Drug Utilization Review Board

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

Wednesday
March 10, 2010
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 – March 10, 2010**

DATE: March 4, 2010

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

Enclosed are the following items related to the March 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 Update Anxiolytic Prior Authorization Category – See Appendix C.

Action Item – Vote to Prior Authorize Twynsta™ – See Appendix D.

Action Item – Vote to Prior Authorize Pennsaid® – See Appendix E.

30 Day Notice to Prior Authorize Mozobil®, Nplate®, and Arcalyst® – See Appendix F.

Action Item – Annual Review of Xopenex® and Albuterol HFA Products – See Appendix G.

FDA and DEA Updates – See Appendix H.

Future Business

Adjournment

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Drug Utilization Review Board

(DUR Board)

Meeting – March 10, 2010 @ 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. February 10, 2010 DUR Minutes – Vote
B. February 11, 2010 DUR Recommendation Memorandum

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 October 2009
B. Medication Coverage Activity Audit for February 2010
C. Help Desk Activity Audit for February 2010

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

5. Action Item – Vote to Update Anxiolytic Prior Authorization Category – See Appendix C.

A. Utilization Review
B. Current Prior Authorization Criteria
C. COP Recommendations

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

6. Action Item – Vote to Prior Authorize Twynsta™ – See Appendix D.

A. COP Recommendations

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

7. Action Item – Vote to Prior Authorize Pennsaid® – See Appendix E.

A. Product Summary
B. COP Recommendations

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

8. 30 Day Notice to Prior Authorize Mozobil®, Nplate®, and Arcalyst® – See Appendix F.

A. Mozobil® Product Information
B. Nplate® Product Information
C. Arcalyst® Product Information

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

9. Action Item – Annual Review of Xopenex® and Albuterol HFA Products – See Appendix G.

A. Current Prior Authorization Criteria
B. Utilization Review
C. COP Recommendations

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

10. FDA and DEA Updates – See Appendix H.

11. Future Business

A. Annual Review of Smoking Cessation Products
B. Annual Review of Growth Hormones
C. FY09 Annual Review
D. New Product Reviews

12. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES of MEETING of FEBRUARY 10, 2010

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	
Jennifer Sipols, Pharm.D.; Clinical Pharmacist	X	
Visiting Pharmacy Student(s): Ross Clark, Brianna O'Malley	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	
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:

Meg Propes, AstraZeneca	Monica Iacobucci, AstraZeneca	Holly Turner, Merck
Mary jean Stevens, Merck	Craig Turner, Merck	Lon Lowrey, Novartis
Linda Cantu, BMS	Toby Thompson, Pfizer	Michael Hathaway, Otsuka
Kelly Rogers, Taro	Terry McCurren, Otsuka	Aaron Mays, Alcon
Charlene Kaiser, Amgen	Paul Davis, MHAT	Ron Thrasher, Chief, Stillwater Police Dept.
Donna Woods Bauer, OCARTA	Steve Erby, Novartis	Gary Wirezener, Chief, Yukon Police Dept.
Lloyd Cronnover, AstraZeneca	Haisam Al-Khouri, M.D.	Albert Appich, Pfizer
Lanette Long, St. Anthony Hospital	Michael Romzkowica, Azur Pharma	Quinn Dinh, Azor Pharma
Tim Warchan, Azor Pharma	Richard Ponder, J&J	Sheila Couch Shaffer, J&J
Chen Ritchie, Bristol Myers	Mark DeClerk, Lilly	Marco Munoz, Lilly
Marcello Kort, Lilly	Bruce Christian, Lilly	Donna Erwin, BMS
David Williams, Forest	Jim Dunlap, Lilly	P. Harwood, Medimmune
Sam Smothers, Medimmune	Janie Huff, Takeda	David Rogers, Capt., Bethany Police Dept.
Jim Cox, OACP	James Osborne, GSK	Mike Isaac, Lt., Norman Police Dept.
Palma Bucher, NAMI	Johnnie Judah, ODMHSAS	Carlonda Simms, NAMI

PRESENT FOR PUBLIC COMMENT:

Agenda Item No. 5	Quinn Dinh, MD, Azur Pharma; Jamie Street, MD, AstraZeneca; Mallery Mayo, PhD, Merck; Leland W. Dennis, MD, Rivers Edge Mental Health; Kirsten Mar, Eli Lilly; Theodore Darkow, BMS; Stacey Puckett, OACP; Paul Davis, MHAT

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: Quinn Dinh, MD, Azur Pharma; Jamie Street, MD, AstraZeneca; Mallery Mayo, PhD, Merck; Leland W. Dennis, Rivers Edge Mental Health; Kirsten Mar, Eli Lilly; Theodore Darkow, BMS; Stacey Puckett, OACP; Paul Davis, MHAT

ACTION: NONE REQUIRED

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

3A: January 13, 2010 DUR Minutes

Dr. Kuhls moved to approve as submitted; seconded by Dr. Winegardener.

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: **UPDATE ON DUR/MEDICATION COVERAGE AUTHORIZATION UNIT**

4A: Retrospective Drug Utilization Review: September 2009

4B: Medication Coverage Activity Audit: January 2010

4C: Help Desk Activity Audit: January 2010

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: **VOTE TO PRIOR AUTHORIZE ANTIPSYCHOTICS**

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

For Public Comment: Quinn Dinh, M.D.; Azur Pharma: Good evening, thank you Chairman and DUR Board members. My name is Quinn Dinh and I'm the senior director of medical affairs for Azur Pharma and happy to be here today and thank you for the opportunity to speak on behalf of Fazaclo. So what is Fazaclo? Fazaclo is a second generation clozapine antipsychotic, atypical antipsychotic that is in the ODT or oral disintegrating tablet formulations. The Fazaclo ODT is considered not equivalent to generic clozapine as you know, and it's not substitutable and this definition is actually is very much related to the FDA in terms of the studies that were conducted to show equivalency. Currently there's no AB rated equivalents for Fazaclo. Currently there are three dosage strengths to Fazaclo; 12.5 mg, 25 mg and 100 mg. And I think these dose strengths allows for the titration which is a key to this treatment space to afford for therapeutic dose to treating therapies. Given the limited time and I would like to relay to the Chairman and the Board here, is that in your consideration of the various therapies across the tiers, it's important to remember some of the advantages that we believe are important to Fazaclo and how that translates into the best treatment for patients and the physicians, therapeutic option point of view and basically those variables could be bucketed in three areas. The first I mentioned earlier, the ODT technology. Second is the Fazaclo patient registry which is a run 24 hours, 7 days a week operations to support the product to insure the registration of patients, the registration of physicians prescribing the therapy and the pharmacies monitoring for laboratories. So that is the only nationwide service that is provided in the space, and lastly I'd like you to consider are the key major landmark studies surrounding antipsychotics. More studies that were conducted not by the pharmaceutical industry but actually by various national healthcare research organizations, so those are the three buckets I would like for you to think about and consider. But before I do that I think I would like to remind you that in terms of from the FDA indications point of view, Fazaclo is indicated for three indications. The first indication is second line indication to treat refractory or resistant schizophrenia when other antipsychotic agents have been tried and there's a lack of efficacy or tolerability issue. I think that's the first important point; and the other two indications are actually first line indications for decrease in suicidal behavior overall, and decrease in decrease in suicidal behavior in schizophrenics. So those are the indications. And as you know psychiatrists and other mental health providers use Fazaclo and clozapine for other disease states, namely first line for schizophrenia, namely even dementia, anxiety, agitation and bipolar disorders, so keep that in mind. And if I can I would like to go back to the three categories that I mentioned earlier about variables that are very important to this product. The ODT technology, I think what it says is that you know we've done research for our physicians and patients are very satisfied with this product, 80% satisfaction leading to adherence and as you know adherence to therapy is very important in this category.

Dr. Muchmore: Okay, we've reached the end of our time. Does anybody have any questions of Dr. Dinh. Thank you very much for coming.

For Public Comment: Jamie Street, MD, AstraZeneca: Good evening ladies and gentlemen. My name is Dr. Jamie Street and I am the field medical physician for AstraZeneca neurosciences. On behalf of AstraZeneca, we openly support equal access to all

the atypical agents in the class in Oklahoma. I would like to point out that indications do matter in this class. Indications are evidence that the FDA has approved the use of a particular drug for a particular disease state and for a particular symptomatology. We feel that it is important that FDA indications be strongly considered when considering and reviewing this class. At the January DUR meeting, our regional scientific manager, Dan Huffman, overview Seroquel and Seroquel XR for the committee. If there are any questions, I'm happy to take them and follow up to that time that was spent in the January meeting. Any questions from the committee?

Dr. Rhymer: I do ma'am ……. any abuse potential for one of those products?

Dr. Street: Seroquel has been identified as having some abuse potential. Seroquel XR because of its' formulation process is not likely to have the same degree. For indications, Seroquel, as of January 2009 is currently indicated in pediatrics for both schizophrenia and bipolar mania. XR has a number of indications and we have identified that XR is most widely appreciated in the Department of Correction and as of January this year, the Federal Department of Correction has placed Seroquel XR on its' formulary.

Dr. Muchmore: Any other questions? Thank you for coming.

For Public Comment: Mallery Mayo, PhD, Merck: Good evening ladies and gentlemen. My name is Dr. Mayo and I represent the medical affairs department at Merck. I support the product called Saphris and I was here two months ago at the meeting and presented some of the clinical data behind Saphris, so I'm really here tonight just to answer any questions that may come up or if you have any questions regarding the product.

Dr. Muchmore: It's only supplied in sublingual tablets, is that right?

Dr. Mayo: It's only supplied in sublingual tablets, that's correct. I do have one question. Slides that are presented, will they be available after the meeting?

Dr. Muchmore: I don't know any reason not to.

Dr. Nesser: Just e-mail me.

Dr. Mayo: Thanks so much for your time, I appreciate it.

For Public Comment: Leland W. Dennis, MD, Rivers Edge Mental Health: Thank you. I am in Elk City, Oklahoma; a general adult psychiatrist with Rivers Edge Mental Health Associates and is Leslie here? Leslie Robinson? No, dogonnit ……. I told her I'd be here last month and things happened, I couldn't get here. I didn't hear the explanation as to why there were so many incomplete reportings and so few denials for January 2010. What was that explanation?

Dr. Muchmore: Sometimes people become more aware of the criteria and realize that the patient doesn't meet those criteria, so they may quit promoting their requests.

Dr. Dennis: I see. And so the 800 plus duplicate requests may have been those of us who are slow learners and request again.

Dr. Muchmore: I don't know that.

Dr. Dennis: In the terms of incomplete, let me tell you, as a practicing psychiatrist, that on November 23rd I turned in a request for a young woman who had just delivered a stillborn child. For an antidepressant. She had tried Prozac in the past, no help; Zoloft in the past, didn't tolerate it. Paxil in the past, didn't tolerate it. She was a very sad woman. Had a 2-year old at home, stillbirth baby, denied on December 9th, November 23rd, December 9th I got a denial "Unable to verify required Tier 2 trials within the last six months for requested medication in claims history. Please provide specific information as indicated." She was pregnant, okay? She really was. She had a stillborn baby. I talked to Leslie about this finally in January and got her approved. Now I kept her on samples. I treated her. I took care of my patient. But it's one of the incomplete in that 7,000 in January, excuse me, 5,000 or so in January. There's one as you break it out as medically necessary that was denied. I wonder if that was my patient who was denied? I want to bring some emotion to this because what we're talking about is approving something that at the last minute changed as we walked in here. I came prepared to talk about open access and the slides came up nothing like the handout that I downloaded this week from the DUR Board's website, from the OCH, you know from the website, about what was going on. Things have changed since I got my handout this week. I want to know in Appendix I, who are the psychiatrists? How do you vet those psychiatrists? What's their relationship to industry? What's their relationship to the DUR Board? How are you going to find a child psychiatrist and then an adult psychiatrist and then what is my appeal as a psychiatrist so that I can get access to my patients' medications that are needed? Because you all say, you published that over 7,000 doctors or providers requested the right diagnosis at the right diagnosis and approved it. That over 5,000 didn't. And so there was 40-plus percent that didn't have right judgment, that didn't have access to right medicine. There are four types of errors in medicine. There's a technical error. As I used to be at the Health Sciences Center teaching students and residents how to do things, there were technical errors that they made and we tried to teach them how to do it. There are errors of judgment. As an attending, if I said to you Chairman, how do you get from here to Wal-Mart and we got in our cars and drove separate ways; if I happen to have an accident on the way to Wal-Mart, did I show worse judgment than you did, or was I just unlucky? There are normative errors. At my level of training, I shouldn't make an error such as missing, you know, not asking about a vital sign. There are pseudo normative errors and that's what's the Board's being asked to make tonight. When you know better but decide anyway. The Board is being asked to approve use of Tier 2 medicines that haven't been identified, to restrict access to patients that are in my office, and I want you to take that to heart. Thank you for your time. Any questions?

Dr. Rhymer: I do. Your patient that was prescribed a drug she wasn't able to get, did you perhaps prescribe alprazolam?

Dr. Dennis: No. We were actually asking simply for Cymbalta.

Dr. Rhymer: Okay, because I've had several that, oh no, they don't want this …… all they want is alprazolam.

Dr. Dennis: Yeah, you can run my numbers. I'm probably writing fewer benzos than any psychiatrist. Yeah I'm in the bottom.

For Public Comment: Kirsten Mar, Eli Lilly: Dr. Muchmore, I'm with the health outcomes research division of Eli Lilly and I'm here to support and answer any questions on Zyprexa that the committee may have tonight, but in light of the time and amount of speakers that you have tonight, I'd like to defer my time to Lt. Isaac.

Dr. Muchmore: Which medication was that?

Ms. Mar: For Zyprexa. If the committee has any questions that I can answer this evening.
Dr. Muchmore: Does anybody have any questions of Kirsten Mar about olanzapine? Okay. The next speaker is Theodore Darkow from BMS, I don't know what that is.
Dr. Feightner: She deferred her time to him, Dr. Muchmore.
Ms. Mar: May I defer my time to Lt. Isaac?
Dr. Muchmore: Oh, I missed that, okay.
For Public Comment: Lt. Mike Isaac, Norman Police Dept.: Mr. Chairman, members, distinguished guests, I'm not a rocket scientist or a psychiatrist, but I am a 26-year veteran of the Norman Police Department where I'm a supervisor. I've trained police officers in the state of Oklahoma for over 20 years. So I hope you won't think that I'm presumptuous when I ask to speak on behalf of law enforcement and the citizens of Norman. We have great services for people throughout our community who have mental illnesses. People from all over this great state have come to Norman expecting an excellent level of care. Some come to Norman because previous cuts in the mental health budget may be one of the decreasing numbers of places left to come for treatment. In my 20-plus years of training law enforcement officers to deal effectively with crisis, especially among people with mental illnesses, I have personally seen the direct and positive effects of the newer generation medications used to treat mental illnesses. Increased treatment compliance is a direct result of people taking these medications without suffering the unpleasant side effects of the older drugs. I know from working with mental health consumers that taking these medications have saved lives. Some people have told me that they say they would not be alive if they did not have these medications. No enforcement officer in this state must be confronted with individuals in crisis forced into a situation made more serious and volatile that it needs to be. Many departments recognize the importance of community oriented policing and how that philosophy, along with (unintelligible) and training helps reduce the severity of calls and more quickly controls dangerous situations. Treatment of mental illness requires the efforts of a properly trained and adequately supplied team of people beginning with the consumer who should not be required to experience treatment failures before being able to participate as full partners in their care so they can experience successful treatment as soon as possible. Oklahoma has made many positive steps forward in seeking and delivering the proper care and treatment of its' citizens with chemical imbalances in the brain that we commonly refer to as mental illness. Previous efforts to meet the stated public policy of assuring the adequate and humane treatment of care of persons with mental illness in Oklahoma should continue by allowing physicians, patients and their families to succeed rather than fail in treatment. I thank you for your time.
Dr. Muchmore: Does anybody have any questions?
Dr. Feightner: I do. First of all, thank you too for your service to the state and to Norman. You state that Tier 3 medications provide a better outcome and are better for the people that you see? Do you have any previous medical training?
Lt. Isaac: Yes, sir.
Dr. Feightner: What's that?
Lt. Isaac: I was an advanced level paramedic. I have research experience at the Dean McGee Eye Institute where I published papers and I was a physician's assistant student for two semesters.
Dr. Feightner: Okay. What percentage of people that you see at the police department do you have access to their medical records? You review the medical records?
Lt. Isaac: I do not.
Dr. Feightner: My question is this …..
Lt. Isaac: How do I know?
Dr. Feightner: yeah. My question is this ….. being a lieutenant how can you tell the Board that a atypical antipsychotic is better than a Tier 1 in working with the field and not having follow-up with the patients, not seeing them on a routine basis and just making that presumption from the field level as far as a police officer? Not that that service is not great, not that you're not smart, it's just how can you make that, that presumption in that from your experience with the people you see.
Lt. Isaac: Let me just broaden my impression a little bit. Maybe that will be more instructive for you. It's not a presumption that I consider to be a presumption anyway. I was on the Board of NAMI Oklahoma. I am in medical for the mental health liaison for the department and I also am on the Board of Directors for Thunderbird Clubhouse. I work closely with the transitioning house in Norman and I've been on the statewide education series with the Department of Mental Health and Substance Abuse Services, and these are stories that are told to me by consumers who struggle with their mental illness every single day. And to a person who has approached me or that I've solicited their input, they said that they want to have a hand in deciding what their medical treatment is by working with their physician and indeed, two of them would not be alive if they had not had the benefit of the antipsychotropes that were talked about in this generation, as opposed to repeatedly required to fail on the first or second level of treatment that you all use. So it's a little bit more than just an anecdotal thing. Without the access to medical records to which I'm not invited.
Dr. Muchmore: Any other questions?
Dr. Kuhls: I'd just like to make a quick statement that since I practice in Norman and deal with the community in Norman and many of Norman's activities, I just want you to know from at least that standpoint I look at this decision and the decision for the state of Oklahoma very seriously. And so, their decisions are based on science, decisions based on the literature, based on where we're at in the state of Oklahoma and I understand your concerns. I understand NAMI's concerns, but I think compared to a lot of insurance companies, and I think compared to even, there was a speaker here from, where was that place last time that was getting Medicare and couldn't get Geodon and Medicare, that all …
(multiple voices): That was a consumer.
Dr. Kuhls: She would qualify for her medications under that program where she can't them in other programs. And so none of these medicines are not available. It's a process of if you're going to be started on one, you start on one before you just jump to the others. But all the products are available. And that's what we're trying to do.

Lt. Isaac: Yes sir. I'm just in that mode for responding to crisis where people are either hostages, have hostages, suicidal ……
Dr. Kuhls: I understand that and I think Dr. Bell, I mean, I didn't want to talk with the last speaker, but Dr. Bell who is a child psychiatrist, is on the Board, and when we try to make our decisions or look at our plan, patients that are needing to be in-patient, okay, those patients aren't going to be put on the medicine in-patient, sent home and said you can't be put on whatever drug you were stabilized on. And so I think there's been a lot of soul searching, decision making, workings that are even beyond this group that have to be made, but I think, I hope you realize that it's not like, UNH, you can't get these drugs or the patient that needs to be stabilized in-patient isn't going to get these drugs. That's not what this is all about.
Dr. Muchmore: I think our program is a lot more accommodating than some third party payers of Medicare. No program is perfect but we certainly have the accommodations, and also we have the ability for someone to contact the prior approval folks and say, you know I have an unusual situation here and they get listened to, and we hope that you don't have to confront any of those people in a crisis because we managed to get them on the right thing.
Dr. Kuhls: So I hear you. I respect that.
Lt. Isaac: Thank you.
Dr. Muchmore: Okay, next item is Theodore Darkow from BMS.
For Public Comment: Theodore Darkow, BMS: That being Bristol Myers Squibb. Thank you for allowing me to speak today. My name is Dr. Theodore Darkow. I'm with the health economics and outcomes research group for Bristol Myers Squibb and I'd like to thank you for your opportunity to provide testimony today on behalf of aripiprazole. My colleague, Dr. Mike McGuire was here last month to provide testimony and he focused on the clinical profile. I'd like to just briefly remind you of a few points that he hit on and then focus on some more outcomes or economic data. In terms of indications, the safety of and efficacy of aripiprazole has been studied in multiple indications in adult and pediatric patients resulting in 14 FDA approved indications for once daily dosing. It has the broadest range of indications across adult and pediatric patients and is only one of two atypical with FDA approvals in individuals less than 19 years of age. And according to the surveillance date incorporated for anonymous patient level data, 75% of those prescriptions are for approved indications. My primary purpose here today however, is to share with you the results of a retrospective analysis of atypicals in bipolar disorder. These results have been published in Clinical Therapeutics and the Journal of Medical Economics. It was a retrospective analysis of health care claims data from a large national commercial managed care plan and the objective was to pair the effectiveness of the atypicals with regard to preventing psychiatric rehospitalization and associated costs in adults with bipolar disorder who are also treated with a mood stabilizer and then added on concurrent atypical therapy. Using data from January 2003 to December 2006, patients 18 to 65 years of age were identified who were newly initiated on an atypical other than clozapine while continuing treatment with a mood stabilizer. The patients had a diagnosis of bipolar as identified by the ICD-9 diagnosis code and no evidence of schizophrenia or schizoaffective disorder. To address the potential for treatment selection bias, patients in each of the comparison cohorts were matched to patients in the aripiprazole cohort using propensity scores which included age, gender, comorbidity, geographical region, calendar year, number of psychiatric hospitalizations, evidence of dyslipedimia or diabetes and also evidence of glucose or lipid monitoring. Patients were followed for up to 90 days and were censored if they were hospitalized, discontinued their therapy or initiated a new antipsychotic. Prior to matching a total of 6,162 qualifying patients were identified of who 840 received aripiprazole and following matching, 690 olanzapine, 840 quetiapine, 829 risperidone and 431 ziprasidone patients were matched to aripiprazole patients and, generally, things were initiated on a dose of recognized antipsychotic that was lower than the recommended, lower than that recommended in the labeling, and there was little evidence of titration to a higher dose in these patients. After adjusting for potential confounders then, the risk of hospitalization was found to be higher for patients taking each of the study atypicals, than for patients receiving aripiprazole. Hazard ratios which indicate the relative risk for hospitalization taking into account time two hospitalizations for the comparison products for 1.6 olanzapine, 1.5 for quetiapine, and also risperidone, and 1.7 for ziprasidone. And all of these differences were statistically significant. Directed pharmacy and medical costs were also measured during the 90-day follow-up period for calculated for both psychiatric service as well as other medical services. And mean costs of these patients were substantial, ranging from $2,195 to $2,706 per patient month. After adjusting for confounders, mean psychiatric costs were significantly higher for patients receiving olanzapine, quetiapine, risperidone and ziprasidone than for patients receiving aripiprazole with these costs being more than 50% higher for olanzapine, risperidone and ziprasidone.
Dr. Muchmore: Thank you very much. Do we have any questions of Dr. Darkow? You know it's clear that all of these drugs including the Tier 1 risperidone are amazing drugs and they do amazing things and our job is to try and funnel people to the right place at the right time if we can, because we certainly do authorize a lot of these medications, including aripiprazole. Okay, next person is Stacey Puckett, OACP.
For Public Comment: Stacey Puckett, OACP: Thank you Mr. Chairman and Board members for allowing us to be here. For those of you who don't know what OACP is, it's the Oklahoma Association of Chiefs of Police. I have some law enforcement representatives with me. If they'd stand up, I'd like for the Board and audience to see. We were not aware of your meeting until very short timeline. This is a very vital issue to law enforcement, as we were made aware of the tiers and the three tiers and the pass/fail systems on those. We have charged or passed with providing crisis intervention training across the state of Oklahoma for law enforcement over the last several years. I also have two family members who have been diagnosed with mental health issues, so I see it from both sides. Their interaction as first responders and on a personal note, with having a son who has attempted suicide three times and is in a long-term mental health facility. As we do these pass/fails with these people who are in the community and they are back in the community and it doesn't work for them while we're trying to get the diagnosis straight, those who represent you and are your first line of defense in your community are your law enforcement officials. And we can't take the risk of the loss of one of your patients. We can't take the risk of the loss of one of our officers because we're trying to determine does this medication work for them or does it not, and do we go on to the next one in the category and try it until they've used all of those medications and then they go to Tier 2 and then Tier 3. These are human beings. These are

lives. These are your brothers, sisters, mothers, and fathers. And I understand tough economic times. We're looking at a 20% reduction in force across the state of Oklahoma in law enforcement. There are going to be fewer officers to respond. There are going to be a greater number of clients who are needing help and assistance and they're going to have to go out there, and so at what value, and I understand we have to make hard decisions and in the chairs that you sit in I respect very much. It's a hard time to make these decisions. But I would ask that you consider when you make these decisions, are you saving dollars here at the state end on these medications at the cost of the community level to these patients, their families, the law enforcement and just the community as a whole, as they try to get these people stabilized and functional and producing members of the community. With that, I thank you for the time.

Dr. Kuhls: I'd just like to make a quick comment also, okay? I hear you, but I think it's very important that number one, you realize that the decisions and the recommendations that have been put forth by the College of Pharmacy are that, number one, nobody that is stabilized right now is going to have medicines changed. There will be no changes.

Ms. Puckett: And I understand that, that they're all to be grandfathered in. It's the new starts from this point forward which is about 5,200 a year.

Dr. Kuhls: Number two. When we looked scientifically at all the literature and everything that was available, there is really no strong data at all to suggest that one antipsychotic, atypical antipsychotic, is better than another, and if there was, this would have been all simple because we want everybody on the first medicine to be on the best and not the worst. But since all the medicines, nobody's shown one is much better than the other in terms of effectiveness, that's why we're making these decisions. And we have a relatively short window of changing therapy to allow physicians not to go through the mega long-term trials of non-effectiveness and so I think we spent a lot of time trying to make your job as safe as possible without putting you at more risk of having more less effective medicines out there and patients that make your job more at risk. I think we spent a lot of time trying to do that the best that we can.

Ms. Puckett: And may I respond to that? On a personal level with my son, while he was trying the 2-week uptake on the medications to see if it's effective or not, while we went through those trial periods and it took several medications before we found that. In the interim, I had the police numerous times at my house to help me get my child into a safe environment. Get him assistance. And so as we go through these, and I understand your literature and your scientific data and their fields, but that is a decision that I think has to be between the patient, the physician and their family support system, because at the end of the day, when I went in and found my son hanging by his curtain in his closet and had to pull him down and do CPR, that was a decision of, when we discussed these medications earlier, that we chose to go with this one because my insurance company, and I have a Cadillac plan, I'll be honest with you, but my insurance company said we're not going to pay for this medication, we want you to try this one first. If I'd have been 30 seconds later, I would be one child less in my family unit.

Dr. Kuhls: And I understand that totally, but at the same time, and what I'm trying to say is, if that psychiatrist, if all the psychiatrists would say this is the one drug to try first because it's the best, it would be simple. But that's, that's where we don't have that data to say that one's better than the other.

Ms. Puckett: Right, and I understand you don't have that data, but you also and I'm sorry, I don't know your name back there, the doctor who spoke first, but he was trying to get what he felt was in his client's best interests, medication to stabilize her life after a traumatic incident. The study was denied and he went though days and weeks and months, and when you're living in that hell every second of every day, it's very difficult. And with the certification and the tiered system, you're starting at the ones first that you've had on this market for a long time and trying to go through those. I think that the cost and the impact not only to law enforcement because the cost to my community and I live in Mustang, and the number of calls that they had to come to my house to respond to my child while we're trying to get him stabilized and going through different medications, that pulled them off the streets to responding to somebody else, and like I said, my insurance said no, try these first. Then if that doesn't work, you can go to this and this, and we finally escalated up to where he got on a plan. But this was months and weeks and how many calls, and how many risks because there were times when I was in fear of my life, my other children's life and the law enforcement officer's life.

Dr. Kuhls: I hear you totally and I agree totally that if we have a plan that we take two months to get the authorization back, if we have a plan who's doing that, we're going to have to change the plan and make it correct, okay? But unlike our other speaker said, I was the major person that said when we have a physician who wants a drug and has a reason that I don't want automatically somebody who doesn't have training to sit there to say no. But we set up a system where there's a psychiatrist that will call that doctor, talk to that doctor, try to get an understanding so that we can make an educated decision very quickly, and if you look at the plan, that plan for those tough cases are there in trying to make rapid decisions. And so I'm hoping that that will take care of the problem that was talked about, about months and months and months of waiting. Because that doesn't work. I agree with you totally.

Dr. Muchmore: The plan as set out is not months and months of waiting. It's 14 days ……

Dr. Kuhls: That's exactly right. Well that's with one medicine, but what I'm saying is that the physician, say, has a good reason to start another drug other than risperidone, okay, and there's some questions here, that's why it will go to the psychiatrist who can call that person, make some decisions very rapidly.

Ms. Puckett: So what is the timeline of their availability. Is there a 24-hour hotline, 48-hour hotline ……..

Dr. Muchmore: Remember, talking about 24 hours. You could have a panel of the finest psychiatrists in the world present a case to them and you won't get agreement over which drug to use on this patient. You still have a process that you go through and that process is what takes time. There's two things that takes time. Convincing the patient to take the medicine and, two, even if you have full access to this list, you still don't always pick the right one next.

Dr. Kuhls: Well I think, I think …… let's ask, okay? You and me. It says on page 24 here, I'll read it for you, okay? It says that the second opinion process; prior auth for the requested medicine is received by the prior authorization unit; clinical pharmacist contacts the on-call psychiatrist and provides information; on-call psychiatrist contacts physician who submitted the PA; on-call

psychiatrist contacts the clinical pharmacist with the review of the results; and then the person, the clinical pharmacist issues the appropriate response. How quickly, Shellie, do you think that this whole process should take?
Dr. Keast: I'm hoping pretty good, I mean we have 24-hour just on a petition turnaround, so just depends on how soon the two docs can get together.
Dr. Kuhls: So you're talking couple a days, a day, two days.
Dr. Keast: At most I would think, yeah, a couple of days.
Dr. Feightner: You can use 72 hour emergency supply as well at the pharmacy. You can get a 72 hour supply at any pharmacy, any, majority of pharmacies in the state. I can't say all, I don't know, but majority of pharmacies is 72 hours' supply of medicine while you're waiting for the authorization.
Dr. Muchmore: And we understand that this is a very important issue and needs to be handled correctly ……
Dr. Kuhls: But I think a second opinion process is very important and I think it should go quickly unlike our other speaker. I really think this is a new component, a very important component in this whole process to give some individualization.
Dr. Muchmore: And I would like to point out that Tier 1 medicine a few years ago would have been Tier 3 and everybody would have been screaming for it, but now it's Tier 1 so ……
Ms. Puckett: I was going to say, it's kind of like dial-up internet. Now we all want DSL and now we're beyond that, we want Wi-Fi. We want access everywhere we are.
Dr. Winegardener: It needs to be pointed out though, that the Tier 1 product that we're talking about, the literature shows that it's every bit as effective as any of the Tier 3 medications. I mean we're not throwing an aspirin at a problem that requires a Percocet. You know the Tier 1 medication is a good, good product and I think that's well supported in the literature and it works.
Dr. Muchmore: And I can remember when it was about the only one besides Clozaril around. It helped a lot of people.
Dr. Dennis (from the audience): Aren't there two drugs on Tier 1?
(unknown): Yes, clozapine and risperidone.
Dr. Dennis (from the audience): Clozapine's the gold standard. Why don't we force fail on that?
Dr. Bell: Because its' indications are so unique that everybody thought it ought to be Tier 1.
Dr. Muchmore: Clozapine's not for everybody. You have some people where it would be impossible to meet the registration requirements.
Dr. Bell: Indications are very specific for that.
Ms. Puckett: I appreciate your time and I appreciate your position. I understand that you're not taking that lightly.
Dr. Muchmore: Next speaker is Paul Davis from MHAT.
For Public Comment: Paul Davis, MHAT: Good evening. I've spoken on this before on behalf of my organization, which is the Mental Health Association in Tulsa, but I'm actually here to speak on behalf of other organizations of which we're members. The first is the Coalition of Advocates. It is an organization, it is a group of organizations actually, that represent mental health and addiction advocates in the state of Oklahoma; and the second is an organization called TOPICC, which the Oklahoma Partnership In Creating Change, and that's a consortium of more law enforcement/public safety minded organizations, the Chiefs of Police Association, Sheriffs' Association, district attorneys are members, as well as (unintelligible). And so those organizations have actually asked me to come speak on their behalf and express to you their concern with the proposal that you're putting forward today as well as their objections to it. Primarily they are concerned about the human cost that we're talking about. You've heard several speakers address this as well. And the comments that you've made about that is the research, and I've read the research because I didn't make my decision lightly either on this proposal. The research is very clear that across the population, all medications are equally effective, but the research is also very clear that the medications are different and individually, people respond to them differently. And so that's why we came to our conclusion that it's extremely important for open access because if we extrapolate from this population wide studies that say that medications are equally effective and we force individuals to try that medication, I think it's pretty clear that everybody that tries Risperdal or risperidone is not going to succeed on it. And so we're forcing everybody to do that though. Because we have determined that there isn't enough difference in success rates in the medications across populations, I think, right? So what we're saying as advocates is that it's pretty clear that right now the science and the research suggests that the medicines do not behave the same in every person and it's not an appropriate time to put this forward. If in the future more generics become available, there's more options that we can put on the front line, then it's probably a good time to look at this again. The Governor said last year that it was a bad time to do it. Nothing's changed since he made that statement except the budget. So what we're doing is we're prioritizing costs. The cost of medication over the cost of a human. And that human life is worth a lot more than that $7 million dollars. That human life is very important to us as advocates and we're asking that you as the Health Care Authority, that you as the Board, takes this a little slower. Let's spend a little bit more time reviewing the research to see if we can all come to a consensus. It's really clear that we have very different interpretations of this research. And what we as advocates are asking, is that you slow this down, that you give us the opportunity to have more input. We did meet with the Health Care Authority. We did have this conversation, and the input wasn't really considered. What we were trying to express is that it's too much to ask for multiple failures for an individual. It's too much to ask for this Board to prescribe medications for the members by requiring that every member take Risperdal, every new start take Risperdal, every new start, fail all Tier 2 medications. You're essentially forcing yourself into that triad that Stacey referred to; that patient, family and consumer to make that decision, and I just don't think it's appropriate to try to do that. So I'll gladly take questions.
Dr. Muchmore: Any questions? Okay, thank you.
Dr. Kuhls: Well I would just say, I would just say you have differences of opinion about the literature, but what I would love to see from you is a psychiatrist that can say this patient will work on this medication, this medication will work on this patient. This medicine will work on that patient, this patient's going to work on that, this medicine going to work on that patient.

Because that's not what out in the literature and it's not in the literature because nobody knows who can predict. And so then when you look at a lot of studies all the medicines are just as effective, and so I think what's important to say to you is that probably the most important thing is not to disagree with the literature, because the literature and the meta analyses and so on are there. But I think what's important for you to say to this Board is probably, there needs to be more better research done and that it's very important that over the next few years, as research comes out, that we reexamine each year the new research that's out there to see if we can start predicting which medicines are better. And if that is true, then we may need to change our recommendations at that time. Do you understand what I'm trying to say?

Mr. Davis: I do, and I kind of wish you had told me what to say before I had spoken, but …….

Dr. Kuhls: I'm just trying to help because I think this is not a one decision and we're going to forget about it and this is going to be the way to do it, be we're going to need to, as a group, look each year at what is the new literature out there, is there one drug that's better. That may happen, that may not happen, but this has got to be a thing that has to be looked at year to year to year.

Mr. Davis: And I think that you're right and you're accurate in the fact that the treatment of mental disease is more of an art than a science today. And that is troubling as an advocate and as a family member and as the full list of my descriptors, but the thing that we're saying isn't that a physician can say this is the right medication at the time. I think what we're saying is that a physician has an informed decision and we're taking that opportunity away from him or her because of this restriction. So I'd also like to actually make a comment. There are several individuals in the audience that weren't able to speak because of the restriction on the numbers because tonight, and which actually are not in pharmaceutical companies, and if the Board wanted to at their discretion, obviously, allow them to speak, that would be great. We'd appreciate by the advocates as well.

Dr. Muchmore: Thank you. I think the thing we need to keep pointing out is that we absolutely understand that certain individuals do better with certain drugs, and just ratchet back a few years when they were all available and all Tier 3 medicines if we'd tiered them. You still have to go through the process of finding the right medicine for the right person and that process still happens here, just a different starting point, but after that, you've got the whole list. Whereas I know a lot of people with good 3rd party insurance where they go, Geodon, nope, you can't have that. We're not doing that. Okay, any other comment? Dr. Bell, any comments? Any other comments from the Board? Okay, do we have a motion.

Dr. Kuhls moved to approve as submitted; seconded by Dr. Bell.

ACTION: MOTION CARRIED

(Post-motion comment: monthly feedback/reporting requested by the Board.)

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE ZIPSOR™, CAMBIA™, AND TO UPDATE NSAID PBPA CRITERIA, AND 30-DAY NOTICE TO PRIOR AUTHORIZE PENNSAID®**

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

Dr. Kuhls recommended changes in tier designations: Tier 1, Tier 2, and change Tier 3 to Special PA.

Tolectin is no longer on market and Dr. Muchmore recommended removing it from the list.*

Dr. Kuhls moved to approve with changes to tier designations and removal of Tolectin; seconded by Dr. Winegardener.

ACTION: MOTION CARRIED

(*Generic Tolectin is still available and will be removed if generic products are no longer available.)

AGENDA ITEM NO. 7: **VOTE TO PRIOR AUTHORIZE RIBAVIRIN CAPSULES, SOLUTION, AND DOSE PACKS**

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

Board recommended to change to " …… or for use in children 3 to 10 years of age" instead of 3 to 17 years of age.

Dr. Winegardener moved to approve as amended; seconded by Dr. Rhymer.

ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: **30-DAY NOTICE TO PRIOR AUTHORIZE TWYNSTA®**

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 9: **FDA & DEA UPDATES**

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 10: **FUTURE BUSINESS**

Materials included in agenda packet; submitted by Dr. Graham.

A: **Anxiolytic Criteria Review**
B: **Annual Review of Smoking Cessation Products**
C: **Annual Review of HFA Products**
D: **Annual Review of Growth Hormones**
E: **New Product Reviews**
ACTION: **NONE REQUIRED**

AGENDA ITEM NO. 11: **ADJOURNMENT**

The meeting was adjourned at 7:20 p.m.

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

Memorandum

Date: February 11, 2010

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 February 10, 2010

Recommendation 1: Vote to Prior Authorize Atypical Antipsychotics

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the addition of the Atypical Antipsychotics class to the Product Based Prior Authorization program. The following Tier lists have been reviewed and determined to be an acceptable combination 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 Healthcare Authority. The following are the recommendations for this category:

- Children less than 5 years of age will require a "second opinion" prior authorization to be reviewed by an OHCA-contracted child psychiatrist. Current users will be allowed to remain on current medication until the petition is submitted and reviewed. See Appendix 1 for second opinion process.
- For all members on atypical antipsychotics, after six months of use, a questionnaire will be sent to the prescriber to be filled out and returned for continuation of therapy. See Appendix 2 for suggested process for questionnaires.
- Requests for unusual dosing or indications will be referred to the OHCA-contracted psychiatrist for review.

- In addition, the College recommends the following tier structure and approval criteria:

Atypical Antipsychotics*

Tier 1	Tier 2	Tier 3†
risperidone (Risperdal®)‡ **clozapine (Clozaril®)**	Supplemental Rebated Tier-3 medications	olanzapine (Zyprexa®) quetiapine (Seroquel®) ziprasidone (Geodon®) aripiprazole (Abilify®) paliperidone (Invega®) quetiapine ER (Seroquel XR®) asenapine (Saphris®) clozapine (Fazaclo®) olanzapine/fluoxetine (Symbyax®) iloperidone (Fanapt™)

*Mandatory Generic Plan Applies
†May be rebated to Tier 2 status only
‡Includes Risperdal Consta

Approval Criteria for Tier 2 Medication:

1. Current users/inpatient discharge:
    a. Members currently stabilized on a higher tiered medication defined by paid claim(s) for the higher tiered medication in the past 90 days will be approved.
    b. Members being released from a hospital and stabilized on a higher tier medication will be approved.
2. Clinical conditions:
    a. Approvals will be granted for members with clinical conditions for which lower tiered drugs are contraindicated.
    b. Approvals will be granted for members whose current regimen includes drugs known to adversely interact with all lowered tiered drugs.
3. Step therapy:
    a. A trial of risperidone, at least 14 days in duration, titrated to recommended dose, that did not yield adequate response or resulted in intolerable adverse effects.

Approval Criteria for Tier 3 Medication:

1. Current users/inpatient discharge:
    a. Members currently stabilized on a higher tiered medication defined by paid claim(s) for the higher tiered medication in the past 90 days will be approved.
    b. Members being released from a hospital and stabilized on a higher tier medication will be approved.
2. Clinical conditions:
    a. Approvals will be granted for members with clinical conditions for which lower tiered drugs are contraindicated.
    b. Approvals will be granted for members whose current regimen includes drugs known to adversely interact with all lowered tiered drugs.

3. Step therapy:
    a. A trial of risperidone, at least 14 days in duration, titrated to recommended dose, that did not yield adequate response or resulted in intolerable adverse effects.
    b. A trial of all available Tier 2 medications, at least 14 days in duration, titrated to recommended dose, that did not yield adequate response or resulted in intolerable adverse effects.
    c. For aripiprazole and quetiapine: a diagnosis of depression requires current use of an antidepressant, and previous trials with at least two other antidepressants.

Recommendation 2: Vote to Prior Authorize Zipsor®, Cambia® and Update PBPA Category

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends placing Zipsor and Cambia into the NSAID Product Based Prior Authorization Program. The College of Pharmacy also recommends the following changes to the Tier Lists and Criteria for the NSAID Category.

NSAIDs (Non-Steroidal Anti-Inflammatory Drugs)		
Tier 1	**Tier 2**	**~~Tier 3~~ Special PA**
diclofenac ER (Voltaren® XR)	celecoxib (Celebrex®)	diclofenac epolamine (Flector®)
diclofenac potassium (Cataflam®)	diclofenac sodium / misoprostol (Arthrotec®)	diclofenac potassium (Zipsor®, Cambia®)
diclofenac sodium (Voltaren®)		diclofenac sodium (Voltaren Gel®)
etodolac (Lodine®)		indomethacin (Indocin®)
etodolac ER (Lodine® XL)		mefanamic acid (Ponstel®)
fenoprofen (Nalfon®)		naproxen sodium (Naprelan®)
flurbiprofen (Ansaid®)		piroxicam (Feldene®)
ibuprofen (Motrin®)		
ketoprofen (Orudis®)		
ketoprofen ER (Oruvail®)		
meclofenamate (Meclomen®)		
meloxicam (Mobic®)		
nabumetone (Relafen®)		
naproxen (Naprosyn®)		
naproxen sodium (Anaprox®)		
naproxen EC (Naprosyn® EC)		
oxaprozin (Daypro®)		
sulindac (Clinoril®)		
tolmetin (Tolectin®)		

Approval Criteria:

1. Criteria for the non-steroidal, anti-inflammatory drugs in Tier 2 are demonstrated by the following conditions:
    a. Previous use of at least two Tier 1 NSAID (from different product lines) plus a PPI
    b. For those with prior GI bleed who must have an NSAID, then a Tier 2 product may be approved (Celebrex should also be taken with a PPI).
2. Criteria for the non-steroidal, anti-inflammatory drugs ~~in Tier 3~~ in the Special PA category are demonstrated by the following conditions:
    a. Special indications, such as the diagnosis of gout for indomethacin, OR
    b. Previous use of at least two Tier 1 NSAID (from different product lines) AND
    c. Reason why a special formulation is needed over a Tier 1 product

Recommendation 3: Vote to Prior Authorize Ribavirin Capsules, Solution, and Dose Packs

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends placing a prior authorization on Ribavirin capsules, suspension and dose packs. Approval would be based on clinical supporting information regarding the inability of member to swallow, hypersensitivity to tablet formulation, medical reasons why member cannot take tablet formulation, or for use in children 3 to ~~17~~ 10 years of age (capsules and suspension only).

Appendix B

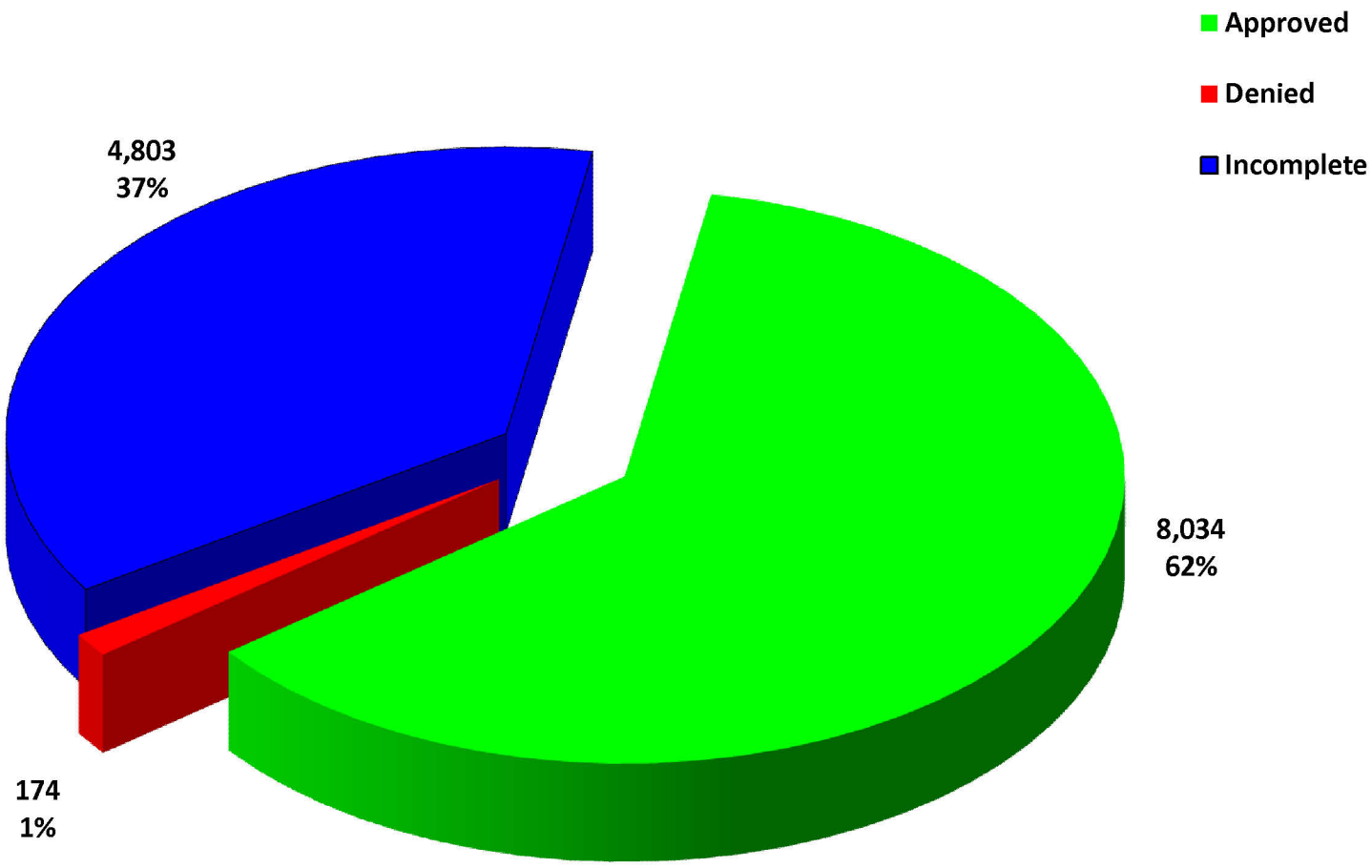
Retrospective Drug Utilization Review Report

Claims Reviewed for October 2009

Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
Total # of messages returned by system when no limits were applied	47,500	60,512	1,082,222	37,073
Limits which were applied	Established, Major, Males and Females, Age 51-60	Males and Females, Narcotics, Age 32-33	Contraindicated, Diabetes Mellitus, Males and Females Age 0-18	High Dose Only, Benzodiazepines, Males and Females, Age 20-70
Total # of messages after limits were applied	99	171	36	79
Total # of members reviewed after limits were applied	99	138	26	79

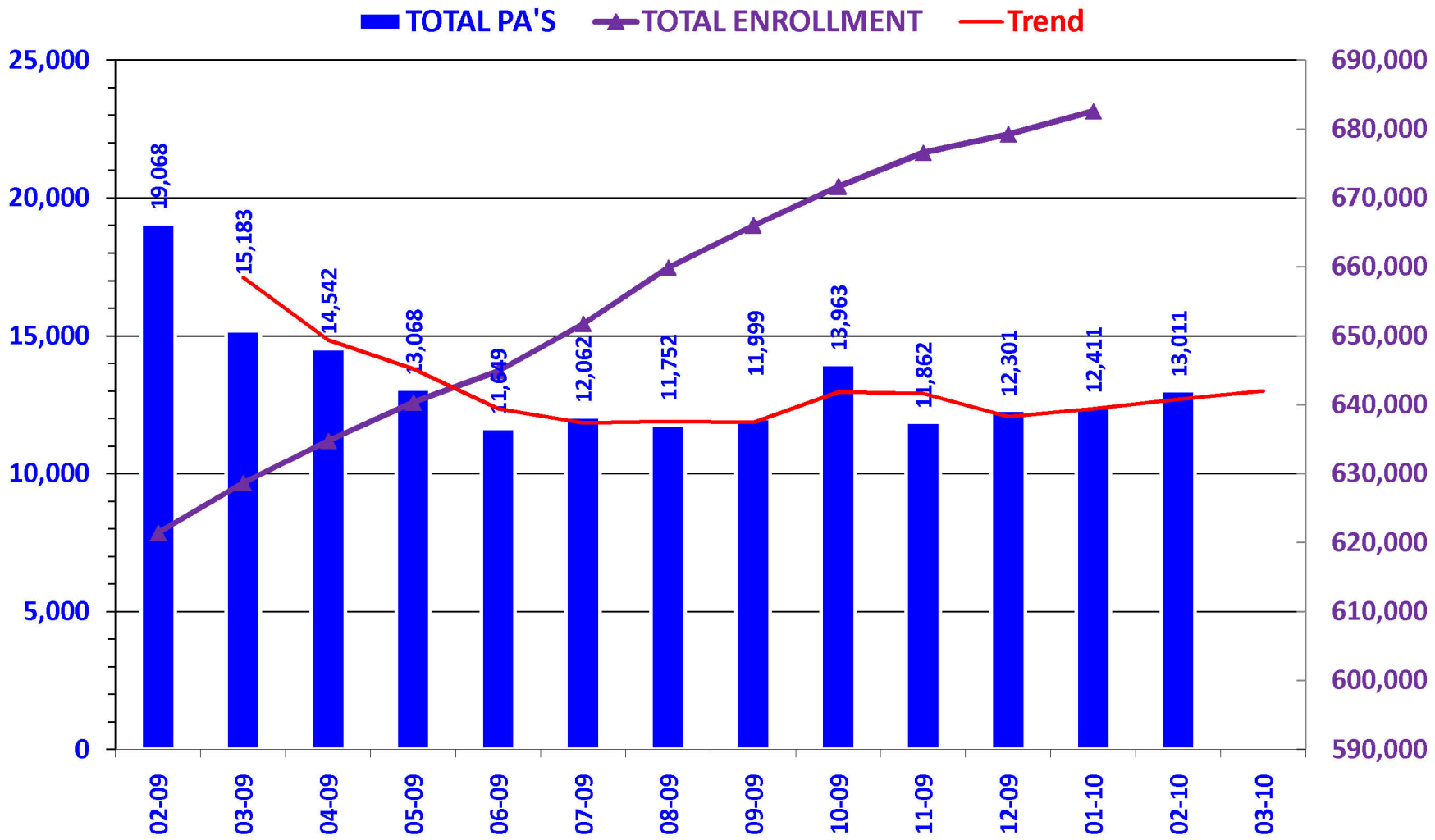
LETTERS			
Category	**Prescribers**	**Pharmacies**	**Total Letters**
Drug Interaction	8	0	8
Duplication of Therapy	84	13	97
Drug-Disease Precautions	0	0	0
Dosing & Duration	36	0	36
Total Letters Sent	128	13	141

PRIOR AUTHORIZATION ACTIVITY REPORT: February 2010



PA totals include overrides

PRIOR AUTHORIZATION REPORT: February 2009 – February 2010



PA totals include overrides

Prior Authorization Activity

February 2010

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort	517	270	2	245	357
Amitiza	25	9	0	16	269
Antidepressant	417	125	1	291	340
Antihistamine	323	172	0	151	286
Antihypertensives	139	53	0	86	338
Antimigraine	132	24	0	108	199
Benzodiazepines	4,577	3,985	11	581	89
Bladder Control	90	17	4	69	339
Byetta	13	2	0	11	364
Elidel/Protopic	40	23	1	16	88
ESA	156	120	2	34	56
Fibric Acid Derivatives	7	0	0	7	0
Fibromyalgia	170	60	3	107	334
Forteo	5	2	0	3	353
Glaucoma	29	6	0	23	362
Growth Hormones	44	36	3	5	155
HFA Rescue Inhalers	92	43	0	49	276
Insomnia	120	30	2	88	126
Misc Analgesics	56	10	19	27	144
Muscle Relaxant	187	72	54	61	46
Nasal Allergy	449	50	2	397	170
NSAIDS	167	39	6	122	218
Nucynta	3	2	0	1	47
Ocular Allergy	16	1	0	15	364
Ocular Antibiotics	24	7	0	17	13
Opioid Analgesic	184	85	4	95	171
Other	564	240	17	307	139
Otic Antibiotic	165	64	0	101	24
Pediculicides	77	29	2	46	17
Plavix	123	99	0	24	360
Proton Pump Inhibitors	641	98	4	539	98
Qualaquin (Quinine)	2	0	1	1	0
Singulair	690	355	1	334	276
Smoking Cessation	84	25	2	57	56
Statins	112	21	1	90	349
Stimulant	945	613	5	327	234
Symlin	2	1	0	1	364
Synagis	153	119	9	25	45
Topical Antibiotics	25	6	0	19	28
Topical Antifungals	30	7	0	23	24
Ultram ER and ODT	9	1	0	8	364
Xolair	2	1	0	1	358
Xopenex Nebs	48	25	0	23	231
Zetia (Ezetimibe)	30	23	0	7	360
Emergency PAs	0	0	0	0	
Total	**11,684**	**6,970**	**156**	**4,558**	

Overrides

Brand	113	94	1	18	182
Dosage Change	454	422	5	27	17
High Dose	2	0	0	2	0
IHS - Brand	80	67	0	13	102
Ingredient Duplication	7	6	0	1	22
Lost/Broken Rx	72	67	1	4	17
Nursing Home Issue	71	62	1	8	15
Other	20	19	0	1	32
Quantity vs. Days Supply	505	325	9	171	238
Stolen	1	0	1	0	0
Wrong D.S. on Previous Rx	2	2	0	0	360
Overrides Total	**1,327**	**1,064**	**18**	**245**	

Total Regular PAs + Overrides	**13,011**	**8,034**	**174**	**4,803**

Denial Reasons

Lack required information to process request.	2,326
Unable to verify required trials.	1,881
Does not meet established criteria.	202
Not an FDA approved indication/diagnosis.	166
Member has active PA for requested medication.	160
Considered duplicate therapy. Member has a prior authorization for similar medication.	114
Requested dose exceeds maximum recommended FDA dose.	68
Medication not covered as pharmacy benefit.	21
Drug Not Deemed Medically Necessary	4

Duplicate Requests: 849

Changes to existing PAs: 817

CALL VOLUME MONTHLY REPORT:
February 2009 – February 2010

Appendix C

VOTE TO UPDATE ANXIOLYTIC PRIOR AUTHORIZATION CATEGORY

OKLAHOMA HEALTHCARE AUTHORITY

MARCH 2010

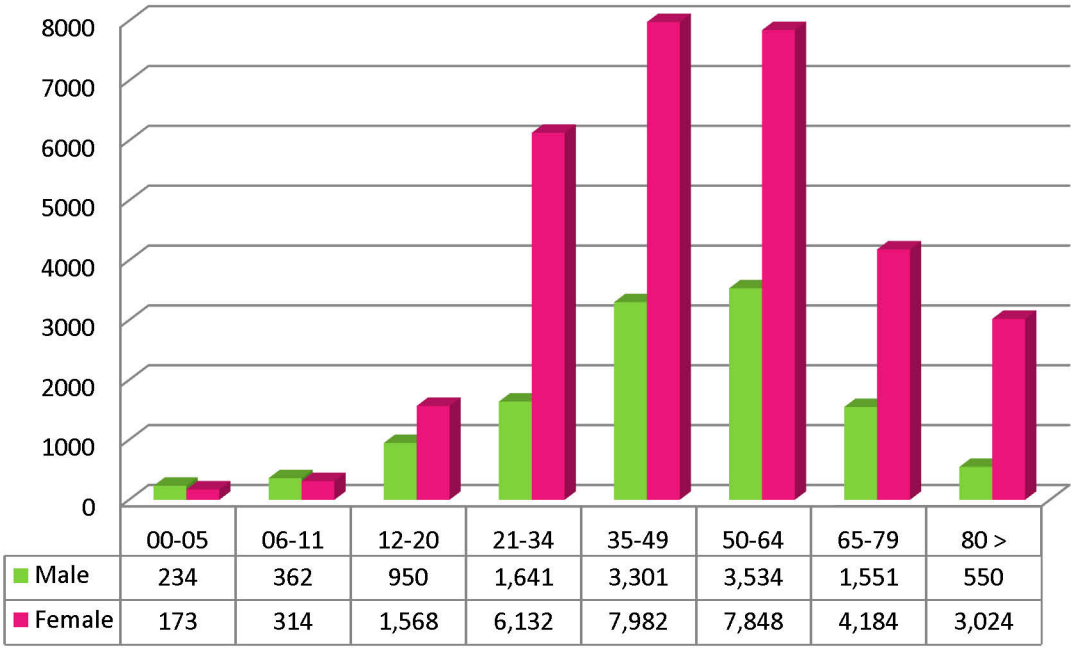
UTILIZATION REVIEW

CALENDAR YEAR 2009

RANK CLAIMS	RANK COST	PRODUCT	CLAIMS	UNITS	DAYS	MEMBERS	AMOUNT PAID	UNITS / DAY	CLAIMS /MEMEBER
1	1	Alprazolam	86,909	6,306,699	2,350,254	19,103	$872,544.82	2.68	4.55
2	2	Clonazepam	58,252	3,882,902	1,687,528	10,648	$552,249.85	2.30	5.47
3	3	Lorazepam	36,922	2,046,147	867,973	9,865	$323,159.51	2.36	3.74
4	4	Diazepam	30,382	2,003,530	769,722	8,703	$231,149.27	2.60	3.49
5	5	Chlorazepate	2,717	182,864	78,235	550	$49,438.66	2.34	4.94
6	7	Chlordiazepoxide	1,576	101,509	38,390	519	$15,102.82	2.64	3.04
7	6	Oxazepam	545	36,452	15,858	110	$16,483.96	2.30	4.95
			217,303	**14,560,103**	**5,807,960**	**43,386***	**$2,060,128.89**	**2.51**	**5.01**

*Unduplicated Members

MEMBER DEMOGRAPHICS



	00-05	06-11	12-20	21-34	35-49	50-64	65-79	80 >
Male	234	362	950	1,641	3,301	3,534	1,551	550
Female	173	314	1,568	6,132	7,982	7,848	4,184	3,024

38 Unknown

MEANS AND TOTALS FOR SELECTED VARIABLES

Variable	Value
Average Day Supply per Member	134
Average Units per Member	336
Number of Dual Eligibles	19,682 (45.4 %)
Number of Claims for Duals	112,032 (51.6 %)
Number of Members Under 21	3,601 (8.3 %)
Number of Claims for Members Under 21	12,038 (5.5 %)

TOP 10 PRESCRIBERS

Prescribers	Percent of Claims
Family Practitioner	34.5
Psychiatrist	16.0
Internist	12.9
General Practitioner	10.6
DDSD-NFM	4.6
Non-Contracted Prescriber	3.0
General Pediatrician	2.8
Physician Assistant	2.7
Nurse Practitioner	2.6
Neurologist	1.6

DAILY TABLET RANGES

Daily Tablet Range	Number of Members
</= 1 tablet daily	6,237
> 1 tablet daily to </= 2 tablets daily	12,848
> 2 tablet daily to </= 3 tablets daily	14,963
> 3 tablet daily to </= 4 tablets daily	6,687
> 4 tablets daily	2,651

PRIOR AUTHORIZATION ISSUES

CURRENT PRIOR AUTHORIZATION CRITERIA

- Members may receive two medications in this category if one is used during the day for one diagnosis and the other is used at night as a hypnotic agent; or if they are using two different strengths to reach a target dose not available in a single unit.
- Clarification of dosing schedule and diagnosis are important to assure that the member is not receiving duplicate therapy (e.g. an anxiolytic and hypnotic both dosed at bedtime).
- Additional information regarding recent attempts at dose reductions should be requested on recurrent petitions for high dose anxiolytic medications.

CURRENT PRIOR AUTHORIZATIONS ANNUALLY

Variable	Total
Total Prior Authorizations*	52,682
Total Approved	43,457 (82.5 %)
Total Denied	1,192
Total Incomplete	7,534
Total Members Requesting PA	18,039

*Currently clonazepam is not prior authorized.

CRITERIA APPROVED JUNE 2007

- Goal of the new criteria was to limit the number of members who use these medications chronically.
- Unable to implement complete criteria due to programming issues.
- Parts of new criteria are being used during manual PA processing, such as diagnostic criteria.
- Goal of this review is to revise the current criteria and lessen PA burden and administrative cost for pharmacies and prescribers.

RECOMMENDATIONS

PRIOR AUTHORIZATION

- Remove current PA requirements for members greater than 18 years of age.
- Members 18 or younger will require prior authorization. The criteria for approval would be as follows:
  - Chronic Behavioral Health Related Diagnosis:
    - Prescription written by a psychiatrist, AND
    - No concurrent ADHD medications (except Strattera), AND
    - No contraindicated indications, *AND*
    - Maximum dosing of 3 times daily.
  - Chronic Physical Diagnosis:
    - Up to TID dosing if a hypnotic is being used concurrently; up to QID otherwise.

SYSTEM EDITS

- Quantity limits set at 3 units per day for all products.
- No requests for dosing greater than 3 times daily will be approved unless a Chronic Physical Diagnosis exists; for these diagnoses the maximum allowed dosing would be 4 times daily.
- Current members will be given 2 months to taper dosing to no more than 3 doses daily.

PRODUR EDITS

- Therapeutic Duplication Module – currently set to notify pharmacies only (claims are suspended until pharmacy responds) of duplications of therapy for most major drug categories.
- Can be limited to antianxiety medications (would include buspirone) and set to deny when more than one product was being filled. (Claims would pay when multiple products are prescribed by a single physician.)

APPROVAL CRITERIA FOR PRODUR EDITS

When a claim fails a system or ProDUR edit a manual prior authorization will be required. Approval will be based on the following criteria related to reason for prior authorization.

QUANTITY LIMIT OVERRIDES

A member may receive more than 3 units per day if the following criteria exist:

1. The number of units per day is greater than 3, but less than the maximum daily dose for the product (or for a total daily dosing of TID).
2. The member has a Chronic Physical Diagnosis and a clinical reason for excessive units has been provided.

PRODUR THERAPEUTIC DUPLICATION OVERRIDES

A member may receive more than one anxiolytic concurrently if the following criteria exist:

1. The duplicate therapy is an injection or sublingual product to be given as needed when oral therapy cannot be administered.
2. The prescription is from a psychiatrist and a clinical reason for multiple products has been provided.
3. The member has a Chronic Physical Diagnosis and a clinical reason for multiple products has been provided.

DIAGNOSES GROUPS

CHRONIC PHYSICAL DIAGNOSES

For these physical medicine diagnoses, a yearly approval will be granted:

- Seizures,
- Epilepsy,
- Paralysis,
- MS,
- CP, and
- Muscular Dystrophy

CHRONIC BEHAVIORAL HEALTH DIAGNOSES

- Post Traumatic Stress Disorder
- Panic Disorder
- Obsessive Compulsive Disorder
- Social Phobia
- Severe Generalized Anxiety Disorder
- Major Depression Recurrent
- Bipolar Disorder

CONTRAINDICATED CO-MORBID CONDITIONS

- History of Substance Abuse/Dependence including Alcoholism.
- Antisocial Personality Disorder
- Cigarette Use

Appendix D

Vote to Prior Authorize Twynsta™ (telmisartan and amlodipine)

Oklahoma Health Care Authority
March 2010

Manufacturer	Boehringer Ingelheim
Classification	Angiotensin II Receptor Blocker (ARB) and Calcium Channel Blocker (CCB)
Status	Prescription Only

Twynsta™(telmisartan and amlodipine) is a combination of telmisartan, an angiotensin II receptor blocker, and amlodipine, a dihydropyridine calcium channel blocker, indicated for treatment of hypertension.

Recommendations

The College of Pharmacy recommends placement of Twynsta™ in Tier 3 of the ARBs (Angiotensin Receptor Blockers) and ARB Combination Products Product Based Prior Authorization Category. The existing criteria for this category will apply.

Tier-1	Tier-2	Tier 3
Any Tier-1 ACE Inhibitor:	amlodopine / valsartan (Exforge®)	amlodipine / olmesartan (Azor™)
benazepril (Lotensin®)	amlodopine / valsartan (Exforge® HCT)	candesartan (Atacand®)
captopril (Capoten®)	irbesartan (Avapro®)	candesartan / HCTZ (Atacand® HCT)
enalapril (Vasotec®)	irbesartan / HCTZ (Avalide®)	losartan (Cozaar®)
enalaprilat (Vasotec® IV)	telmisartan (Micardis®)	losartan / HCTZ (Hyzaar®)
fosinopril (Monopril®)	telmisartan / HCTZ (Micardis® HCT)	eprosartan (Teveten®)
lisinopril (Prinivil®, Zestril®)	valsartan (Diovan®)	eprosartan / HCTZ (Teveten® HCT)
moexipril (Univasc®)	valsartan / HCTZ (Diovan HCT®)	telmisartan/amlodipine (Twynsta™)
quinapril (Accupril®)	olmesartan (Benicar®)	
trandolapril (Mavik®)	olmesartan / HCTZ (Benicar HCT®)	

Mandatory Generic Plan applies.

Criteria

To qualify for a Tier 2 antihypertensive medication (or Tier 3 medication when no Tier 2 medications exist) there must be

- documented inadequate response to two Tier 1 medications, or
- adverse drug reaction to all Tier 1 class of medications, or
- previous stabilization on the Tier 2 medication, or
- a unique indication for which the Tier 1 antihypertensives lack

To qualify for a Tier 3 antihypertensive medication there must be

- documented inadequate response to two Tier 1 medications and documented inadequate response to all available Tier 2 medications, or
- adverse drug reaction to all Tier 1 or Tier 2 classes of medications, or
- previous stabilization on the Tier 3 medication, or
- a unique indication for which the lower tiered antihypertensives lack

Appendix E

Vote to Prior Authorize PENNSAID® (diclofenac sodium)

Oklahoma Health Care Authority, March 2010

Manufacturer Mallinckrodt Brand Pharmaceuticals, Inc.
Classification Non-Steroidal Anti-Inflammatory Drug
Status Prescription Only

PENNSAID® Summary

PENNSAID® is a non-steroidal anti-inflammatory drug indicated for treatment of the symptoms associated with osteoarthritis of the knee(s) only for a treatment regimen of not more than three months duration, whether continuous or intermittent. PENNSAID® is a solution formulation of diclofenac sodium containing 45% dimethyl sulfoxide (DMSO), propylene glycol, glycerin and alcohol and is intended for external use only. PENNSAID® is not recommended for use with other NSAIDs because of the absence of any evidence demonstrating synergistic benefits and the potential for additive side effects.

The dose of PENNSAID® is 40 drops per knee, 4 times a day. The procedure is to dispense 10 drops into the hand or directly onto the knee and then spread evenly around the front, back and sides of the knee and repeat this procedure until the recommended dose has been applied and the knee is completely covered. The most common adverse reactions were related to the application site. In the open-label uncontrolled long-term safety study, the withdrawal rate for an application site event was 14%.

Recommendations

The College of Pharmacy recommends placing PENNSAID® into the Special PA Category of the NSIAD Product Based Prior Authorization Program. The existing criteria will apply.

NSAIDs (Non-Steroidal Anti-Inflammatory Drugs)		
Tier 1	**Tier 2**	**Special PA**
diclofenac ER (Voltaren® XR)	celecoxib (Celebrex®)	diclofenac epolamine (Flector®)
diclofenac potassium (Cataflam®)	diclofenac sodium / misoprostol (Arthrotec®)	diclofenac potassium (Zipsor®, Cambia®)
diclofenac sodium (Voltaren®)		**diclofenac sodium (PENNSAID®)**
etodolac (Lodine®)		diclofenac sodium (Voltaren Gel®)
etodolac ER (Lodine® XL)		indomethacin (Indocin®)
fenoprofen (Nalfon®)		mefanamic acid (Ponstel®)
flurbiprofen (Ansaid®)		naproxen sodium (Naprelan®)
ibuprofen (Motrin®)		piroxicam (Feldene®)
ketoprofen (Orudis®)		
ketoprofen ER (Oruvail®)		
meclofenamate (Meclomen®)		
meloxicam (Mobic®)		
nabumetone (Relafen®)		
naproxen (Naprosyn®)		
naproxen sodium (Anaprox®)		
naproxen EC (Naprosyn® EC)		
oxaprozin (Daypro®)		
sulindac (Clinoril®)		
tolmetin (Tolectin®)		

Appendix F

30 Day Notice to Prior Authorize Mozobil® (plerixafor)

Oklahoma Health Care Authority, March 2010

Manufacturer	Genzyme
Classification	Hematopoietic
Status	Prescription Only

Plerixafor Summary

Plerixafor is a hematopoietic stem cell mobilizer indicated in combination with granulocyte-colony stimulating factor (G-CSF) for the harvesting of peripheral blood stem cells in patients with non-Hodgkin's lymphoma (NHL) and multiple myeloma (MM). Perixafor is a first in class CXCR4 receptor antagonist. CXCR4 and stromal cell derived factor-1 alpha (SDF-1α) have key regulatory roles in stem cell movement into and out of the bone marrow. Plerixafor blocks the CXCR4/SDF-1α interaction, releasing stem cells from the bone marrow into the circulating blood. Clinical studies show an increase in the number of stem cells harvested in fewer apheresis sessions, and more patients were able to proceed to transplant on this therapy than those receiving placebo.

Plerixafor treatment should be administered after the patient has received G-CSF once daily for four days. It is then administered as a subcutaneous injection beginning approximately 11 hours prior to initiation of each apheresis session, for up to four consecutive days. The most common adverse reactions (occurring in greater than or equal to 10% of patients) during HSC mobilization and apheresis were: diarrhea, nausea, fatigue, injection site reaction, headache, arthralgia, dizziness, and vomiting. Thrombocytopenia has been observed in patients receiving plerixafor, and monitoring platelet counts during therapy is recommended.

Plerixafor is currently contraindicated for use in patients with leukemia due to the potential to mobilize leukemia cells and subsequently contaminate the apheresis product. However, this potential is present with all types of tumor cells, and the effect of possible reinfusion of tumor cells has not been well-studied to date. Plerixafor has also been shown to cause splenomegaly in rats, so patients with abdominal pain during therapy should be evaluated. Also, this compound has been shown to be teratogenic in animals, so women of child-bearing potential should be counseled and advised to take measures to avoid pregnancy during therapy.

The current cost of a 24 mg/1.2mL vial of Mozobil® is $5,500. The cost per milligram is approximately $229. At the recommended dosing of 0.24 mg/kg, using an average patient weight of 75 kg, the cost of one cycle of therapy would be $16,488 if the patient has the maximum four days of treatment. The number of cycles needed would depend on the patient's response to transplant.

Plerixafor is currently being evaluated in clinical trials for use in other types of cancers such as myelodysplastic syndromes (MDS), acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL), chronic lymphocytic leukemia (CLL), and small lymphocytic lymphoma (SLL). It is also being evaluated for use in a condition called WHIMS (warts, hypogammaglobulinemia, infection, and myelokathexis syndrome), a genetic disorder that causes mature neutrophils to be retained within the bone marrow rather than being released to the general blood circulation.

Recommendations

Currently, this medication has been placed on prior authorization status for medical claims. The College of Pharmacy recommends pharmacy prior authorization of Mozobil® (plerixafor) with the following criteria.

Criteria for approval:

1. FDA approved indication of use in combination with granulocyte-colony stimulating factor (G-CSF) to mobilize hematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in patients with non-Hodgkin's lymphoma (NHL) and multiple myeloma (MM).
2. MUST have a cancer diagnosis of non-Hodgkins's lymphoma (NHL) or multiple myeloma (MM). This medication is NOT covered for the diagnosis of leukemia.
3. Prescribed by an oncologist only.
4. Patient must be at least 18 years of age.
5. Patient must not be pregnant or become pregnant during treatment. Female patients with reproductive potential need to use effective contraceptive methods during plerixafor use.
6. Must have either a prior stem cell collection failure or a history of heavy pre-treatment.
7. Must be given in combination with the granulocyte-colony stimulating factor (G-CSF) Neupogen® (filgrastim).
8. **Dosing (requires current body weight in kilograms):**
    a. Recommended dose is 0.24 mg/kg, maximum dose is 40mg/day, administered 11 hours prior to apheresis for up to 4 consecutive days. (USE ACTUAL BODY WEIGHT).
    b. Dosing for renal impairment:
        i. Creatinine clearance ≤ 50 mL/min: 0.16 mg/kg, maximum of 27 mg/day.
9. Approval period will be for two months.

Product Details

Indication- Plerixafor is for use in combination with granulocyte-colony stimulating factor (G-CSF) for the harvesting of peripheral blood stem cells in patients with non-Hodgkin's lymphoma (NHL) and multiple myeloma (MM).

Dosage Forms- Plerixafor is supplied as a solution for subcutaneous injection at a concentration of 20mg/mL. Inactive ingredients in the solution are sodium chloride, hydrochloric acid, water, and sodium hydroxide.

Contraindications- as of February 4, 2010, no specific contraindications have been determined.

Pregnancy Risk Category D

Warnings and Precautions-

- **Tumor cell mobilization in leukemia patients-** this drug may mobilize leukemic cells and contaminate the apheresis product; use of plerixafor is not recommended in these cases.
- **Leukocytosis-** if peripheral blood counts are above 50,000/mL, monitoring is recommended.
- Dose reduction recommended for patients with moderate to severe renal impairment (CrCl less than 50mL/min).
- **Thrombocytopenia-** has been reported; monitoring platelets is recommended
- **Pregnancy-** teratogenic in animals, so women of childbearing potential should avoid pregnancy using effective contraception.
- **Splenomegaly-** has been reported in rats; evaluate patients who report abdominal pain and/or scapular or shoulder pain for splenic integrity.
- **Renal impairment-** adjust dose for CrCl ≤ 50.

Common Adverse Reactions-

- **Dermatologic-** Injection site reactions including erythema, hematoma, hemorrhage, induration, inflammation, irritation, pain, paresthesia, pruritus, rash, swelling, and urticaria (34%).
- **Gastrointestinal-** Diarrhea (37%), nausea (34%), vomiting (10%), flatulence (7%).
- **Hematologic-** Thrombocytopenia.
- **Musculoskeletal-** Arthralgia (13%).
- **Neurologic-** Headache (22%), dizziness (11%), insomnia (7%).
- **Other-** Fatigue (27%).

Drug Interactions-

- No known significant drug interactions.

Patient Information-

- Do not use this medication if you have experienced or suspect an allergic reaction to it.

- Do not use this medication if you are pregnant, and avoid becoming pregnant while you are on this medication by using effective contraception.
- This drug is given as a shot under your skin and will be administered by a nurse or other trained health care professional.
- This drug should be started after you have received G-CSF (filgrastim, pegfilgrastim) and will be given once a day for 4 consecutive days.
- Make sure your doctor knows if you are breastfeeding, or if you have kidney disease, an enlarged spleen, bone marrow problems (such as leukemia), or blood disorders (such as leukocytosis, thrombocytopenia).
- If you experience pain in the upper left part of your abdomen or at the tip of the left shoulder, alert your doctor right away. This could be a symptom of a serious side effect with your spleen.
- If you experience a slow heartbeat, severe or unusual tiredness/weakness, cold sweats, confusion, dizziness, faintness, or lightheadedness when getting up from a lying or sitting position after you get the injection, notify your doctor.
- If you develop a skin rash, hives, swelling around the eyes, shortness of breath, or any allergic reaction to this medicine, stop taking the medicine and check with your doctor right away.
- This medicine can cause diarrhea, nausea, vomiting, or stomach upset, but these side effects can be controlled, ask your doctor or nurse for control methods if you experience any of these side effects.
- Your blood will need to be checked during your regular doctor's appointments, so be sure you attend all of your scheduled appointments.

REFERENCE

Product Information: MOZOBIL®subcutaneous injection, plerixafor subcutaneous injection. Genzyme Corporation, Cambridge, MA, 2008. Plerixafor monograph. Lexi-Comp, Inc. (Lexi-Drugs) Lexi-Comp, Inc. Accessed February 17, 2010.

30 Day Notice to Prior Authorize Nplate® (romiplostim)

Oklahoma Health Care Authority, March 2010

Manufacturer	Amgen, Inc.
Classification	Thrombopoietin Receptor Agonist
Status	Prescription Only

Nplate® Summary

Nplate® is a thrombopoietin (TPO) receptor agonist indicated for the treatment of thrombocytopenia in patients with chronic immune (idiopathic) thrombocytopenia purpura (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. It should be reserved for patients with ITP whose severity of thrombocytopenia and clinical presentation increases the risk for bleeding and should not be used as an attempt to normalize platelet counts. Nplate® increases platelet production through binding and activation of the TPO receptor, increasing platelet production at a rate that outpaces destruction due to disease.

Nplate® is administered weekly as a subcutaneous injection, and is available only through a restricted distribution program called the Nplate® NEXUS (Network of Experts Understanding and Supporting Nplate® and Patients) Program. Only prescribers and patients registered with the program are able to prescribe, administer, and receive the product. CBC's, including platelet counts and peripheral blood smears, must be monitored very closely during therapy. Weekly monitoring is required until a stable dose has been achieved, then at least monthly thereafter. It is important to keep the patient's platelet levels from approximately 50 x 10^9/L to 200 x 10^9/L to reduce the risk of thrombotic/thromboembolic complications.

The most serious adverse reactions associated with Nplate® in clinical studies were bone marrow reticulin deposition and worsening thrombocytopenia after Nplate® discontinuation. Other adverse events seen at a high rate include headache, fatigue, arthralgia, and epistaxis. Patients should be monitored carefully for response to therapy. It should be noted that hyporesponsiveness or failure to maintain a platelet response with Nplate may be due to factors such as neutralizing antibodies to the product or bone marrow fibrosis. Antibody formation can be detected by submitting a blood sample to Amgen for assay.

The current cost of a 250 mcg vial of Nplate® is $1145, and the cost of a 500 mcg vial is $2289. The cost per microgram is $4.58. In phase 3 clinical trials, the median weekly dose for non-splenectomized patients was 2 mcg/kg and 3 mcg/kg for splenectomized patients. Using an average patient weight of 75 kg, the cost of one year of therapy would be approximately $35,724-$53,586.

Nplate® is currently being evaluated in clinical trials for treatment of thrombocytopenia in patients with patients who have low or intermediate risk Myelodysplastic Syndrome (MDS); patients with advanced malignancy receiving treatment with carboplatin; and in patients with Non-Hodgkin's Lymphoma.

Recommendations

The College of Pharmacy recommends prior authorization of Nplate® with the following criteria.

Criteria for approval:

1. FDA approved indication of chronic immune (idiopathic) thrombocytopenia purpura (ITP)
2. Previous insufficient response to treatment with corticosteroids, immunoglobulin, or splenectomy
3. Recent platelet count of < 50 x 10^9/L
4. Prescriber must be enrolled in the Nplate NEXUS (Network of Experts Understanding and Supporting Nplate and Patients) Program
5. Recent patient weight in kilograms for dosing purposes; initial dosing is 1 mcg/kg once weekly as a subcutaneous injection
6. **Continuation criteria:**
    a. Weekly CBCs with platelet count and peripheral blood smears until stable platelet count (≥ 50 x 109/L for at least 4 weeks without dose adjustment) has been achieved; then obtain monthly thereafter
    b. Dosing adjustments:
        i. Platelets < 50 x 10^9/L, increase dose by 1 mcg/kg
        ii. Platelets > 200 x 10^9/L for 2 consecutive weeks, reduce dose by 1 mcg/kg
        iii. Platelets > 400 x 10^9/L, do not dose. Continue to assess platelet count weekly. When platelets < 200 x 10^9/L, resume at a dose reduced by 1 mcg/kg
7. **Discontinuation criteria:**
    a. Platelet count does not increase to a level sufficient to avoid clinically important bleeding after 4 weeks of therapy at the maximum weekly dose of 10 mcg/kg
8. Approval period will be for four weeks initially, and then quarterly.

Product Details

Indication – Nplate® is indicated as a treatment for thrombocytopenia in patients with chronic immune idiopathic thrombocytopenic purpura (ITP) who have had an insufficient response to corticosteroids, immunoglobulin, or splenectomy. It should be reserved for patients with ITP whose severity of thrombocytopenia and clinical presentation increases the risk for bleeding and should not be used as an attempt to normalize platelet counts.

Dosage forms –Nplate® is available as a single-dose vial containing 250 mcg or 500 mcg of romiplostim as a sterile, lyophilized, solid white powder. The inactive ingredients are L-histidine, sucrose, mannitol, polysorbate 20, and hydrochloric acid.

Contraindications – None reported as of February 3, 2010.

Pregnancy Risk Category: C

Warnings and Precautions – Prescribers and patients must be enrolled in the Nplate® NEXUS (Network of Experts Understanding and Supporting Nplate and Patients) Program. Only those registered may prescribe, administer, or receive this product.

- **Antibody development-** has been reported; if suspected, contact Amgen for assays to detect neutralizing antibodies to romiplostim and thrombopoietin
- **Bone marrow fibrosis-** new or worsening; increased risk; monitoring recommended
- **Bone marrow reticulin formation-** has been reported; monitoring recommended
- **Failure to respond or maintain a response-** possibly due to neutralizing antibodies to romiplostim or bone marrow fibrosis
- **Worsened thrombocytopenia upon discontinuation-** may increase risk of bleeding, monitoring recommended.
- **Thrombotic and thromboembolic complications-** may result from excessive platelet count increases; romiplostim should not be used to normalize platelet counts.

Common adverse reactions –

- **Central nervous system –** headache (35%), fatigue (33%), dizziness (17%), insomnia (16%).
- **Gastrointestinal –** diarrhea (17%), nausea (13%), abdominal pain (11%), dyspepsia (7%).
- **Neuromuscular & skeletal –** arthralgia (26%), myalgia (14%), back pain (13%), limb pain (13%), shoulder pain (8%), paresthesia (6%).
- **Respiratory –** epistaxis (32%), upper respiratory infection (17%).
- **Miscellaneous –** antibody formation (romiplostim 10%; TPO 5%).

Drug interactions – No formal drug interactions studies have been performed as of February 3, 2010.

Patient information –

- **Lab monitoring -** CBC with differential at baseline, during treatment (weekly until platelet response stable for 4 weeks, then monthly), and weekly for 2 weeks after treatment is completed.
- You should also receive a Medication Guide, discuss therapy and associated risks with your prescriber, and sign an enrollment form prior to beginning treatment. You should receive and read a new Medication Guide prior to each treatment, as information may be added.
- You must be enrolled in Nplate NEXUS program and may only receive injections from prescribers also enrolled in the program to ensure proper use.
- Doses may be adjusted by your physician according to changes in your platelet count.
- You will receive a weekly subcutaneous injection under the skin.

- If a dose is missed, contact your provider as soon as possible. Missed doses can increase your bleeding risk.
- Nplate is not intended to restore your platelet counts to normal.

REFERENCE
Product Information: Nplate(TM) subcutaneous injection, romiplostim subcutaneous injection. Amgen, Inc, Thousand Oaks, CA, 2008.
Romiplostim monograph. Lexi-Comp, Inc. (Lexi-Drugs) Lexi-Comp, Inc. Accessed February 17, 2010.

30 Day Notice to Prior Authorize Arcalyst® (rilonacept)

Oklahoma Health Care Authority, March 2010

Manufacturer	Regeneron Pharmaceuticals, Inc.
Classification	Immunological Agent/Interleukin-1 Inhibitor
Status	Prescription Only

Rilonacept Summary

Rilonacept is an interleukin-1 blocker indicated for the treatment of Cryopyrin-Associated Periodic Syndromes (CAPS), including Familial Cold Auto-Inflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS) in adults and children 12 and older. CAPS refer to rare genetic syndromes, generally caused by mutations in the NLRP-3 gene, which encodes the protein cryopyrin. This protein is an important component of the inflammasome, which becomes overactive causing an excessive release of activated interleukin-1 beta (IL-1β) that drives inflammation. Symptoms include fever, urticaria-like rash, arthralgia, myalgia, fatigue, and conjunctivitis. Rilonacept is a dimeric fusion protein containing portions of human IL-1 receptor (IL-1RI and IL-1RAcP) and is expressed in recombinant Chinese Hamster Ovary (CHO) cells. Rilonacept blocks IL-1β by acting as a soluble decoy receptor, binding IL-1β and preventing its interaction with cell surface receptors.

Rilonacept is given as subcutaneous injection once weekly. The first injection should be performed under the supervision of a qualified healthcare professional. If a patient or caregiver is to administer this medication, he/she must be instructed on aseptic handling and proper injection technique, including rotation of injection sites. Prior to initiation of therapy vaccination history should be reviewed. There is an increased risk of secondary transmission of infection by live vaccines and also the possibility of reduced effectiveness of immunization while taking rilonacept.

The most common adverse reactions reported with rilonacept are injection site reactions, reported in 48% of patients. These were generally mild to moderate effects lasting 1-2 days and included erythema, swelling, pruritus, mass, bruising, inflammation, pain, edema, dermatitis, discomfort, urticaria, vesicles, warmth, and hemorrhage. Increased risk of infections was also been associated with rilonacept therapy. Upper respiratory infections, including bronchitis and sinusitis, occurred in a significant percentage of patients during trials. Some of the most serious adverse events were related to infection, including a case of *Mycobacterium intracellulare* and a case of *Streptococcus pneumoniae* meningitis. For this reason, it is not recommended to take other medications that block IL-1 or TNF-blocking agents concomitantly with rilonacept due to the increased risk of serious infections and neutropenia.

The current cost of a 220mg vial of rilonacept is $5280. It is given as a weekly injection, with a loading dose the first week of 320mg then 160mg weekly thereafter. For the first year of therapy for one adult patient, the cost would be approximately $279,840.

Rilonacept is currently being evaluated in clinical trials for treatment of several other conditions, including diabetes mellitus type 1, juvenile idiopathic arthritis, atherosclerosis, and the prevention of gout exacerbations.

Recommendations

The College of Pharmacy recommends prior authorization of Arcalyst® with the following criteria.

Criteria for approval:

1. FDA approved indication of Cryopyrin-Associated Periodic Syndromes (CAPS). This includes Familial Cold Auto-inflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS) in adults and children 12 and older.
2. Arcalyst should not be given to patients concomitantly with TNF-blocking agents, such as Enbrel (etanercept).
3. Should not be initiated in patients with active or chronic infection.
4. Dosing should not be more often than once weekly.
5. **Approved dosing schedule for adults 18 and over:**
    a. Initial treatment: loading dose of 320 mg delivered as two 2mL subcutaneous injections of 160 mg each given on the same day at two different injection sites.
    b. Continued treatment is one 160 mg injection given once weekly.
6. **Approved dosing schedule for pediatric patients aged 12-17 years (must have patient weight in kilograms):**
    a. Initial treatment: loading dose of 4.4 mg/kg, up to a maximum of 320 mg, delivered as one or two subcutaneous injections with a maximum single-injection volume of 2mL.
    b. Continued treatment is 2.2 mg/kg, up to a maximum of 160 mg, given once weekly.
7. Approval period is for one year.

Product Details

Indication- Cryopyrin-Associated Periodic Syndromes (CAPS) which includes Familial Cold Autoinflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS) in patients 12 years of age and older.

Dosage Forms- Rilonacept is supplied as a lyophilized powder for injection (220mg per vial). It must be reconstituted with 2.3mL of sterile water leaving it at a concentration of 80mg/mL. The inactive ingredients are histidine, arginine, polyethylene glycol 3350, sucrose, and glycine.

Contraindications- as of February 17, 2010, no specific contraindications have been indicated for rilonacept.

Pregnancy Risk Category C

Warnings and Precautions-

- **Concurrent use of live vaccines or tumor necrosis factor (TNF) inhibitors** is not recommended
- **Infections, chronic or active-** potential for exacerbation; discontinue if a serious infection develops
- **Hypersensitivity** reactions have occurred
- **Latent tuberculosis** should be treated prior to initiating rilonacept
- **Lipid profile changes-** monitoring is recommended, especially in patients with cardiovascular risk factors
- **Increased risk of malignancies-** treatment with immunosuppressants may result in an increase in the risk of malignancies

Common Adverse Reactions-

- **Dermatologic-** injection site reactions (48%) including erythema, swelling, pruritus, bruising, inflammation, pain, edema, dermatitis, urticaria, and hemorrhage, usually lasting 1 to 2 days.
- **Immunologic-** antibody development (35%), infectious disease (18-48%)
- **Neurologic-** hypoalgesia (9%)
- **Respiratory effects-** upper respiratory infection (26%), cough (9%), sinusitis (9%)
- **Endocrine/metabolic-** increased lipid profiles

Drug Interactions-

- **TNF blocking agents and IL-1 blocking agents (anakinra, adalimumab, etanercept, infliximab) -** increased risk of serious infections and neutropenia as well as increased adverse reactions.
- **CYP450 Substrates-** production of CYP450 enzymes are suppressed when cytokines, such as IL-1, are increased during chronic inflammation. Rilonacept may decrease this chronic inflammation and possibly lead to a normalization of P450 levels. Drugs that may require additional monitoring: alfentanil, astemizole, cisapride, cyclosporine, tacrolimus, ergotamines, fentanyl, paclitaxel, quinidine, phenytoin, pimozide, sirolimus, terfenadine, theophylline, thioridazine, tizanidine, and warfarin.
- **Live vaccines-** increased risk of secondary transmission of infection by the live vaccine and reduced effectiveness of immunization

Patient Information-

- Arcalyst® can lower you ability to fight off infections, serious life-threatening infections and death have occurred while taking it.
- Do not use Arcalyst® if you have an infection or have one that keeps coming back (chronic infection).
- If you get any sign of an infection, such as a fever, cough, flu-like symptoms or open sores on your body, contact your doctor immediately.

- Do not take other medications that block IL-1 or TNF, such as: etanercept, adalimumab, infliximab, or anakinra. These may increase your risk of getting a serious infection.
- Before starting Arcalyst® tell your doctor if you think you have an infection, are begin treated for an infection, have signs of an infection or open sores on your body, if you have asthma, diabetes or an immune system problem, if you have HIV, Hepatitis B or Hepatitis C, if you have TB or have been in close contact with someone with TB, or if you are taking other medications that may affect your immune system.
- Ask your doctor if you require any vaccinations, including pneumonia and influenza vaccines.
- Tell your doctor if you are scheduled to receive any vaccines, if you are pregnant or are planning to become pregnant, or if you are breast feeding.
- Tell your doctor all the medications you are taking including vitamins, herbals and especially corticosteroids.
- Arcalyst® is given as a once a week injection under the skin, do not attempt to give the injections until you or your caregiver fully understands how to do so. Your healthcare provider or pharmacist can answer any questions about preparing and injecting your dose.
- Arcalyst® should be stored in the refrigerator and away from light before use; once it is reconstituted it can be kept at room temperature, but must be used within three hours of mixing.
- If you miss a dose, inject it as soon as you can, up to the day that the next injection is due. Take the next dose on your regular schedule and do not double up or increase your dose to make up for a missed one.
- Do not injected into areas that are tender, red or hard.
- Injection sites should be rotated to avoid irritation and to ensure proper absorption of the medication.

- Steps for Arcalyst® use:
    - Wash your hands with soap and water before handling injection supplies.
    - Be sure and clean the tops of the vials you are withdrawing and injecting into with alcohol swabs before entry, use a different alcohol swab for each vial.
    - Inject 2.3mL of air into the sterile water vial and then 2.3mL of sterile water should be withdrawn from the sterile water vial into a syringe.
    - Make sure all air bubbles are removed from the syringe before injecting into the Arcalyst® vial.
    - Inject the sterile water into the Arcalyst® vial and let it sit for 1 minute, if it is not completely dissolved, shake it for 30 seconds and then wait 1 more minute (repeat this process until all of the Arcalyst® is dissolved). The mixed Arcalyst® should be thick, clear and colorless to pale yellow. Do not use the Arcalyst® if the solution is discolored, cloudy or has particulates in it.
    - Using a new syringe and needle inject 2mL of air into the Arcalyst® vial and then withdraw 2mL of the Arcalyst® solution into the syringe, making sure no air bubbles are in the syringe.
    - The Arcalyst® vial can now be discarded into the puncture resistant container, never save the remaining medication in the vial for another use.
    - You should inject yourself in the left or right abdomen or the left or right thigh, if the injection is being given to you by a caregiver the upper left and right arms may be used. Be sure to clean the area of skin to be injected with an alcohol swab before the injection occurs and let it dry completely.
    - A small amount of skin should be pinched up and with a quick dart like motion enter that skin with the needle at a 90° angle (for small children or people with little fat under their skin the injection angle can be at 45°.
    - Once the needle is properly inserted into the skin pull back on the plunger gently and if NO blood appears in the syringe then inject the full contents of the syringe. If blood appears withdraw the needle from your skin and restart from the first step with all new supplies.
    - Once the injection is complete withdraw the needle from your skin and place a piece of sterile gauze over the injection site for several seconds.

- Once the injection is complete do not attempt to recap the needle.
- Throw the syringe and needle away in the in the puncture resistant container.
- Do not reuse needles or syringes and do not try to recap the needle.
- Never throw away needles, syringes or vials in your household trash.

REFERENCE

Product Information: ARCALYST(TM) subcutaneous injection, rilonacept subcutaneous injection. Regeneron Pharmaceuticals,Inc, Tarrytown, NY, 2008.

Rilonacept monograph. Lexi-Comp, Inc. (Lexi-Drugs) Lexi-Comp, Inc. Accessed February 17, 2010.

Appendix G

Annual Review of Xopenex and Albuterol HFA Products

Calendar Year 2009

Oklahoma HealthCare Authority

March 2010

Current Prior Authorization Criteria*

Short Acting B2 Agonists	
Tier 1	**Tier 2**
ProAir® HFA 90mcg/inhalation**	**Xopenex® HFA 45mcg/inhalation**
Proventil® HFA 90mcg/inhalation**	
Ventolin® HFA 90mcg/inhalation**	

* Voted on November 2008, Implemented January 14, 2009

**supplemental rebate

The following is the approval criteria:

1. Approved or clinically accepted indication, and
2. Specific reason member cannot use all available tier one products.
3. Quantity limits per 30 day supply:

Product	Quantity
Proair HFA	**2 units (17 grams)**
Xopenex HFA	**2 unit (30 grams)**
Proventil HFA	**2 unit (13.4 grams)**
Ventolin HFA	**2 unit (36 grams)**

Utilization and Comparison: HFA Products CY 2008 and CY 2009

Tier-1 HFA Products

Calendar Year	Total Members	Total Claims	Total Cost	Cost per Claim	Per-Diem	Total Units	Total Days
2008†							
	43,075	90,687	$3,853,529.08	$42.49	$1.82	949,364	2,121,745
2009*							
	64,861	140,935	$6,472,572.21	$45.93	$1.94	1,637,651	3,343,052
Percent Change	**50.6%**	**55.4%**	**68.0%**	**8.1%**	**6.6%**	**72.5%**	**57.6%**
	21,786	**50,248**	**$2,619,043.13**	**$3.44**	**$0.12**	**688,287**	**1,221,307**

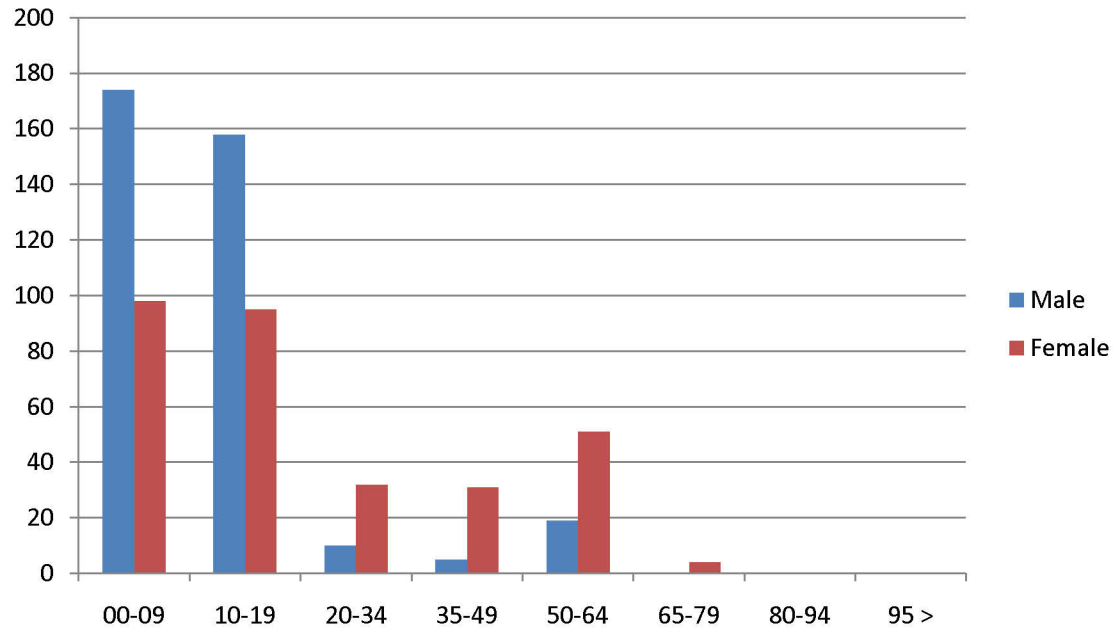
†In 2008 there were approximately 42,791 claims for MDI products which would have cost $1,818,190 if HFAs had been dispensed.
*Generic MDI no longer available.

Xopenex HFA

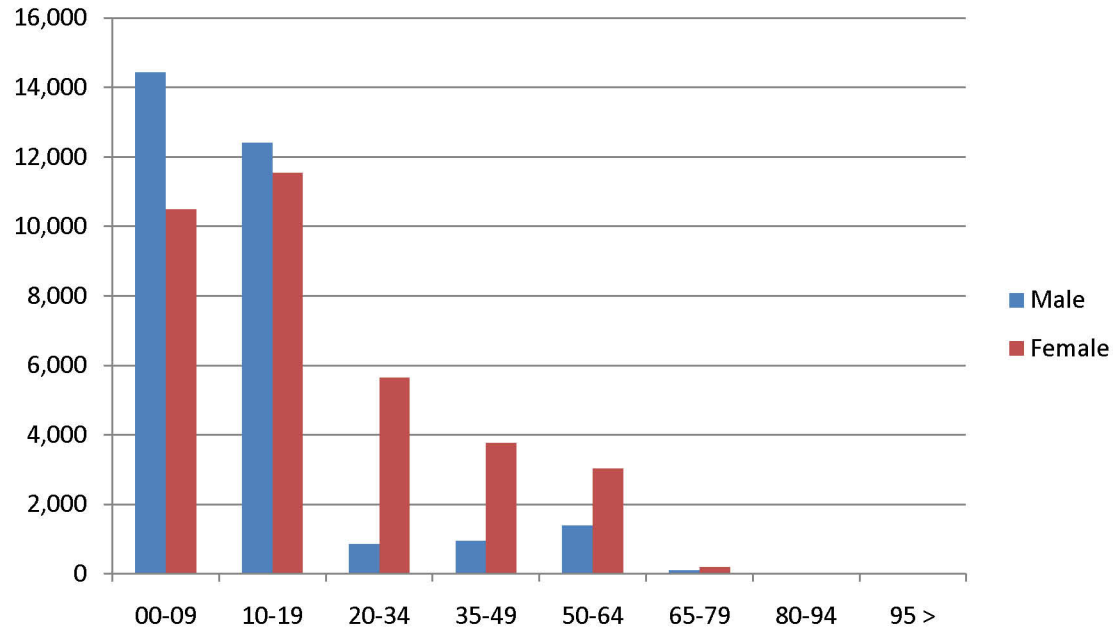
Calendar Year	Total Members	Total Claims	Total Cost	Cost per Claim	Per-Diem	Total Units	Total Days
2008							
	3,095	6,455	$381,106.74	$59.04	$2.36	113,363	161,253
2009							
	677	1,396	$81,911.55	$58.68	$2.33	24,675	35,118
Percent Change	**-78.1%**	**-78.4%**	**-78.5%**	**-0.6%**	**-1.3%**	**-78.2%**	**-78.2%**
	-2,418	**-5,059**	**($299,195.19)**	**($0.36)**	**($0.03)**	**-88,688**	**-126,135**

Age and Gender CY 2009

Xopenex HFA



Tier-1 HFA



Prescriber Specialty CY 2009

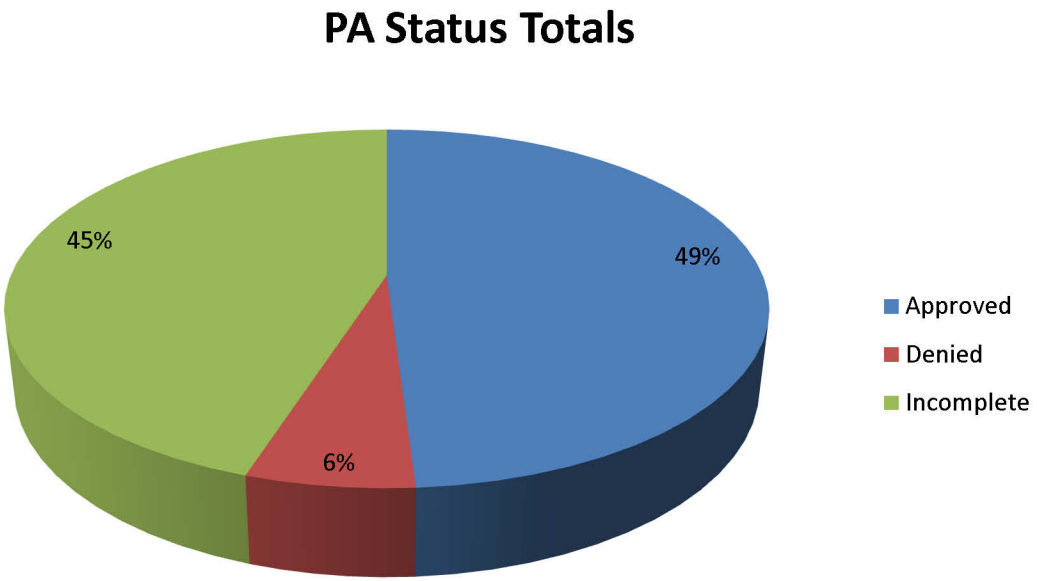
Tier-1 HFA Products

Specialty	Percentage of Claims
Family Practitioner	28
General Pediatrician	24
Nurse Practitioner (Other)	10
Physician Assistant	10
PRESCRIBER ONLY	7
General Practitioner	6
Internist	4
Emergency Medicine Practitioner	3
DDSD-NFM	1
Obstetrician/Gynecologist	1

Xopenex HFA

Specialty	Percentage of Claims
General Pediatrician	37
Family Practitioner	22
Nurse Practitioner (Other)	10
Physician Assistant	10
General Practitioner	6
PRESCRIBER ONLY	4
Internist	3
Emergency Medicine Practitioner	2
Unknown	1
DDSD-NFM	1

Prior Authorization Totals



Recommendations

The College of Pharmacy does not recommend any changes to this category at this time.

Tier-1 Product Utilization CY 2009

BRAND NAME	CLAIMS	UNITS	DAYS	MEMBERS	COST	UNITS/ DAY	CLAIMS/ MEMBERS	COST/ DAY
PROAIR HFA AER	98,059	990,055	2,304,955	45,908	$4,642,083.39	0.43	2.14	$2.01
VENTOLIN HFA AER	25,905	521,960	627,905	14,959	$1,012,536.66	0.83	1.73	$1.61
PROVENTIL AER HFA	16,971	125,636	410,192	9,396	$817,952.16	0.31	1.81	$1.99
Totals	140,935	1,637,651	3,343,052		$6,472,572.21	0.49	2.01	$1.94

Xopenex HFA Utilization CY 2009

BRAND NAME	CLAIMS	UNITS	DAYS	MEMBERS	COST	UNITS/ DAY	CLAIMS/ MEMBERS	COST/DAY
XOPENEX HFA AER	1,396	24,675	35,118	677	$81,911.55	0.7	2.06	2.33

Appendix H

U.S. Food and Drug Administration

About FDA

Drug Safety Oversight Board Meeting, January 21, 2010

Public Summary

The Executive Director updated the Drug Safety Oversight Board (DSB or Board) on risk communications [Public Health Advisories (PHA), Early Communications about Ongoing Safety Reviews (EC), and Information for Healthcare Professionals (HCP)] posted and in development since the November 19, 2009 meeting. The following is a list of the posted risk communications:

Risk Communications Posted since the November 19, 2009 DSB meeting:

- November 20, 2009: Sibutramine hydrochloride[1]
- December 2, 2009: Valproate and neural tube defects[2]
- December 22, 2009: Ezetimibe/Simvastatin (marketed as Vytorin), Simvastatin (marketed as Zocor) and Ezetimibe (marketed as Zetia) and the SEAS Trial Report[3]
- January 14, 2010: Tiotropium (Spiriva) and potential increase risk of stroke, heart attack, and death[4]

The DSB heard presentations and discussed three topics:

1. An update from the Office of Communications
2. How to communicate FDA's updated recommendations about long acting beta agonists (LABAs)
3. Propoxyphene safety issue

The views expressed by non-CDER employees are those of the individual and not necessarily the opinion of their respective government agency.

An update from the Office of Communications

The Director from FDA's Office of Communications (OCOMM) provided an update on developments over the past year and the many challenges OCOMM faces when writing and issuing risk communications to health care professionals and the public. OCOMM has expanded its vision of how to communicate to the public beyond the traditional ways, including talking directly with health care professionals and the media. Dr. Baruch Fischhoff, a Howard Heinz University Professor at Carnegie Mellon University and Chair of FDA's Risk Communications Advisory Committee attended as a guest speaker. He provided an overview of the issues involved when communicating risks and benefits to the public.

The Board discussed the following:

- The many factors that are considered when writing risk communications, such as who is the audience; what does the audience want; and what is the best way to deliver information to them
- Challenges FDA encounters when communicating risks to the public, including legal and regulatory constraints, emerging science, the audiences' needs, and helping the public understand FDA's role in overseeing drug safety throughout the product's life cycle
- What is the most effective approach for communicating messages to the public (e.g. multiple, multi-tiered, or single communications)
- Different social media and communication products that FDA is using or may use in the future to disseminate messages to the public, such as texting, facebook, twitter, widgets, RSS feed, and other social media products
- Methods for testing the impact of safety communications

How to communicate FDA's updated recommendations about long acting beta agonists (LABAs)

LABAs are FDA-approved medications used to treat adult and pediatric patients with asthma, chronic obstructive pulmonary disease, or exercise-induced bronchospasm. LABAs work by relaxing muscles in the airways in the lungs allowing for better airflow for up to 12 hours. The DSB heard presentations and discussed how FDA might communicate FDA's updated recommendations when LABAs are used to treat patients with asthma.

Board members from the Department of Defense, Veterans Health Administration, and the Indian Health Service provided information on LABA usage patterns including LABA combination products (with an inhaled corticosteroid) used in their hospitals and clinics. They also provided input on how the updated recommendations might affect their health systems.

The Board discussed the following:

- The pathophysiology of asthma and the risks and benefits of LABAs
- The National Asthma Education and Prevention Program's (NAEPP) published asthma treatment guidelines for patients 12 years of age and older
- The Serevent Nationwide Surveillance (SNS) study, the Salmeterol Multicenter Asthma Research Trial (SMART), and FDA's 2008 LABA meta-analysis
- Recommendations for LABA use from the Advisory Committee meeting held in December 2008
- FDA's updated recommendations for using LABAs in patients with asthma
- Specific labeling concepts, goals, and rationale for each labeling change
- Key messages regarding LABAs that should be included in a communication to healthcare professionals and consumers
- The importance for FDA to discuss the updated recommendations with stakeholders, professional societies and healthcare professionals to help disseminate the message

Propoxyphene Issue

The Board discussed whether and how additional safety data from the Drug Abuse Warning Network-Medical Examiner (DAWN-ME) and the Florida Department of Law Enforcement (FDLE) could impact the risk-benefit assessment for propoxyphene. Propoxyphene is an opioid analgesic used to relieve mild to moderate pain.

The Board discussed the following:

- The regulatory history of propoxyphene products
- Efficacy and safety of propoxyphene products
- Non-clinical toxicology safety issues associated with propoxyphene

- Propoxyphene's receptor activity and cardiotoxicity in relationship to other opiates
- An overview of propoxyphene pharmcokinetics, including the effect of food, hepatic and renal impairment, and age on its metabolism
- Safety findings from FDA's Propoxyphene Working Group, including data from the DAWN-ME and FDLE
- Propoxyphene drug utilization trends in the US
- The use of summary safety data (overall data rather than individual patient data) from a large database when making regulatory decisions; an what standards should FDA use to make regulatory decisions using summary safety data

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Links on this page:

1. http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/ucm191650.htm
2. http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/ucm192649.htm
3. http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/ucm194964.htm
4. http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/ucm197429.htm

U.S. Food and Drug Administration

Drugs

FDA Drug Safety Communication: Ongoing review of Avandia (rosiglitazone) and cardiovascular safety

Safety Announcement

[02-22-2010] The U.S. Food and Drug Administration (FDA) is reviewing data, submitted in August 2009, from a large, long-term clinical study on possible risks with the diabetes drug, Avandia* (rosiglitazone). The clinical study, called the **R**osiglitazone **E**valuated for **C**ardiovascular **O**utcomes and **R**egulation of Glycemia in **D**iabetes or RECORD study was designed to evaluate the cardiovascular safety of rosiglitazone, a medication used to treat type 2 diabetes mellitus.

In addition to the RECORD study, a number of observational studies of the cardiovascular safety of rosiglitazone have been published. FDA has been reviewing these on an ongoing basis.

FDA is now reviewing the primary data from the completed RECORD study, conducting follow-up audits, and reviewing additional studies. This work is ongoing and no new conclusions or recommendations about the use of rosiglitazone in the treatment of type 2 diabetes have been made at this time.

Once FDA completes its review of the data from the RECORD study, the agency will present the totality of new and existing cardiovascular safety data on rosiglitazone at a joint public meeting of the Endocrinologic and Metabolic Drugs and Drug Safety and Risk Management Advisory Committees in July 2010. At that meeting, the Advisory Committee will provide an updated assessment of the risks and benefits of rosiglitazone in the treatment of type 2 diabetes.

When prescribing rosiglitazone, healthcare professionals should follow the recommendations in the drug label. Patients should continue taking rosiglitazone unless told by their healthcare professional to stop. Patients who are concerned about the possible risks associated with using rosiglitazone should talk to their healthcare professional.

FDA previously communicated to the public about the possible association between rosiglitazone and increased cardiovascular risk in a 2007 safety alert[1]. The agency also sought advice from external experts at the July 30th 2007[2] joint meeting of the FDA Endocrinologic and Metabolic Drugs and Drug Safety and Risk Management Advisory Committees. The RECORD study data represent the only new information from a completed randomized, controlled clinical trial of rosiglitazone received by FDA since the 2007 announcements.

The RECORD study was designed to evaluate the cardiovascular safety of rosiglitazone, which is consistent with FDA's December 2008 Guidance for Industry[3] recommending that manufacturers of new treatments for diabetes carefully design their clinical trials to include an evaluation of cardiovascular safety. The RECORD study will be evaluated in the context of this recent Guidance.

** Rosiglitazone is sold as a single-ingredient product under the brand name Avandia. It is also available in combination with other diabetes medications, metformin under the brand name Avandamet or glimepiride under the brand name Avandaryl.*

Additional Information for Patients

FDA recommends that patients currently using rosiglitazone:

- Not stop taking their medication without talking with their healthcare professional.
- Discuss any questions or concerns they have about rosiglitazone with their healthcare professional.
- Read the *Medication Guide* that comes with each rosiglitazone prescription to better understand the risks and benefits of their medication.
- Report any side effects with rosiglitazone to FDA's MedWatch program using the information at the bottom of the page.

Additional Information for Healthcare Professionals

FDA recommends that healthcare professionals:

- Follow the recommendations in the drug label when prescribing rosiglitazone. This includes a *Boxed Warning* stating that:
  - Use of rosiglitazone in patients with established NYHA Class III or IV heart failure is contraindicated. Further, rosiglitazone is not recommended in patients with symptomatic heart failure.
  - Rosiglitazone causes or exacerbates congestive heart failure in some patients. Healthcare professionals should monitor for the signs and symptoms of heart failure (including excessive, rapid weight gain, difficulty breathing, and/or swelling) after starting treatment and after dose increases of rosiglitazone. If heart failure signs and symptoms occur, the heart failure should be managed appropriately and discontinuation or dose reduction of rosiglitazone must be considered.
  - Available data on rosiglitazone and risk of myocardial ischemia are inconclusive. A meta-analysis of 42 clinical studies (mean duration 6 months; 14,237 total patients), most of which compared rosiglitazone to placebo, found an association between rosiglitazone use and a increased risk of myocardial ischemic events such as angina or heart attack. Three other studies (mean duration 41 months; 14,067 total patients), comparing rosiglitazone to other oral diabetes medications or placebo, have not confirmed or excluded this risk. The recently completed RECORD study, currently being reviewed by FDA, is one of these three studies.
- Discuss with patients the risks of rosiglitazone treatment, taking into account the clinical utility of rosiglitazone, the risks/benefits of other antidiabetic medications, and the risks associated with poorly controlled blood glucose.
- Discuss with patients the importance of adhering to their diabetes medication regimen.
- Report any adverse events associated with the use of rosiglitazone to FDA's MedWatch program using the information at the bottom of the page.

Data Summary

Part of a post-approval commitment between the European Medicines Agency (EMA) and the manufacturer, the RECORD study compared cardiovascular safety outcomes in 2,220 patients with type 2 diabetes taking rosiglitazone plus other diabetes medications (metformin or a sulfonylurea) to 2,227 patients taking metformin and a sulfonylurea.

Patients in the study were followed on average 5.5 years and were monitored for the occurrence of the primary endpoint (cardiovascular death and cardiovascular hospitalizations). There were several secondary endpoints including the composite endpoint for major cardiovascular events (cardiovascular death, heart attack or stroke). All CV endpoints were determined by a team of cardiologists who were unaware of which patients were receiving rosiglitazone. The study reported no difference in the primary endpoint in the rosiglitazone group [hazard ratio = 0.99 (95% Confidence Interval of 0.85 to 1.16)] compared to combined use of metformin and a sulfonylurea. In addition, there was no significant treatment difference in any of the secondary composite endpoints except an increase in heart failure, which is a well-known side effect of drugs in this class, including Actos (pioglitazone). The increase in risk of heart failure is consistent with the warnings contained in the current drug label. The RECORD study findings were published in the June 2009 issue of *Lancet*[1].

FDA will present a summary of any new observational studies of rosiglitazone safety at the upcoming Advisory Committee meeting in July 2010.

References:

1. Home PD, Pocock, SJ, Beck-Neilsen H, et al. Rosiglitazone evaluated for cardiovascular outcomes in oral agent combination therapy for type 2 diabetes (RECORD): a multicentre, randomized, open-label trial. *Lancet* 2009; 373: 2125–35.

Related Information

- Rosiglitazone maleate (marketed as Avandia, Avandamet, and Avandaryl) Information[4]
- Information for Healthcare Professionals Rosiglitazone maleate (marketed as Avandia, Avandamet, and Avandaryl)[5]
  Issued 5/21/2007, updated 11/19/2007
- Diabetes Mellitus -- Evaluating Cardiovascular Risk in New Antidiabetic Therapies to Treat Type 2 Diabetes (PDF - 51KB)[6]
- 2007 Endocrinologic and Metabolic Drugs Advisory Committee[7]

Labeling and Regulatory History from Drugs@FDA

- Avandia (rosiglitazone maleate) Prescribing Information[8]
  Avandia (rosiglitazone)
- Prescribing Information and Medication Guide[9]
  Avandamet (rosiglitazone and metformin)
- Avandaryl Prescribing Information Nov 2009[10]
  Avandaryl – (rosiglitazone and glimepiride)

Contact Us

- **Report a Serious Problem**
- 1-800-332-1088
- 1-800-FDA-0178 Fax

  MedWatch Online[11]

  Regular Mail: Use postage-paid FDA Form 3500[12]

  Mail to: MedWatch 5600 Fishers Lane

  Rockville, MD 20852-9787

Links on this page:

1. http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm143406.htm
2. http://www.fda.gov/ohrms/dockets/ac/cder07.htm#EndocrinologicMetabolic
3. http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM071627.pdf
4. http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm143349.htm
5. http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm143406.htm
6. http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM071627.pdf
7. http://www.fda.gov/ohrms/dockets/ac/cder07.htm#EndocrinologicMetabolic
8. http://www.accessdata.fda.gov/drugsatfda_docs/label/2008/021071s034lbl.pdf
9. http://www.accessdata.fda.gov/drugsatfda_docs/label/2008/021410s025lbl.pdf
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11. http://www.fda.govhttps://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm
12. http://www.fda.gov/downloads/Safety/MedWatch/DownloadForms/UCM082725.pdf

U.S. Food and Drug Administration

Drugs

Drug Safety Communication: Erythropoiesis-Stimulating Agents (ESAs): Procrit, Epogen and Aranesp

Safety Announcement

The FDA is requiring all drugs called Erythropoiesis-Stimulating Agents (ESAs) to be prescribed and used under a risk management program, known as a risk evaluation and mitigation strategy (REMS), to ensure the safe use of these drugs. The ESAs that are part of the REMS are marketed under the names Epogen, Procrit, and Aranesp. FDA required Amgen, the manufacturer of these products, to develop a risk management program because studies show that ESAs can increase the risk of tumor growth and shorten survival in patients with cancer who use these products. Studies also show that ESAs can increase the risk of heart attack, heart failure, stroke or blood clots in patients who use these drugs for other conditions.

ESAs work by stimulating the bone marrow to produce red blood cells. ESAs are approved for the treatment of anemia (low red blood cells) resulting from chronic kidney failure, chemotherapy, certain treatments for Human Immunodeficiency Virus (HIV), and also to reduce the number of blood transfusions during and after certain major surgeries.

As part of the REMS, a *Medication Guide* explaining the risks and benefits of ESAs must be provided to all patients receiving ESAs. In addition to the Medication Guide, Amgen was required to develop the ESA APPRISE (Assisting Providers and Cancer Patients with Risk Information for the Safe use of ESAs) Oncology program for healthcare professionals who prescribe ESAs to patients with cancer.

Under the ESA APPRISE Oncology program, Amgen will ensure that only those hospitals and healthcare professionals who have enrolled and completed training in the program will prescribe and dispense ESAs to patients with cancer. Amgen is also required to oversee and monitor the program to ensure that hospitals and healthcare professionals are fully compliant with all aspects of the program.

The goals of the REMS for the ESAs are:

- To support informed decisions between patients and their healthcare professionals who are considering treatment with an ESA by educating them on the risks of ESAs.
- To mitigate the risk of decreased survival and/or poorer tumor outcomes in patients with cancer by implementing the part of the REMS called the ESA APPRISE Oncology Program.

Additional Information for Patients:

Patients with cancer

Patients using ESAs should:

- Understand the risks associated with use of ESAs. These risks include:
  - ESAs may cause tumors to grow faster.
  - ESAs may cause some patients to die sooner.
  - ESAs may cause some patients to develop blood clots, and serious heart problems such as a heart attack, heart failure or stroke.
- Be aware that their healthcare professional has received special training about the use of ESAs in patients with cancer.
- Read the ***Medication Guide*** to understand the benefits and risks of using an ESA.
- Talk with their healthcare professional about any questions they may have about using ESAs.
- Be aware that they will be asked to sign an acknowledgment form that says they have talked with their healthcare professional about the risks of ESAs. This form must be signed before patients begin a course of treatment with an ESA.

Patients with chronic kidney failure (includes patients on dialysis and those not on dialysis)

Patients using ESAs should:

- Know that the use of ESAs can increase the risk for stroke, heart attack, heart failure, blood clots, and death.
- Read the ***Medication Guide*** to understand the benefits and risks of using an ESA.
- Get blood tests while using ESAs. The test results may help guide the course of therapy and lower the risks of using these drugs.Patients' healthcare professionals should make them aware of how often to have blood tests.
- Talk with their healthcare professional about any questions they have about the risks and benefits of using ESAs.

Additional Information for Healthcare Professionals and Hospitals: ESA use in cancer

Healthcare Professionals

The ESA APPRISE Oncology program requires that all healthcare professionals who prescribe ESAs for patients with cancer do the following:

- Complete a training module that covers the use of ESAs. Completion of the training module is required for enrollment in the ESA APPRISE Oncology program.
- Sign the patient/healthcare professional acknowledgement form prior to the patient receiving an ESA. The acknowledgement form attests that the healthcare professional and patient have discussed the risks of using an ESA.
- Re-enroll in the ESA APPRISE Oncology program every three years.

Healthcare professionals not enrolled in the ESA APPRISE Oncology program will not be able to prescribe ESAs for use in patients with cancer.

As part of the enrollment in the ESA APPRISE Oncology program, healthcare professionals must attest to their understanding of the following:

- That ESAs shortened overall survival and/or increased the risk of tumor progression or recurrence in clinical studies in patients with breast, nor -small cell lung, head and neck, lymphoid, and cervical cancer.
- To decrease the risks of ESAs, the lowest dose needed should be used to avoid red blood cell transfusion.
- ESAs should be discontinued following completion of a chemotherapy course of treatment.
- Aranesp® is indicated for the treatment of anemia due to the effect of concomitantly administered chemotherapy, based on studies that have shown a reduction in the need for red blood cell transfusions in patients with metastatic, non-myeloid malignancies.
- Epogen®/Procrit® is indicated for the treatment of anemia due to the effect of concomitantly administered chemotherapy, based on studies tha have shown a reduction in the need for red blood cell transfusions in patients with metastatic, non-myeloid malignancies receiving chemotherapy for a minimum of 2 months.
- ESAs are not indicated for use in patients receiving hormonal agents, therapeutic biologic products, or radiotherapy unless receiving concomitant myelosuppressive chemotherapy.
- ESAs are not indicated for patients receiving myelosuppressive therapy when the anticipated outcome is cure.
- ESA use has not been demonstrated in controlled clinical trials to improve symptoms of anemia, quality of life, fatigue, or patient well-being.

Hospitals

Hospitals must do the following:

- Be enrolled in the ESA APPRISE Oncology program in order to dispense ESAs to patients with cancer, even if the prescribing healthcare professional is certified under the program.
- Have a system in place that ensures that all healthcare providers who prescribe ESAs in the hospital are enrolled and comply with the ESA APPRISE Oncology program.

Additional Information for Healthcare Professionals: non-cancer use of ESAs

- Healthcare professionals who prescribe ESAs for anemia not caused by cancer chemotherapy are required to provide a copy of the *Medication Guide* to each patient or their representative when an ESA is dispensed.
- Healthcare professionals who use ESAs only for non-cancer uses are not required to enroll in the ESA APPRISE Oncology program.

Evaluation and Monitoring of the APPRISE Oncology Program

Amgen will be responsible for ensuring compliance with the program:

- Amgen will conduct real-time monitoring of prescribing and purchases in private-practice settings and clinic audits.
- Hospitals in the program will be audited to ensure compliance with the ESA APPRISE Oncology Program.
- Failure to comply will result in a suspension of access to ESAs.

Table of Key Safety Studies

Study/Tumor/(n)	Hemoglobin Target	Achieved Hemoglobin (Median Q1, Q3)	Primary Endpoint	Adverse Outcome for ESA-containing Arm
Chemotherapy				
Cancer Study 1 Metastatic breast cancer (n=939)	12-14g/dL	12.9 g/dL 12.2, 13.3 g/dL	12 month overall survival	Decreased 12-month survival
Cancer Study 2 Lymphoid malignancy (n=344)	13-15 g/dL (M) 13-14 g/dL (F)	11.0 g/dL 9.8, 12.1 g/dL	Proportion of patients achieving a hemoglobin response	Decreased overall survival
Cancer Study 3 Early breast cancer (n=733)	12.5-13 g/dL	13.1 g/dL 12.5, 13.7 g/dL	Relapse-free and overall survival	Decreased 3 yr. relapse-free and overall survival
Cancer Study 4 Cervical Cancer (n=114)	12-14 g/dL	12.7 g/dL 12.1, 13.3 g/dL	Progression-free and overall survival and locoregional control	Decreased 3 yr. progression-free and overall survival and locoregional control
Radiotherapy Alone				
Cancer Study 5 Head and neck cancer (n=351)	≥15 g/dL (M) ≥14 g/dL (F)	Not available	Locoregional progression-free survival	Decreased 5-year locoregional progression-free survival Decreased overall survival
Cancer Study 6 Hand and neck cancer (n=522)	14-15.5 g/dL	Not available	Locoregional disease control	Decreased locoregional disease control
No Chemotherapy or Radiotherapy				
Cancer Study 7 Non-small cell lung cancer (n=70)	12-14 g/dL	Not available	Quality of Life	Decreased overall survival
Cancer Study 8 Non-myeloid malignancy	12-13 g/dL	10.6 g/dL 9.4, 11.8 g/dL	RBC transfusions	Decreased overall survival

(n=989)

Related Information

- Information on Erythropoiesis-Stimulating Agents (ESA) Epoetin alfa (marketed as Procrit, Epogen) Darbepoetin alfa (marketed as Aranesp)[1]
- Aranesp REMS (PDF - 11146KB)[2]
- Aranesp Medication Guide (PDF - 59KB)[3]
- Darbepoetin Alfa (marketed as Aransep) Label - 2/16/2010[4]
- Epogen/Procrit REMS (PDF - 11043KB)[5]
- Epogen Medication Guide (PDF - 62KB)[6]
- Procrit Medication Guide (PDF - 57KB)[7]
- Epoetin Alfa (marketed as Epoetin, Procrit) Label - 2/16/2010[8]
- FDA Announces New Safety Plan for Agents Used to Treat Chemotherapy-Related Anemia[9]
  2/16/2010

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- 1-800-FDA-0178 Fax

  MedWatch Online[10]

  Regular Mail: Use postage-paid FDA Form 3500[11]

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  Rockville, MD 20852-9787

Links on this page:

1. http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm109375.htm
2. http://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM200104.pdf
3. http://www.fda.gov/downloads/Drugs/DrugSafety/UCM085918.pdf
4. http://www.accessdata.fda.gov/drugsatfda_docs/label/2010/103951s5197lbl.pdf
5. http://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM200105.pdf
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8. http://www.accessdata.fda.gov/drugsatfda_docs/label/2010/103234s5199lbl.pdf
9. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm200471.htm
10. http://www.fda.govhttps://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm
11. http://www.fda.gov/downloads/Safety/MedWatch/DownloadForms/UCM082725.pdf

U.S. Food and Drug Administration

Safety

Maalox Total Relief and Maalox Liquid Products: Medication Use Errors

Audience: Consumers, Healthcare professionals

[Posted 02/17/2010] FDA notified consumers and healthcare professionals about reports of serious medication errors involving consumers who used Maalox Total Relief when they had intended to use a Maalox liquid antacid product. Maalox Total Relief and the traditional Maalox products are both liquid medications available without a prescription, but are not interchangeable and are intended to treat different medical conditions. Maalox Total Relief is an upset stomach reliever and anti-diarrheal medication, while traditional Maalox liquid products Maalox Advanced Regular Strength and Maalox Advanced Maximum Strength are antacids.

Maalox Total Relief is not appropriate for individuals who want to use an antacid, since it contains the active ingredient bismuth subsalicylate which is chemically related to aspirin and may cause serious adverse effects such as bleeding. Maalox Total Relief should not be used in people who have or have a history of gastrointestinal ulcers or a bleeding disorder. It also should not be taken by children and teens if they are recovering from a viral infection, nor by individuals who are taking certain medications including: oral antidiabetic drugs (OADs), anticoagulation (thinning the blood) drugs such as warfarin (Coumadin) and clopidogrel (Plavix), non-steroidal anti-inflammatory drugs (NSAIDS), and other anti-inflammatory drugs.

The Drug Safety Communication and Consumer Update contain additional information for healthcare professionals and consumers, as well as product label photos.

[02/17/2010 - Drug Safety Communication [1] - FDA]
[02/17/2010 - News Release [2] - FDA]
[02/17/2010 - Consumer Update [3] - FDA]

Links on this page:

1. http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm199476.htm
2. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm200795.htm
3. http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm199331.htm

U.S. Food and Drug Administration

Drugs

Facts and Myths about Generic Drugs

Today, 7 in 10 prescriptions filled in the United States are for generic drugs. This fact sheet explains how generic drugs are made and approved and debunks some common myths about these products.

FACT: FDA requires generic drugs to have the same quality and performance as the brand name drugs.

- When a generic drug product is approved, it has met rigorous standards established by the FDA with respect to identity, strength, quality, purity and potency. Some variability can and does occur during manufacturing, for both brand name and generic drugs. When a drug, generic or brand name, is mass produced, very small variations in purity, size, strength and other parameters are permitted. FDA puts limits on how much variability in composition or performance of a drug is acceptable.
- Generic drugs are required to have the same active ingredient, strength, dosage form, and route of administration as the brand name (or reference) product. Generic drugs do not need to contain the same inactive ingredients as the brand product.
- Through review of bioequivalence data, FDA assures that the generic product will perform the same as its respective brand name (or reference product. This standard applies to all generic drugs, whether immediate or controlled release.
- A generic drug must be shown to be bioequivalent to the reference drug; that is, it must be shown to give blood levels that are very similar to those of the reference product. If blood levels are the same, the therapeutic effect will be the same. In that case, there is no need to carry ou a clinical effectiveness study and they are not required.
- All generic manufacturing, packaging and testing sites must pass the same quality standards as those of brand name drugs and the generic products must meet the same exacting specifications as any innovator brand name product. In fact, many generic drugs are made in the same plants as innovator brand name drug products.
- If an innovator of a brand name drug switches drug production to an alternative manufacturing site, or they change formulation of their brand name drug, these companies are held to the same rigorous manufacturing requirements as those that apply to generic drug companies.

FACT: Research shows that generics work just as well as brand name drugs.

- A recent study evaluated the results of 38 published clinical trials that compared cardiovascular generic drugs to their brand-name counterparts. There was no evidence that brand-name heart drugs worked any better than generic heart drugs. [Kesselheim et al. Clinical equivalence of generic and brand-name drugs used in cardiovascular disease: a systematic review and meta-analysis. JAMA. 2008;300(21) 2514-2526].

FACT: When it comes to price, there is a big difference between generic and brand name drugs. On average, the cost of a generic drug is 80 to 85% lower than the brand name product.

- An IMS National Prescription Audit shows that a typical formulary now charges $6 for generic medications, $29 for preferred branded drugs, and $40 or more for non-preferred branded drugs. [Aitken et al. Prescription drug spending trends in the United States: looking beyond the turning point. Health Aff (Millwood). 2009;28(1):w151-60].
- Independent research has shown that total prescription drug expenditures in the United States only increased by 4.0% from 2006 to 2007, wit total spending rising from $276 billion to $287 billion. This is a sharp decrease from the 8.9% growth rate observed in prescription drug expenditures in 2006. One factor cited as a reason for the slowdown is an increase in availability and use of generic drugs [Hoffman et al. Projecting future drug expenditures--2009. Am J Health Syst Pharm. 2009;66(3):237-57].

Recently, some misinformation has raised concerns over generic drugs. Below are some common myths in circulation.

MYTH: FDA lets generic drugs differ from the brand name counterpart by up to 45 percent.

FACT: This claim is false. Anyone who repeats this myth does not understand how FDA reviews and approves generic drugs.

- FDA recently evaluated 2,070 human studies conducted between 1996 and 2007. These studies compared the absorption of brand name and generic drugs into a person's body. These studies were submitted to FDA to support approval of generics. The average difference in absorption into the body between the generic and the brand name was **only 3.5 percent** [Davit et al. Comparing generic and innovator drugs: a review c 12 years of bioequivalence data from the United States Food and Drug Administration. Ann Pharmacother. 2009;43(10):1583-97]. Some generics were absorbed slightly more, some slightly less. This amount of difference would be expected and acceptable, whether for one batch of brand name drug tested against another batch of the same brand, or for a generic tested against a brand name. In fact, there have been studies in which branded drugs were compared with themselves as well as with a generic. As a rule, the difference for the generic-to-brand comparison was about the same as the brand-to-brand comparison.
- Any generic drug modeled after a single, brand name drug (the reference) must perform approximately the same in the body as the brand name drug. There will always be a slight, but not medically important, level of natural variability – just as there is for one batch of brand name drug to the next.

MYTH: People who are switched to a generic drug are risking treatment failure.

FACT: There is no evidence for this claim. Treatment failures can and do occur when taking generic or brand name drugs. If someone is switched to a generic drug around the time they are relapsing, they may attribute the problem to the switch.

- Many people who have recovered from major depression have a relapse despite continued treatment. These relapses have been shown in trials of long-term therapy. [Byrne and Rothschild. Loss of antidepressant efficacy during maintenance therapy: possible mechanisms and treatments. J Clin Psychiatry. 1998;59(6):279-88].
- Many people who are on a seizure medications will re-experience a seizure despite continued treatment. [Randomised study of antiepileptic drug withdrawal in patients in remission. Medical Research Council Antiepileptic Drug Withdrawal Study Group. Lancet. 1991;337(8751):1175-80].
- A percentage of people will re-experience gastric ulcers, despite an initial, positive response to and continued treatment with prescription strength antacids (cimetidine tablets; http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?id=8131#nlm34067-[1]9).

MYTH: Generic drugs cost less because they are inferior to brand name drugs.

FACT: Generic manufacturers are able to sell their products for lower prices, not because the products are of lesser quality, but becaus generic manufacturers generally do not engage in costly advertising, marketing and promotion, or significant research and development.

- When a brand name drug comes off patent and generic drugs are permitted to compete with the brand name drug, the generic products compete by offering lower prices. Unlike the manufacturers of brand name drugs, generic drug companies do not have significant expenses to recoup for advertising, marketing and promotion, or research and development activities.

MYTH: There are quality problems with generic drug manufacturing. A recent recall of generic digoxin (called Digitek) shows that generic drugs put patients at risk.

FACT: FDA's aggressive action in this case demonstrates the high standards to which all prescription drugs – generic and brand name - are held.

- In March 2008, FDA performed a scheduled inspection of the Actavis production facility and identified products that were not manufactured to required specifications over a period of time extending back to the year 2006. Included in this list of products was one particular lot of Digitek.
- Actavis detected a very small number of oversized tablets in this lot (specifically, 20 double-sized tablets in a sample of approximately 4.8 million tablets).
- Although Actavis attempted to remove the affected Digitek tablets through visual inspection, FDA determined that this method of removal was inadequate to assure the product's quality and consistency in accordance with the current Good Manufacturing Practice (cGMP) regulations.
- Since the detection of the manufacturing problem, FDA has been actively engaged with this company to ensure that **ALL** potentially affected lots of Digitek tablets have been recalled. In our best judgment, given the very small number of defective tablets that may have reached the market and the lack of reported adverse events before the recall, harm to patients was very unlikely.
- FDA takes action whenever we find that a drug manufacturer is not following cGMPs. Over the last ten years, FDA has taken enforcement action against many brand name and generic firms for failing to meet FDA manufacturing quality standards.

MYTH: FDA's enforcement action against the generic drug company Ranbaxy demonstrates quality problems with imported generic drugs.

FACT: FDA's action demonstrates FDA's commitment to safe generic drugs.

- FDA has taken several regulatory actions against the generic drug manufacturer Ranbaxy, on the basis of problems at two of Ranbaxy's manufacturing facilities. Ranbaxy is one of many non-U.S. based generic and brand drug manufacturers.
- On Sept. 2008, the FDA issued two warning letters and instituted an Import Alert barring the entry of all finished drug products and active pharmaceutical ingredients from Ranbaxy's Dewas, Paonta Sahib and Batamandi Unit facilities due to violations of U.S. cGMP requirements. That action barred the commercial importation of 30 different generic drugs into the United States and remains in effect today (http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm149532.htm[2]).
- Subsequent FDA investigations also revealed a pattern of questionable data raising significant questions regarding the reliability of certain generic drug applications from Ranbaxy.
- To address the allegedly falsified data, the FDA has invoked its Application Integrity Policy (AIP) against the Paonta Sahib facility. When the AII is implemented, the FDA stops all substantive scientific review of any new or pending drug approval applications that contain data generated b the Paonta Sahib facility. This AIP covers applications that rely on data generated by the Paonta Sahib facility only.
- In the fiscal year 2008, FDA performed 2,221 drug-related inspections. FDA takes many different enforcement actions, not just against generic drug manufacturers. For a list of enforcement actions in the fiscal year 2008, see http://www.fda.gov/downloads/ICECI/EnforcementActions/EnforcementStory/UCM129812.pdf[3]. It is FDA's responsibility to ensure that the drugs people use, generic or brand name, are safe and effective.

MYTH: Brand name drugs are safer than generic drugs.

FACT: FDA receives very few reports of adverse events about specific generic drugs. Most reports of adverse events are related to side effects of the drug ingredient itself.

- The monitoring of postmarket adverse events for all drug products, including generic drugs, is one aspect of the overall FDA effort to evaluate the safety of drugs after approval. In most cases, reports of adverse events generally describe a **known reaction** to the active drug ingredient.

MYTH: FDA does not care about concerns over generic drugs.

FACT: FDA is actively engaged in making all regulated products – including generic drugs – safer.

- We are aware that there are reports noting that some people may experience an undesired effect when switching from brand name drug to a generic formulation or from one generic drug to another generic drug. Evidence indicates that if problems with interchangeability of drug formulations occur, they occur only for a very small subset of people.
- FDA is encouraging the generic industry to investigate whether, and under what circumstances, such problems occur. The Agency does not have the resources to perform independent clinical studies, and lacks the regulatory authority to require industry to conduct such studies. FDA will continue to investigate these reports to ensure that it has all the facts about these treatment failures and will make recommendations to healthcare professionals and the public if the need arises.

Links on this page:

1. http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?id=8131#nlm34067-
2. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2009/ucm149532.htm
3. http://www.fda.gov/downloads/ICECI/EnforcementActions/EnforcementStory/UCM129812.pdf

U.S. Department of Health & Human Services

U.S. Food and Drug Administration

News & Events

FDA NEWS RELEASE

For Immediate Release: March 2, 2010
Media Inquiries: Sandy Walsh, 301-796-4669, sandy.walsh@fda.hhs.gov
Consumer Inquiries: 888-INFO-FDA

FDA Approves First Generic Tamsulosin to Treat Enlarged Prostate Gland

Condition known as benign prostatic hyperplasia common in older men

The U.S. Food and Drug Administration today approved the first generic version of Flomax Capsules 0.4 mg (tamsulosin hydrochloride) to treat benign prostatic hyperplasia (BPH), a condition in which an enlarged prostate gland causes problems with urination.

The most common symptoms of BPH include a weak stream during urination, urgency, leaking or dribbling, as well as more frequent urination, especially at night.

BPH is common among older men. According to the National Institutes of Health, it rarely causes symptoms before age 40, but more than half of men in their 60s and as many as 90 percent of men older than 70 have BPH symptoms.

"The approval of generic tamsulosin offers greater access to a widely used treatment for BPH," said Gary Buehler, director of the FDA's Office of Generic Drugs. "FDA is committed to making generic drugs available to patients and these drugs meet the same rigid standards as the brand name drugs."

The prescribing information and safety warnings for the generic version of tamsulosin are the same as those for Flomax Capsules. Generic tamsulosin capsules are manufactured by IMPAX Laboratories Inc. of Hayward, Calif. Information about the marketing and availability of this generic drug can be obtained from the manufacturer.

For more information:

- Consumer Information: Generic Drugs [1]
- What BPH Means to Men – A Healthy Moments Podcast from the National Institutes of Health [2]
- Information on specific drug products, Drugs@FDA [3]

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RSS Feed for FDA News Releases [4] [what is RSS? [5]]

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