the drug.

[10/02/2009 - Information for Healthcare Professionals - Authorization of Use of Expired Tamiflu for Oral Suspension - FDA]
[10/02/2009 - Treatment of Influenza During Pregnancy - FDA]
[09/25/2009 - Emergency Compounding of an Oral Suspension from Tamiflu 75 mg Capsules (Final Concentration 15 mg/mL) - FDA]

[09/25/2009 - Emergency Use of Tamiflu in Infants Less than 1 Year of Age - FDA]

[09/24/2009 - Public Health Alert - FDA]

[09/23/2009 - Dear Healthcare Professional Letter - Roche]

[09/23/2009 - Information for Pharmacists - CDC]

Safety

Sitagliptin (marketed as Januvia and Janumet) - acute pancreatitis

Audience: Diabetes healthcare professionals, patients

[Posted 09/25/2009] FDA notified healthcare professionals and patients of revisions to the prescribing information for Januvia (sitagliptin) and Janumet (sitagliptin/metformin) to include information on reported cases of acute pancreatitis in patients using these products. Eighty-eight post-marketing cases of acute pancreatitis, including two cases of hemorrhagic or necrotizing pancreatitis in patients using sitagliptin, were reported to the Agency between October 2006 and February 2009. It is recommended that healthcare professionals monitor patients carefully for the development of pancreatitis after initiation or dose increases of sitagliptin or sitagliptin/metformin. Sitagliptin has not been studied in patients with a history of pancreatitis. Therefore, it is not known whether these patients are at an increased risk for developing pancreatitis and the medication should be used with caution and with appropriate monitoring in patients with a history of pancreatitis. Considerations for healthcare professionals, information for patients, and a Data Summary are provided.

[09/25/2009 - Information for Healthcare Professionals - FDA]