Drug Utilization Review Board

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

Wednesday
June 9, 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 – June 9, 2010**

DATE: June 3, 2010

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

Enclosed are the following items related to the June 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.

Review of Albuterol HFA Products

Action Item – Vote to Prior Authorize Ilaris® – See Appendix C.

Action Item – Vote to Prior Authorize Requip XL™ and Mirapex ER™ – See Appendix D.

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

Action Item – Vote to Prior Authorize Livalo® and Statin Utilization Review – See Appendix F.

Action Item – Vote to Prior Authorize Oleptro® – See Appendix G.

Action Item – Annual Review of Ophthalmic Anti-Infectives and Vote to Prior Authorize Besivance™ – See Appendix H.

Action Item – Annual Review of Stimulants and 30 Day Notice to Prior Authorize ProCentra™ - See Appendix I.

FDA and DEA Updates – See Appendix J.

Future Business

Adjournment

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Drug Utilization Review Board

(DUR Board)

Meeting – June 9, 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. May 12, 2010 DUR Minutes – Vote
B. May 13, 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 January 2010
B. Retrospective Drug Utilization Review Response for November 2009
C. Medication Coverage Activity Audit for May 2010
D. Help Desk Activity Audit for May 2010

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

5. Review of Albuterol HFA Products

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

6. Action Item – Vote to Prior Authorize Ilaris® – See Appendix C.

A. COP Recommendations

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

7. Action Item – Vote to Prior Authorize Requip XL™ and Mirapex ER™ – See Appendix D.

A. Product Summaries
B. COP Recommendations

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

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

A. COP Recommendations

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

9. Action Item – Vote to Prior Authorize Livalo® and Statin Utilization Review – See Appendix F.

A. Utilization Review
B. COP Recommendations

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

10. Action Item – Vote to Prior Authorize Oleptro® – See Appendix G.

A. COP Recommendations

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

11. Action Item – Annual Review of Ophthalmic Anti-Infectives and Vote to Prior Authorize Besivance™ – See Appendix H.

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

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

12. Action Item – Annual Review of Stimulants and 30 Day Notice to Prior Authorize ProCentra™ – See Appendix I.

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

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

13. FDA and DEA Updates – See Appendix J.

14. Future Business

A. Review Ribavirin Prior Authorization
B. Annual Review of Growth Hormones
C. Utilization Review of Epilepsy Medications
D. New Product Reviews

15. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES of MEETING of MAY 12, 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:

David Lee, Merck	David Williams, Forest	Ric Uhles, Forest
Aaron Mays, Alcon	Allen Haag, Astra Zeneca	Jeff Himmelberg, GSK
Randy Beckner, GSK	Jon White, Three Rivers Pharma	Paul Brinknar, Three Rivers Pharma
Frances Bauman, Novo Nordisk	Pam Sardo, Abbott	John Harris, Abbott
William Dozier, Gilead	Tyler Hunter, Gilead	Donna Erwin, BMS
Richard Ponder, Johnson & Johnson	Mark Veerman, Johnson & Johnson	Carlos Palasciano, Hawthorn
Holly Turner, Merck	Warren Tayes, Merck	Michael Hathaway, Otsuka
Terry McCurren, Otsuka	Kelly Rogers, Taro	John Seidenberger, Boehringer Ingelheim
Jim Dunlap, Lilly USA	Mario Munoz, Lilly USA	Lisa Sherman, Strativa

PRESENT FOR PUBLIC COMMENT:

(ad hoc)	Dr. Harlan Wright
Agenda Item No. 9:	Randy Beckner, GSK

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

1A: Roll Call

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

ACTION: NONE REQUIRED

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

Dr. Muchmore recognized the speakers for public comment.

(ad hoc) Dr. Harlan Wright

Agenda Item No. 9: Randy Beckner, GSK

Dr. Dan McNeill was introduced as special guest speaker.

Dr. Dan McNeill: Thank you Dr. Graham. I have been asked about three to four weeks ago, I was asked to come out here and give a presentation, and this was a task that I accepted with much glee, having spent nine years on this Board and even longer in service with other committees or boards within the Health Care Authority. Of course the topic that I'd like to present tonight is Dr. Mitchell. Many of you know that Dr. Mitchell will be leaving the life of the Health Care Authority and enter the dark of other State government agencies, but before she goes, I think a few words in front of those here assembled are required. In trying to assemble the material for my presentation, I have this background app on my brand new iPhone. Unfortunately it only recorded the criminal history of Lynn Von Mitchell, so I turned to other resources such as the State Medical Board and her trusted assistant, Kay. Dr. Mitchell graduated from the OU College of Medicine in 1984. After completing residencies in family medicine and occupational medicine, she was hired by OU as a faculty member in the Department of Family Medicine. One of her tasks as a faculty member was to serve as the Medical Director of the physician assistant program which she assumed in 1989, and that was my first contact with Dr. Mitchell. She remained as medical director of the PA program until 1995 when she landed a part-time job here at the Health Care Authority. For those of you that were around during that time in Oklahoma, you might remember that the Health Care Authority was transitioning to this new model of health care delivery called managed care. I remember going to many meetings with Dr. Mitchell across the state as she tried to explain this managed care process to many people; providers, lay people, administrators, etc. I heard her on many an occasion, though, disembowel some of the Authority's harshest critics with her kind, sincere, motherly explanations of managed care. In 2000 she became our State Medicaid Director, the job she's held for the last ten years. I can say without doubt Dr. Mitchell had been instrumental in assuring that hundreds of thousands of Oklahomans have received and continue to receive quality medical care through the many different components of this agency. On behalf of the Drug Utilization Review Board, her presentation is in order. So let me read this to you: "Lynn V. Mitchell, MD, MPH; With Gratitude for Your Exceptional Leadership, Visionary Guidance, and Committment to Excellence; Drug Utilization Review Board 1995 to 2010". So Dr. Mitchell, if you please ..... (applause).

Dr. Mitchell: Yeah, I promised everybody that if they did anything, they were going to be in serious trouble, starting with Kay in the back, going to Nancy ..... it was Ron? It has been a delight to work with each and every one of you. I so appreciate the collegiality of the role that you've led me to play, but it hasn't been me, let me assure you. It has been all the fine staff that sit around this table and the volunteers. They come and spend time here every month, as well as the staff of the Health Care Authority. It has been my delight to be here and be allowed to serve in this role, and I hope to be able to continue to collaborate with this group and many folks here at the Health Care Authority as I'm kind of transitioned into my new role including when the dark side, one of which is Dr. McNeill's employer. As he referred to the dark side because I'm going to be going to the Health Department, but also to OU as well, so thank you for all the time that you all spend doing what you do on behalf of the members and I certainly appreciate it, and I look forward to continuing to be able to work with each and every one of you. Thank you very much.

ACTION: NONE REQUIRED

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

3A: February 10, 2010 DUR Minutes

Ms. Varalli-Claypool moved to approve as submitted; seconded by Dr. Harrell.

ACTION: MOTION CARRIED

(ad hoc) For Public Comment: Dr. Harlan Wright: Thank you. I'll make it short and brief. Hepatitis C represents about 2% of the liver population in the United States with a liver disease. In African-Americans, it represents close to 3%, so we're talking about a large population of people. Treatment includes a combination of two drugs that are very expensive. One is Interferon and one is Ribavarin. And the combination treatment goes on for a few, so we're talking about cost savings, important that we get bang for our buck. When you treat a patient, you really want to be sure the patient is going to clear the virus. Economic wise, especially through the Health Care Authority, we need to remember if this patient doesn't clear, he either goes on to my second endeavor, and that's called liver transplant, and that is not, as you well know, a cost effective process until considerably later with a very high (unintelligible). So what happens in the treatment of Hep C is that Ribavarin it is very key that the doses be maintained during a key period of treatment, which usually occurs in the first six to eight months of treatment. If the virus

at that point is clear, then you can adjust doses if necessary. Prior to that, if you miss doses, you'll have a greater possibility of not clearing your virus. It is very expensive treatment for over a year, then it's lost by missing out on doses or making dosing of this drug key to the patient compliance, key to viral clearance. Now Ribavarin was approved in 1986 as an antiviral therapy. It was not found to be effective in the treatment of Hep C until really 1997-98. So the drug has a new indication and because of that Ribavarin in the old days was scheduled out as a 200 mg pill, capsule. And the current doses of Ribavarin the patient was taking, according to his weight, we do know that our weight here in Oklahoma tends to be a little heavier than most, is anywhere from 1,200 to 1,400 mg per day, split in two doses, 200 tablets. We're looking at three pills in the morning, three pills in the evening.

The patient is also not doing well because he's doing poorly on an Interferon dose which he gets once a week. So compliance is the key. One of the keys that would help compliance, and these studies have actually shown this, is that if you can actually use a pill formulation where the number of pills are less. And this particular company, Ribavarin, Three Rivers, actually has a formulation for that. Generic formulation of 600 mg, two pills a day. And when they've done studies actually to show patient compliance and viral clearance, less number of pills often makes a patient more compliant. The patient then clears the virus and you can save money at the other end. But we have to look at this as a difference process. Thank you.

Dr. Muchmore: The same group of people that may be treated for Hepatitis C may also be treated for liver transplant at some point in time, in which they have to take handfuls of pills on schedule or lose their liver. So what better time to start teaching compliance than when you're treating them for Hepatitis C? I mean, we have a whole mechanism for getting these patients post-liver transplant to take their pills.

Dr. Wright: That's correct. And we initiate in the beginning. But you need to understand the patient population you deal with and it's not always .... sometimes they have to stumble a couple of times. They've already stumbled a couple of times to get Hep C to start with. They have to stumble a couple of times through the process. And so oftentimes if we make it easier in the process of compliance, it's important to them.

Dr. Muchmore: But in terms of efficacy, if the Ribavarin is taken as directed, one is not more efficacious than the other.

Dr. Wright: That's true. The dose is what's important, not the formulation.

Dr. Muchmore: Can you imagine what the State budget looks like, medications in this current era?

Dr. Wright: I can very much imagine. So especially when I talk about transplant ..... especially when we talk about Interferon all the time, what are we talking about, close to $1,800 a month for therapy with a response rate ideally around 55-60% believe me I understand, but I also understand missing 10% or 20% adds up over a long period of time. Some of these patients really do (unintelligible)

Dr. Muchmore: I have no doubt about that. The question is what is practical and what is reasonable. You can get to Dallas better in Cadillac than a kiddie-car, but you can still get to Dallas.

Dr. Kuhls: Well, I think, we have never formally reviewed this drug, right?

Dr. Muchmore: No, we have. We approved the 200 mg generic Ribavirin ...

Dr. Kuhls: No, I know, but did we look at this drug specifically? I don't remember this drug specifically being looked at.

Dr. Nesser: Yeah it was on individual item on the .....

Dr. Wright: As an individual item but it was not looked at and unfortunately it's the combined therapy that's important. You look at it as an individual item, but you have to think about the other drug that is important to the process because it's key to this whole business and in this particular case (unintelligible)

Dr. Kuhls: Well I think what we should do is put this on the agenda again, this medicine specifically, review it, and at least look at the prices, because I don't have a good concept right now of price difference and all those kind of things.

Dr. Muchmore: We can bring it up next meeting ..... some more data and .....

Dr. Kuhls: Have some more data with the actual numbers and to at least look at it.

Dr. Muchmore: Well that's the thing we wrestled with in this before. We recognize the increased convenience of 600 mg pills, but seeing no difference in efficacy and limited budget, it's hard to deal with.

Dr. Kuhls: I'd just like to look at the numbers.

Dr. Wright: We'll look at the numbers, but there is actually some studies now that actually show the difference between six pills versus two. There's some data on overall compliance and is a consequence of clear virus. Remember we're talking about the other drug that is being very expensive is (unintelligible) Interferon. You're still giving it but you may not be efficacious because you're not getting the proper dose of Ribavirin and that could be a problem.

Dr. Muchmore: Thank you.

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

4A: Retrospective Drug Utilization Review: November 2009
4B: Retrospective Drug Utilization Review: December 2009
4C: Retrospective Drug Utilization Review Response: September 2009
4D: Retrospective Drug Utilization Review: October 2009
4E: Medication Coverage Activity Audit: March & April 2010
4F: Help Desk Activity Audit: March & April 2010

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: **VOTE TO PRIOR AUTHORIZE MOZOBIL®, NPLATE,® AND ARCALYST®**
Reports included in agenda packet; presented by Dr. Sipols.
Dr. Kuhls moved to approve; seconded by Dr. Preslar.
ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: **30-DAY NOTICE TO PRIOR AUTHORIZE ILARIS®**
Materials included in agenda packet; presented by Dr. Sipols.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 7: **30-DAY NOTICE TO PRIOR AUTHORIZE BESIVANCE™**
Materials included in agenda packet; presented by Dr. Moore.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 8: **30-DAY NOTICE TO PRIOR AUTHORIZE REQUIP XL™ AND MIRAPEX ER™**
Materials included in agenda packet; presented by Dr. Chonlahan.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 9: **30-DAY NOTICE TO PRIOR AUTHORIZE LOVAZA®**
For Public Comment, Randy Beckner: I appreciate the opportunity to have a few brief moments with the Committee. My name is Randy Beckner and I'm a Pharm.D. with the medical department of GSK. We're here talking about Lovaza the central fatty acids esterified ester. It is FDA approved for elevated triglycerides, equal to or greater than 500 mg per deciliter. The efficacy of Lovaza is comparable to the fibrates monotherapy when baseline is elevated will get drops of 40% in triglycerides increases of ATL 10 to 15% and drops in non-HDL 15%. The real beauty of Lovaza is, about the safest medication that anybody can prescribe or take. It's relatively free of side effects. GI for placebo is 2 to 3% versus Lovaza itself which is a 4 to 5% eructation event for that. Compared to the other agents, fibrates and niacin, no dosage adjustment is required for Lovaza. Fibrates, as you are aware, individuals with renal impairment require a dosage adjustment, so this one dose, 4 grams for Lovaza, can be either taken once a day, twice a day. Niacin, another competitive agent, while being a very effective agent, is difficult to tolerate for a lot of patients. The other competition for Lovaza are the over-the-counter supplements and where Lovaza differs from the supplements is in potency and purity. Not only are heavy metals removed by a five step purification process, also PCB's, petroleum distillates, anything that is protein bound. So adverse events are further reduced by the purification process. Potency and (unintelligible) supplements (unintelligible) Lovaza capsules (unintelligible). So in summary it's a very well tolerated, effective agent for lowering triglycerides and 500 or greater. So I would recommend changes to the recommendation. One is minor in that triglycerides equal to or greater than 500 mg, it just says 500 mg. And then I would urge the committee to consider a first line therapeutic placement. Any questions? (unintelligible)
Dr. Kuhls: You know, if you just took multiple over the counter pills, right, and I know there are a lot of pills, okay, compared to your product.
Dr. Beckner: Sixteen
Dr. Kuhls: Sixteen pills. So say you prescribe sixteen pills a day and which is probably still going to end up cheaper than your product, how important is mercury in all those kind of things when you take sixteen pills a day?
Dr. Beckner: If you look at the purification process for fatty acids, heavy metals, lead, mercury, actually come up fairly readily for all the products. There are case reports on their toxicity. Recently PCB has become an issue for the supplements. Now the FDA guidelines for PCB's is less than 1500 parts per million. California, which is a stricter State on PCB's, recommends no greater than 80 or 90 parts per million. Each Lovaza capsule is less than 4 parts per million. The other issue with multiple capsules, becomes a caloric aspect. Each Lovaza capsule is 10 kilocalories per capsule. When you start getting into multiple capsules, in each capsule may be 20, 25 kilocalories and (unintelligible). In addition, adherence for Lovaza is higher than supplements because if you open up a bottle of Lovaza and smell it, it generally has no smell. If you open up a bottle of most of the fish oil products, you already have the fish oil being exposed to the air or oxygen, then you breakdown products. The reason you don't see them with Lovaza is it's prepared in an oxygen-free environment (unintelligible) that allows for chemical reaction.
Dr. Kuhls: And platelet problems?
Dr. Beckner: Well as you are aware, omega-3's have the opposite effect of omega-6's, and there is an increase in bleeding time. In several studies it has been documented that the bleeding time, even in CABG patients, is not deemed to be clinically significant, so it is not a recommendation to withhold Lovaza prior to surgical interventions.
Dr. Feightner: Any projected supply issues with the oil spill since this comes from marine life?
Dr. Beckner: No, and actually if you look at supply of the fish that's utilized, it's cold water fish, primarily off of Peru and Argentina.

Dr. Feightner: I was just kidding, really, that's okay.
Dr. Muchmore: Any other questions or comments for Mr. Beckner? Okay. We run into the same problem with niacins over the counter and niacins as formulated as a prescription product, being that there are real differences, and it's very hard to say don't take the prescription niacin (unintelligible) over the counter when we know that its' release is more prolonged than the over the counter and can lead to more hepatic issues, and in this one, it's very difficult to say don't take Lovaza, take the over the counter one. You go to buy any of the hundred brands of over the counter fish oil, you have no idea what the load of PCB's, mercury, lead or anything else is.
Dr. Graham: So you wonder how long it would take to have an effect.
Dr. Muchmore: Well we don't know. But that's the issue that comes to mind. There are over the counter fish oils that are promoted as highly purified. If you go to the website IFOS, you know, they do have things like this, but they're more expensive by far.
Dr. Graham: What makes it a prescription item?
Dr. Preslar: It's a 5-stage process and nitrogen.
Dr. Beckner: More or less.
Dr. Muchmore: Well and it's gone through the FDA approval process as opposed to a food product, which all fish oil's sold as a food product.
Dr. Beckner: And everything is standardized .....
Dr. Graham: But as far as the activity, it's not the activity of the product that you're marketing.
Dr. Beckner: Right, and then we insure the potency and purity. Thank you.
Materials included in agenda packet; presented by Dr. Le.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 10: **ANNUAL REVIEW OF STATINS AND STATIN COMBINATION PRODUCTS AND 30-DAY NOTICE TO PRIOR AUTHORIZE LIVALO®**

Reports included in agenda packet; presented by Dr. Le.
Dr. Kuhls moved to table to the June 2010 DUR Board meeting; seconded by Dr. Preslar.
ACTION: MOTION TABLED

AGENDA ITEM NO. 11: **ANNUAL REVIEW OF ANTIDEPRESSANTS AND 30-DAY NOTICE TO PRIOR AUTHORIZE OLEPTRO™**

Reports included in agenda packet; presented by Dr. Le.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 12: **FDA & DEA UPDATES**

Materials included in agenda packet; presented by Dr. Graham.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: **FUTURE BUSINESS**

Materials included in agenda packet; submitted by Dr. Graham.
A: Annual Review of Smoking Cessation Products
B: Annual Review of Growth Hormones
C: Utilization Review of Epilepsy Medications
D: New Product Reviews
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: **ADJOURNMENT**

The meeting was adjourned at 7:26 p.m.

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

Memorandum

Date: May 17, 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 May 12, 2010

Recommendation 1: Vote to Prior Authorize Mozobil®, Nplate®, and Arcalyst®

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the addition of the Mozobil®, Nplate®, and Arcalyst® to the prior authorization program with the following product specific criteria:

Mozobil® (plerixafor) 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. Must be given in combination with the granulocyte-colony stimulating factor (G-CSF) Neupogen® (filgrastim).
6. **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.

7. Approval period will be for two months.

Nplate® (romiplostim) criteria for approval:

1. FDA approved indication of chronic immune (idiopathic) thrombocytopenia purpura (ITP) in adults 18 and over.
2. Previous insufficient response with at least two of the following treatments: corticosteroids, immunoglobulins, or splenectomy
3. Recent platelet count of < 50 x 10^9/L
4. Initial dosing of 1 mcg/kg once weekly as a subcutaneous injection with recent patient weight in kilograms provided
5. **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
6. **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
7. Approval period will be for four weeks initially, and then quarterly.

Arcalyst® (rilonacept) criteria for approval:

1. FDA approved indication of Cryopyrin-Associated Periodic Syndromes (CAPS) verified by genetic testing. This includes Familial Cold Auto-inflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS) in adults and children 12 and older.
2. The member should not be using a tumor necrosis factor blocking agent (e.g. adalimumab, etanercept, and infliximab) or anakinra
3. Should not be initiated in patients with active or chronic infection including hepatitis B, hepatitis C, human immunodeficiency virus, or tuberculosis.
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.

Recommendation 2: Annual Review of Statins and Statin Combination Products

No action required.

The DUR Board recommends additional review of this class to determine the advantages and disadvantages of allowing grandfathering of this category.

Recommendation 3: Annual Review of Antidepressants

No action required.

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

Appendix B

RETROSPECTIVE DRUG UTILIZATION REVIEW REPORT
January 2010

MODULE	DRUG INTERACTION	DUPLICATION OF THERAPY	DRUG-DISEASE PRECAUTIONS	DOSING & DURATION
Total # of messages	48,825	61,252	1,117,619	30,437
Limits applied	Established, Major, Males and Females, Age 22-50	Males and Females, Narcotics, Age 38-40	Contraindicated, Diabetes Mellitus, Males and Females Age 46-52	High Dose & Low Dose, Biguanides, Males and Females, Age 0-40
Total # of messages after limits were applied	124	317	191	88
Total # of members reviewed	124	243	144	88

LETTERS			
Category	**Prescribers**	**Pharmacies**	**Total Letters**
Drug Interaction	35	0	35
Duplication of Therapy	140	22	162
Drug-Disease Precautions	5	0	5
Dosing & Duration	39	0	39
Total Letters Sent	219	22	241

Retrospective Drug Utilization Review Report

Claims Reviewed for November 2009

Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
Limits which were applied	Established, Major, Males and Females, Age 61-150	Narcotics, Males and Females, Age 34-35	Contraindicated, Diabetes Mellitus, Males and Females, Age 19-35	High Dose, Benzodiazepines, Males and Females, Age 71-150

Response Summary (Prescriber)
Letters Sent: 129
Response Forms Returned: 84

The response forms returned yielded the following results:

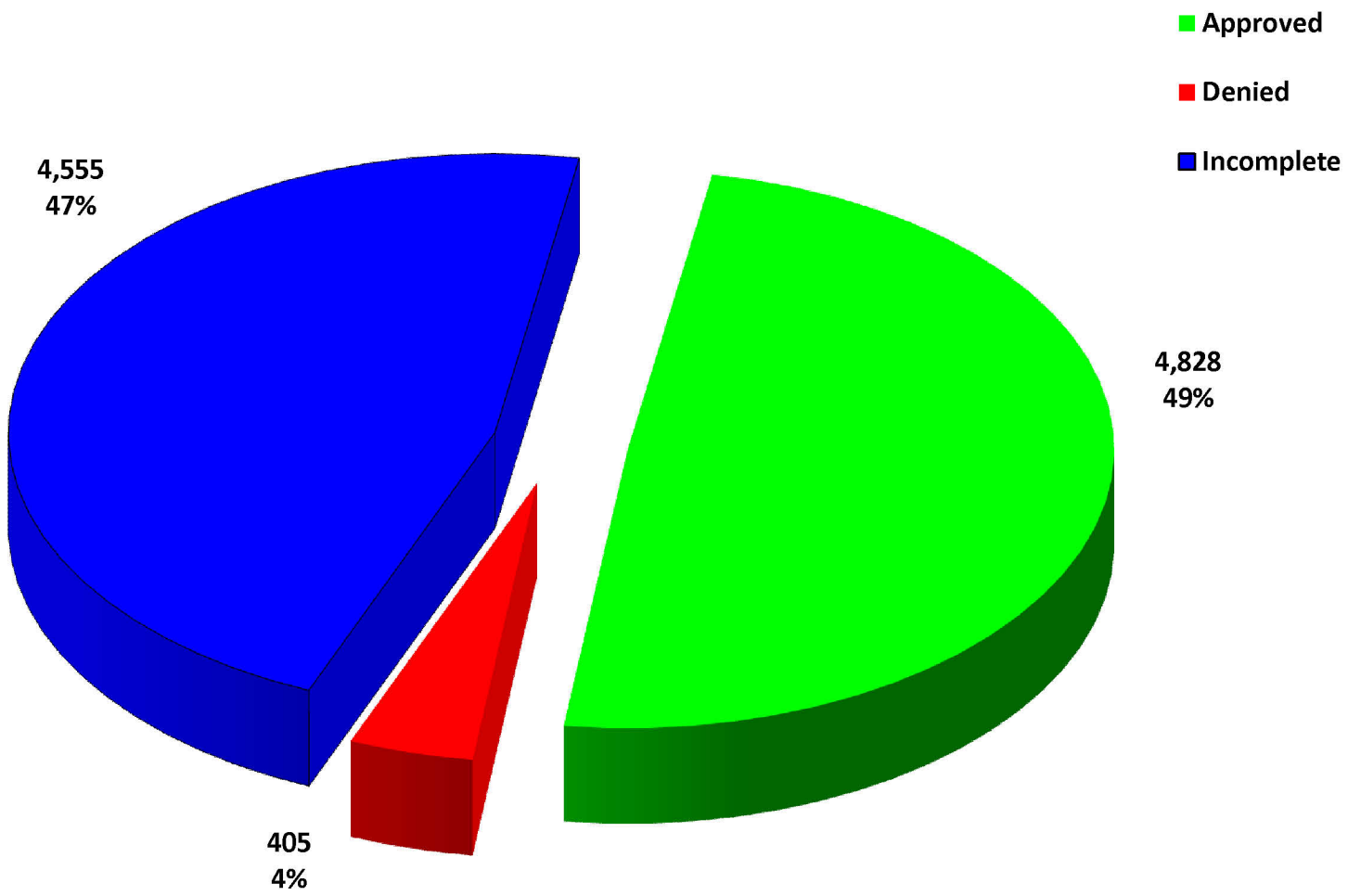
6 (7%)	*Record Error—Not my patient.*
8 (10%)	*No longer my patient.*
2 (2%)	*Medication has been changed prior to date of review letter.*
25 (30%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
29 (35%)	*I am aware of this situation and will plan to continue monitoring therapy.*
14 (17%)	*Other*

Response Summary (Pharmacy)
Letters Sent: 21
Response Forms Returned: 13

The response forms returned yielded the following results:

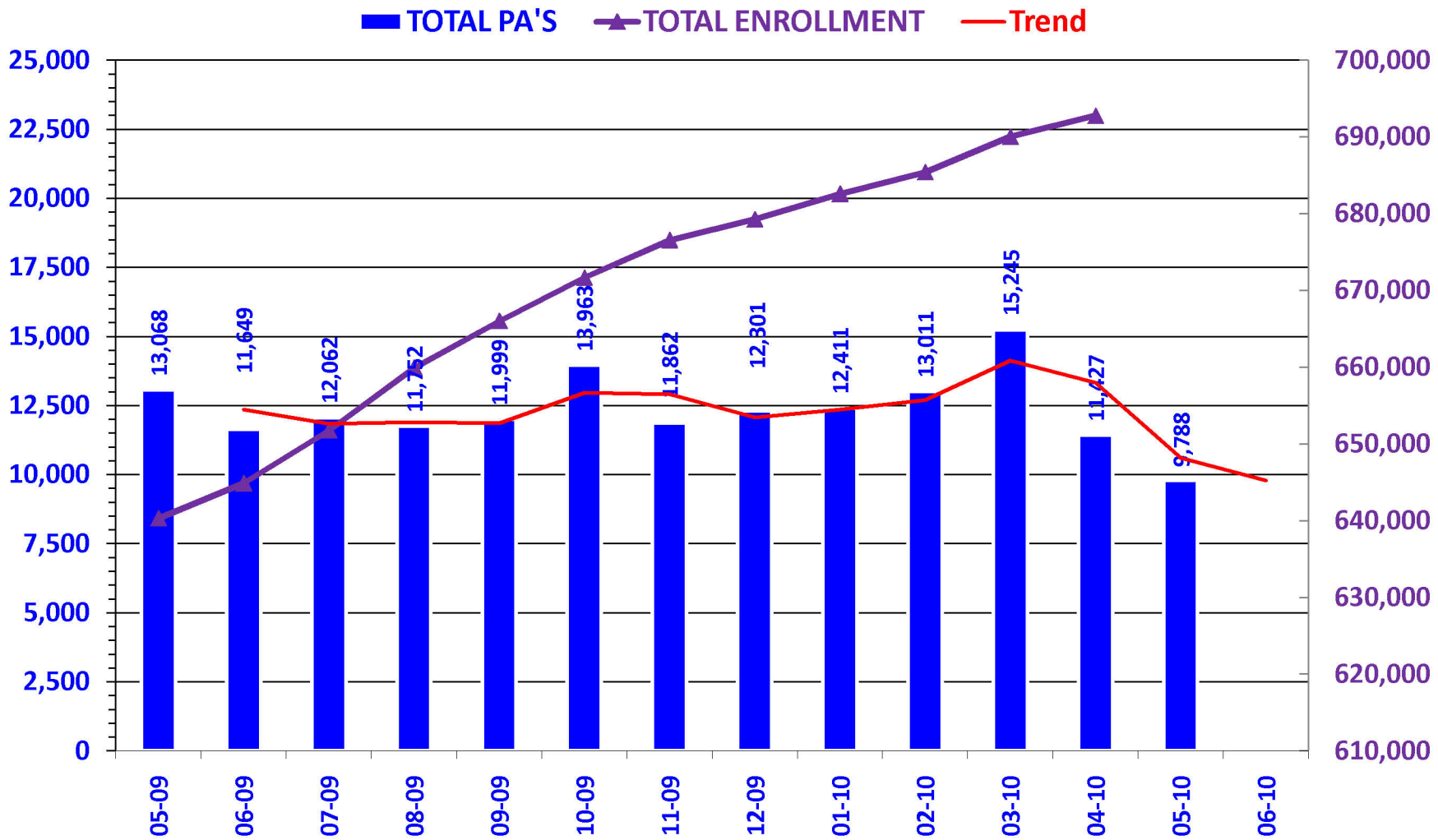
0 (0%)	*Record Error—Not my patient.*
0 (0%)	*No longer my patient.*
0 (0%)	*Medication has been changed prior to date of review letter.*
6 (46%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
3 (23%)	*I am aware of this situation and will plan to continue monitoring therapy.*
4 (31%)	*Other*

PRIOR AUTHORIZATION ACTIVITY REPORT: May 2010



PA totals include overrides

PRIOR AUTHORIZATION REPORT: May 2009 – May 2010



PA totals include overrides

Prior Authorization Activity

May 2010

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort	495	232	5	258	358
Amitiza	27	8	4	15	218
Antidepressant	394	113	20	261	342
Antihistamine	479	263	16	200	323
Antihypertensives	110	46	8	56	333
Antimigraine	110	23	4	83	254
Atypical Antipsychotics	694	339	14	341	347
Benzodiazepines	171	49	0	122	202
Bladder Control	68	10	5	53	333
Brovana (Arformoterol)	2	0	1	1	0
Byetta	10	5	0	5	361
Elidel/Protopic	42	23	0	19	91
ESA	289	168	53	68	61
Fibric Acid Derivatives	9	2	1	6	228
Fibromyalgia	139	46	7	86	326
Fortamet/Glumetza	3	0	0	3	0
Forteo	5	4	0	1	361
Glaucoma	17	10	0	7	269
Growth Hormones	46	37	3	6	182
HFA Rescue Inhalers	93	38	2	53	275
Insomnia	82	17	5	60	180
Misc Analgesics	37	7	14	16	179
Muscle Relaxant	180	49	58	73	72
Nasal Allergy	449	104	26	319	150
NSAIDS	136	27	8	101	334
Ocular Allergy	42	8	1	33	155
Ocular Antibiotics	138	50	2	86	11
Opioid Analgesic	150	64	4	82	179
Other	457	125	34	298	143
Otic Antibiotic	140	73	2	65	11
Pediculicides	89	39	0	50	19
Plavix	305	194	3	108	294
Proton Pump Inhibitors	511	112	15	384	100
Qualaquin (Quinine)	4	0	4	0	0
Singulair	1,059	672	19	368	254
Smoking Cessation	51	15	2	34	50
Statins	121	34	4	83	346
Stimulant	954	579	19	356	237
Symlin	2	0	0	2	0
Topical Antibiotics	23	3	0	20	33
Topical Antifungals	21	6	0	15	33
Ultram ER and ODT	8	3	0	5	238
Xolair	6	1	3	2	361
Xopenex Nebs	53	24	1	28	243
Zetia (Ezetimibe)	22	13	0	9	360
Emergency PAs	12	12	0	0	
Total	**8,255**	**3,647**	**367**	**4,241**	

Overrides					
Brand	31	18	1	12	214
Dosage Change	497	477	2	18	13
High Dose	11	7	0	4	157
IHS - Brand	37	33	2	2	138
IHS – Brand	2	0	0	2	0
Ingredient Duplication	4	4	0	0	11
Lost/Broken Rx	104	97	6	1	9
NDC vs Age	42	41	0	1	258
Nursing Home Issue	102	97	0	5	16
Other	18	12	0	6	56
Quantity vs. Days Supply	720	428	26	266	250
Stolen	9	8	1	0	3
Overrides Total	**1,533**	**1,181**	**38**	**314**	
Total Regular PAs + Overrides	**9,788**	**4,828**	**405**	**4,555**	

Denial Reasons

Unable to verify required trials.	2,354
Lack required information to process request.	2,112
Does not meet established criteria.	236
Not an FDA approved indication/diagnosis.	131
Member has active PA for requested medication.	50
Medication not covered as pharmacy benefit.	44
Considered duplicate therapy. Member has a prior authorization for similar medication.	20
Requested dose exceeds maximum recommended FDA dose.	20
Drug Not Deemed Medically Necessary	1

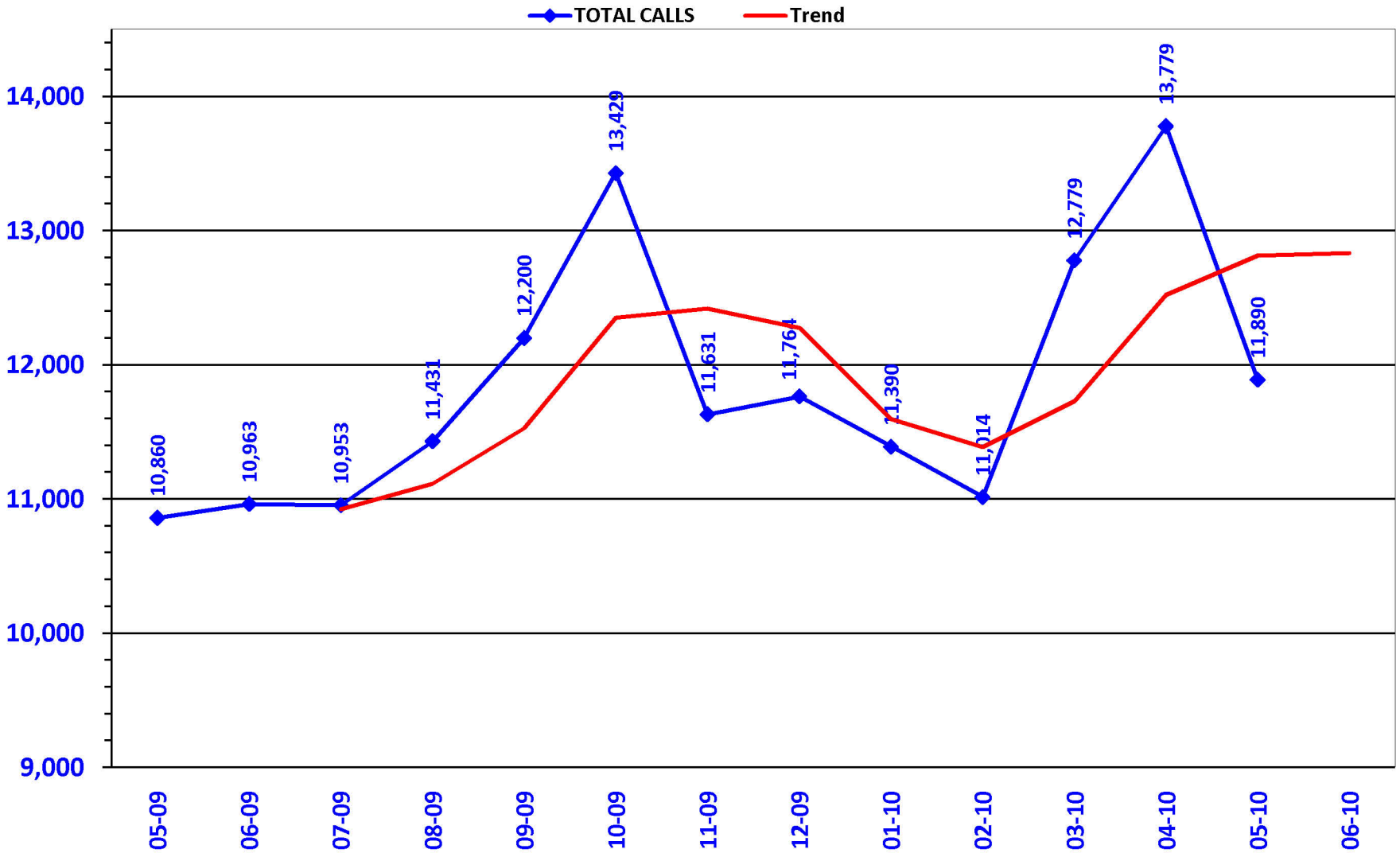
Duplicate Requests: 650

Letters: 1,393

No Process: 407

Changes to existing PAs: 439

CALL VOLUME MONTHLY REPORT:
May 2009 – May 2010



Appendix C

Vote to Prior Authorize ILARIS®

Oklahoma Health Care Authority, June 2010

Recommendations:

The College of Pharmacy recommends pharmacy prior authorization of ILARIS® (canakinumab) with the following criteria.

ILARIS® (canakinumab) criteria for approval:

Criteria for approval:

1. FDA approved indication of Cryopyrin-Associated Periodic Syndromes (CAPS) verified by genetic testing. This includes Familial Cold Auto-inflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS) in adults and children 4 and older.
2. The member should not be using a tumor necrosis factor blocking agent (e.g. adalimumab, etanercept, and infliximab) or anakinra
3. Should not be initiated in patients with active or chronic infection including hepatitis B, hepatitis C, human immunodeficiency virus, or tuberculosis.
4. Dosing should not be more often than once every 8 weeks.
5. **Approved dosing schedule based on weight:**
    a. Body weight >40 kg: 150mg
    b. Body weight 15 kg – 40 kg: 2mg/kg. If inadequate response, may be increased to 3mg/kg
6. Approval period is for one year.

Appendix D

Vote to Prior Authorize Requip XL™ (ropinirole) and Mirapex ER™ (pramipexole extended release)

Oklahoma Health Care Authority
June 2010

Requip XL™ (ropinirole)

Manufacturer	GlaxoSmithKline
Classification	non-ergoline dopamine agonist
Status	Prescription Only

Requip XL™ Summary

Requip XL™ extended-release tablets contain ropinirole, a non-ergoline dopamine agonist indicated for the treatment of signs and symptoms of idiopathic Parkinson's disease. The once daily formulation may be prescribed as monotherapy or adjunct therapy.

Dosage Forms: 2mg, 4mg, 6mg, 8mg, or 12mg extended-release tablets

Mirapex ER™ (pramipexole extended release)

Manufacturer	Boehringer Ingelheim
Classification	Non-ergot dopamine agonist
Status	Prescription Only

Mirapex ER™ Summary

Mirapex ER™ tablets contain pramipexole, a non-ergot dopamine agonist indicated for the treatment of idiopathic Parkinson's Disease at once a day dosing.

Dosage Forms: 0.375mg, 0.75mg, 1.5mg, 3mg, or 4.5mg extended-release tablets

Recommendations

The College of Pharmacy recommends prior authorization for Requip XL™ (ropinirole) tablets and Mirapex ER™ (pramipexole) tablets to ensure appropriate utilization for the FDA approved indication for the treatment of signs and symptoms of Parkinson's Disease.

Appendix E

Vote to Prior Authorize Lovaza® (omega-3-acid ethyl esters)

Oklahoma Health Care Authority
June 2010

Manufacturer	GlaxoSmithKline
Classification	Anti-Hypertriglyceridemia
Status	Prescription Only

Recommendations

The College of Pharmacy recommends prior authorization of Lovaza® with the following criteria:

1. Laboratory documentation of severe hypertriglyceridemia (fasting triglycerides ≥500 mg/dL).
2. Previous failure with both nicotinic acid and fibric acid medications.

Appendix F

STepped **A**pproach **T**o **IN**creased **C**ost **E**ffectiveness (STATIN-CE) and Vote to Prior Authorize Livalo® (pitavastatin)

Oklahoma Health Care Authority

June 2010

Introduction and Background

There is no question regarding the place of statins in the clinical management of cardiovascular disease as this class is the most potent lipid lowering class to date, and has been clearly shown to decrease the number of cardiac events and reduced risk of stroke in patients who take them.[1] The use of statins has been further expanded as clinical evidence shaped guidelines to recommend lipid lowering strategies for primary prevention and included diabetes and metabolic syndrome as risk factors.[2] These medications were a major proponent that propelled the class of lipid regulators to be the 2nd most costly drug category, only second to the atypical antipsychotics, and the class with the most retail prescriptions dispensed in 2008.[3]

As a result of the cost of these medications, there have been numerous cost-effectiveness strategies that have been considered and implemented by various payor systems to date. Most significantly, the introduction of generic simvastatin prompted a worldwide response from various countries such as Australia, Germany, and the United Kingdom, to name a few, to alter pricing structures or coverage benefit designs. A little closer to home, private pharmacy benefits managers all over the U.S. employed such strategies as tier restructuring, prior authorizations, and even zero copays resulting in free medications, or other incentives to get people to switch from the brand name medication to the generic.

Considerations for Maximizing Cost-Effectiveness

A review of available published reviews on the use of atorvastatin and simvastatin medications show that dosing[4] and compliance play a key role in goal LDL goal attainment and overall cost-efficacy of using these medications. The statins vary in LDL lowering capacity, but similar LDL lowering can be attained between Lipitor® 10mg and 20mg and simvastatin 40mg. One review[5] showed that patient care groups with a high proportion of simvastatin and pravastatin use were just as successful at achieving cholesterol targets for patients with coronary heart disease, diabetes and stroke as those that used more atorvastatin, rosuvastatin or fluvastatin. A lot of effort is centered on demonstrating LDL lowering percentages and associated endpoints, but the bottom line lies with compliance. Medication persistence studies for the class of statins show compliance rates between only 40% and 70%[6], and that the compliance rate decreases over time.[7] One trial estimates that with compliance rates of only 40%, the risk reduction is less than half of that shown in clinical trials.[8] These are two important points to consider in the approach to increase cost-effectiveness of these medications.

Utilization of Statins

Trends in Utilization of Statins and Statin Combination Products

Calendar Year	Members	Claims	Paid	Paid/ Claim	Paid/ Day	Units	Days
2004	23,999	109,803	$15,496,853.11	$141.13	$3.12	5,002,082	4,971,840
2005	28,986	143,797	$20,421,439.46	$142.02	$3.21	6,330,961	6,359,937
2006	10,228	43,686	$6,079,728.88	$139.17	$3.27	1,846,769	1,860,539
2007	10,579	48,596	$4,679,850.00	$96.30	$2.32	2,004,344	2,016,639
2008	11,818	55,204	$4,631,396.72	$83.90	$2.08	2,230,090	2,225,081
2009	12,245	55,228	$4,387,536.24	$79.44	$1.96	2,259,312	2,243,610

Medication Totals for Calendar Year 2009

BRAND NAME	CLAIMS	UNITS	DAYS	MEMBERS	PAID	PAID/ DAY	PERCENT PAID
Lipitor® Totals	20,333	849,233	847,587	4,803	$3,284,031.81	$3.87	74.85%
Simvastatin Totals	20,117	783,369	785,574	5,232	$197,583.04	$0.25	4.51%
Pravastatin Totals	6,280	255,915	249,225	1,991	$66,285.78	$0.27	1.52%
Lovastatin Totals	3,331	144,942	134,126	914	$33,969.72	$0.25	0.78%
Crestor® Totals	2,107	91,208	91,973	508	$346,316.63	$3.77	7.90%
Vytorin® Totals	1,796	79,976	80,694	379	$277,317.93	$3.44	0.06%
Zetia® Totals	822	38,287	38,590	187	$131,825.07	$3.42	3.00%
Simcor Totals	213	6,762	6,491	84	$17,611.79	$2.71	0.004%
Lescol® and XL Totals	141	6,770	6,620	29	$21,806.09	$3.29	0.005%
Advicor® Totals	77	2,520	2,400	12	$8,925.41	$3.72	0.002%
Altoprev® Totals	11	330	330	3	$1,862.97	$5.65	0.04%
Grand Totals	**55,228**	**2,259,312**	**2,243,610**	**12,245**	**$4,387,536.24**	**$1.96**	**100.00%**

MEDICATION	CLAIMS	UNITS	DAYS	MEMBERS	PAID	UNITS/ DAY	CLAIMS/ MEMBER	PAID/ DAY
LIPITOR® TAB 10MG	5,161	212,169	210,212	1,151	$626,145.21	1.01	4.48	$2.98
LIPITOR® TAB 20MG	7,421	311,491	311,569	1,753	$1,298,464.28	1	4.23	$4.17
LIPITOR® TAB 40MG	5,817	244,845	243,596	1,419	$1,022,090.26	1.01	4.1	$4.20
LIPITOR® TAB 80MG	1,934	80,728	82,210	480	$337,332.06	0.98	4.03	$4.10
TOTALS	**20,333**	**849,233**	**847,587**		**$3,284,031.81**	**1**	**4.21**	**$3.86**
SIMVASTATIN TAB 5MG	30	1,170	1,170	12	$262.95	1	2.5	$0.22
SIMVASTATIN TAB 10MG	1,391	53,440	52,916	366	$11,823.93	1.01	3.8	$0.22
SIMVASTATIN TAB 20MG	8,219	315,970	314,012	2,117	$76,206.09	1.01	3.88	$0.24
SIMVASTATIN TAB 40MG	7,910	314,285	314,880	2,070	$82,050.09	1	3.82	$0.26
SIMVASTATIN TAB 80MG	2,567	98,504	102,596	667	$27,239.98	0.96	3.85	$0.27
TOTALS	**20,117**	**783,369**	**785,574**		**$197,583.04**	**0.996**	**3.57**	**0.242**

Clinical Comparison of Simvastatin and Atorvastatin

Comparison of LDL-Lowering Capacity*

Medication	% LDL Reduction	Medication	% LDL Reduction
Simvastatin TAB 5MG	26	Atorvastatin TAB 10MG	39
Simvastatin TAB 10MG	30	Atorvastatin TAB 20MG	43
Simvastatin TAB 20MG	38	Atorvastatin TAB 40MG	50
Simvastatin TAB 40MG	41	Atorvastatin TAB 80MG	60
Simvastatin TAB 80MG	47		

*From Product Label.

Comparison of Adverse Effects*

Description	Simvastatin	Atorvastatin
Contraindications	▪ hypersensitivity to atorvastatin or any component of the product ▪ active liver disease which may include unexplained persistent elevations in hepatic transaminase levels. ▪ women who are pregnant or may become pregnant.	▪ hypersensitivity to atorvastatin or any component of the product ▪ active liver disease ▪ serum transaminases, unexplained persistent elevation ▪ pregnancy or lactation; may cause fetal harm
Warnings & Precautions	▪ **Skeletal muscle effects** (e.g., myopathy and rhabdomyolysis): Risks increase with higher doses and concomitant use of certain CYP3A4 inhibitors, gemfibrozil, cyclosporine, danazol, amiodarone, verapamil, and diltiazem. Predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, and renal impairment. ▪ Patients should be advised to **report promptly any symptoms of myopathy.** Simvastatin therapy should be discontinued immediately if myopathy is diagnosed or suspected. ▪ **Liver enzyme abnormalities** and monitoring: Persistent elevations in hepatic transaminase can occur. Monitor liver enzymes before and during treatment. Patients titrated to the 80-mg dose should receive more frequent liver function tests than patients on lower doses.	▪ **Skeletal muscle effects** (e.g., myopathy and rhabdomyolysis): Risks increase when higher doses are used concomitantly with cyclosporine, fibrates, and strong CYP3A4 inhibitors (e.g., clarithromycin, itraconazole, HIV protease inhibitors). Predisposing factors include advanced age (> 65), uncontrolled hypothyroidism, and renal impairment. Rare cases of rhabdomyolysis with acute renal failure secondary to myoglobinuria have been reported. In cases of myopathy or rhabdomyolysis, therapy should be temporarily withheld or discontinued ▪ **Liver enzyme abnormalities** and monitoring: Persistent elevations in hepatic transaminases can occur. Monitor liver enzymes before and during treatment ▪ **A higher incidence of hemorrhagic stroke** was seen in patients without CHD but with stroke or TIA within the previous 6 months in the LIPITOR 80 mg group vs. placebo
Common Adverse Effects	**Incidence ≥5.0%:** ▪ upper respiratory infection ▪ headache ▪ abdominal pain ▪ constipation ▪ nausea	**Incidence ≥ 2%:** ▪ nasopharyngitis ▪ arthralgia ▪ diarrhea ▪ pain in extremity ▪ urinary tract infection
Specific Populations	**Severe renal impairment**: patients should be started at 5 mg/day and be closely monitored.	**Hepatic impairment**: Plasma concentrations markedly increased in patients with chronic alcoholic liver disease

*From Product Label

Drug-Drug Interactions*

Simvastatin	
Interacting Agent	**Prescribing Recommendations**
Itraconazole, ketoconazole, erythromycin, clarithromycin, telithromycin, HIV protease inhibitors, nefazodone	Avoid simvastatin, or suspend use of simvastatin during course of treatment.
Gemfibrozil, cyclosporine, danazol	Do not exceed 10 mg simvastatin daily
Amiodarone, verapamil	Do not exceed 20 mg simvastatin daily
Diltiazem	Do not exceed 40 mg simvastatin daily
Grapefruit juice	Avoid large quantities of grapefruit juice (>1 quart daily)
Coumarin anticoagulants	Concomitant use with ZOCOR prolongs INR. Achieve stable INR prior to starting ZOCOR. Monitor INR frequently until stable upon initiation or alteration of ZOCOR therapy.

Atorvastatin	
Interacting Agent	**Prescribing Recommendations**
Clarithromycin, itraconazole, HIV protease inhibitors (ritonavir plus saquinavir or lopinavir plus ritonavir)	Caution when exceeding doses > 20 mg atorvastatin daily. The lowest dose necessary should be used.
Cyclosporine	Do not exceed 10 mg atorvastatin daily
Digoxin	Patients should be monitored appropriately
Rifampin	should be simultaneously co-administered with LIPITOR
Oral Contraceptives	Values for norethindrone and ethinyl estradiol may be increased

***From Product Label**

Economic Impact of Switching from Atorvastatin to Simvastatin

Estimated Savings per Conversion Scenario

Conversion Rate	Lipitor® 10mg to Simvastatin 40mg	Lipitor® 20mg to Simvastatin 40mg	Lipitor® 40mg to Simvastatin 40mg	Total Raw Savings 10mg & 20mg	Total Raw Savings 10mg, 20mg, & 40mg
100%	$571,490.09	$1,217,456.34	$958,755.30	$1,788,946.43	$2,747,701.73
75%	$510,528.61	$1,034,409.55	$813,815.68	$1,544,938.16	$2,358,753.84
50%	$340,256.89	$689,346.89	$542,206.14	$1,029,603.78	$1,571,809.92
25%	$169,985.17	$344,284.22	$270,596.60	$514,269.39	$784,865.99

Based on the utilization data, this will affect approximately 2,900 members who are currently on Lipitor® 10mg and 20mg, or 4,300 members if Lipitor 40mg is included. Approximately 440 members will be affected if Crestor® 5mg, 10mg and 20mg doses are included. Previously, it has been theorized that total cost per petition to the *healthcare system* (includes cost to physicians, pharmacists, and program) is between $7.12 and $13.78. Total cost per petition to the *healthcare system* is estimated to be between $33,748.80 and $65,317.20 annually.

Strategies for Switching from Lipitor® to Simvastatin in the SoonerCare Population

Prescriber Targeted Intervention

Communication to prescribers is a key component for the successful implementation of this proposed cost-effectiveness initiative. For further input from the DUR Board, the College of Pharmacy recommends the following:

- Set a date for implementation of conversion.
- Notify prescribers of Lipitor® and Crestor® regarding the initiative, including the number of members currently on these medications along with the member's identity, and a request to switch these members to a preferred product.
- A faxblast to all prescribers and pharmacies notifying them of the date of of implementation and request generic utilization or recommendation for all members when appropriate.

Member Targeted Education

The College of Pharmacy also recommends members currently on Lipitor® and Crestor® receive a postcard with the following:

- Information regarding effectiveness of available generic statins on the $0.00 copay list.
- General information regarding generic medications that are available that are also on the $0.00 copay list.
- Importance of compliance when taking medications for chronic diseases, specifically pertaining to statins.

Recommendation

In conclusion, the College of Pharmacy recommends the DUR Board discuss and consider the **ST**epped **A**pproach **T**o **IN**creased **C**ost **E**ffectiveness (STATIN-CE) initiative in the SoonerCare population, and the addition of Livalo® to Tier 2 of the Statin PBPA Category. The existing criteria for this category will apply.

HMG-CoA Reductase Inhibitors (Statins)		
Tier One	***Tier Two***	***Tier Three***
Fluvastatin (Lescol® & Lescol® XL)	**Atorvastatin (Lipitor®)**	**Lovastatin (brand Altoprev®)**
Lovastatin (Mevacor®)	**Rosuvastatin (Crestor®)**	**Simvastatin/Ezetimibe (Vytorin®)**
Pravastatin (Pravachol®)	**Pitavastatin (Livalo®)**	**Ezetemibe (Zetia®)**
Simvastatin (Zocor®)		
Statin/Niaspan® Combination Products		
Tier 1 Statins and/or Niaspan®	**Lovastatin/Niacin CR (Advicor®)**	
	Simvastatin/Niacin CR (Simcor®)	

To qualify for a Tier 2 medication, there must be:

1. A trial, defined by at least 8 weeks of continuous therapy titrated to recommended dose, of a Tier 1 medication that did not yield adequate LDL reduction.
2. Documented adverse effect or contraindication to all available lower tiered products.
3. Clinical exception for atorvastatin 80mg: members hospitalized for recent acute myocardial infarction or acute coronary syndrome.

To qualify for a Tier 3 medication, there must be:

1. A trial, defined by at least 8 weeks of continuous therapy titrated to recommended dose, of a Tier 2 medication that did not yield adequate LDL reduction.
2. Documented adverse effect or contraindication to all available lower tiered products.
3. Clinical exceptions for Ezetimibe:
    a. Documented active liver disease.
    b. Documented unexplained, persistent elevations of serum transaminases.
    c. Documented statin related myopathy.

[1] Law MR, Wald NJ, Rudnicka AR (June 2003). "Quantifying effect of statins on low density lipoprotein cholesterol, ischaemic heart disease, and stroke: systematic review and meta-analysis". *BMJ* **326** (7404): 1423.

2 Third Report of the Expert Panel on Detection, Evaluation, and Treatment of the High Blood Cholesterol in Adults (Adult Treatment Panel III): Executive Summary. Available online at: **http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3xsum.pdf**

[3] http://seekingalpha.com/article/128003-u-s-prescription-drug-sales-grow-slowly-hydrocodone-most-prescribed

[4] Rublee DA. Burke JP. LDL-C goal attainment in patients who remain on atorvastatin or switch to equivalent or non-equivalent doses of simvastatin: a retrospective matched cohort study in clinical practice. Postgraduate Medicine. 122(2):16-24, 2010 Mar.

[5] **Duncan Petty , David Lloyd.** Can cheap generic statins achieve national cholesterol lowering targets? J Health Serv Res Policy 2008;**13**:99-102

[6] CONNIE A. VALDEZ, PHARMD, MSED, AND HEATHER ULRICH, PHARMD. Similar Medication Compliance and Control of Dyslipidemia With Simvastatin or Atorvastatin in a Staff-Model HMO Medical Clinic. J Manag Care Pharm. 2005;11(6):499-504.

[7] Joshua S. Benner; Robert J. Glynn; Helen Mogun; et al. **Long-term Persistence in Use of Statin Therapy in Elderly Patients.** JAMA, July 24/31, 2002—Vol 288, No. 4

[8] Branko Kopjar, MD, MS, PhD, Anne E.B. Sales, RNS, PhD, Sandra L. Pin˜eros, PA-C, MPH, Haili Sun, PhD, Yu-Fang Li, PhD, and Ashley N. Hedeen, MPH, MD. Adherence With Statin Therapy in Secondary Prevention of Coronary Heart Disease in Veterans Administration Male Population. Am J Cardiol 2003;92:1106–1108

Appendix G

Vote to Prior Authorization Oleptro™ (trazodone extended release)

Oklahoma Health Care Authority, June 2010

Recommendations

The College of Pharmacy recommends placement of Oleptro™ in Tier 3 of the Antidepressants PBPA Category. The existing criteria for this category will apply.

SSRIs (Selective Serotonin Reuptake Inhibitors)		
Tier 1	**Tier 2**	**Tier 3**
citalopram (Celexa®)	escitalopram (Lexapro®)	
fluoxetine (Prozac®, Sarafem®)	fluoxetine (40mg caps, Prozac Weekly™)	
fluvoxamine (Luvox®)	fluvoxamine CR (Luvox® CR)	
paroxetine (Paxil®, Paxil CR®)	paroxetine (Pexeva®)	
sertraline (Zoloft®)		
Dual Acting Antidepressants		
Tier 1	**Tier 2**	**Tier 3**
bupropion (Wellbutrin®)	Venlafaxine Extended Release Tabs	bupropion (Aplenzin®)
bupropion (Wellbutrin SR®, Wellbutrin XL®)		duloxetine (Cymbalta®)
mirtazapine (Remeron®, Remeron SolTab®)		nefazodone (Serzone®)
trazodone (Desyrel®)		trazodone ER (Oleptro™)
venlafaxine (Effexor®)		venlafaxine ER (Effexor XR® Caps)
		desvenlafaxine (Pristiq®)
Monoamine Oxidase Inhibitors		
Tier 1	**Tier 2**	**Tier 3**
		selegiline transderm patch (Emsam®)
		tranylcypromine (Parnate®)
		phenelzine (Nardil®)
		selegiline (Zelapar®)

Mandatory generic plan applies , Current tiers based on Supplemental Rebate participation

Tier-2 Authorization Criteria

1. A documented, recent (within 6 months) trial of a Tier 1 medication at least 4 weeks in duration and titrated to recommended dosing, that did not provide an adequate response. Tier 1 selection can be from any classification.
2. Prior stabilization on the Tier 2 medication documented within the last 100 days. A past history of success on the Tier 2 medication will also be considered with adequate documentation.
3. A unique FDA-approved indication not covered by Tier 1 products or other products from a different therapeutic class.
4. A petition may be submitted for consideration whenever a unique member specific situation exists.

Tier-3 Authorization Criteria

1. A documented, recent (within 6 months) trial with a Tier 1 and a Tier 2 medication at least 4 weeks in duration and titrated to recommended dose, that did not provide an adequate response. Tier 1 and Tier 2 selection can be from any classification.
2. Prior stabilization on the Tier 3 medication documented within the last 100 days. A past history of success on the Tier 3 medication will also be considered with adequate documentation.
3. A unique FDA-approved indication not covered by a lowered tiered product or other products from a different therapeutic class.
4. A petition may be submitted for consideration whenever a unique member specific situation exists.

Appendix H

Fiscal Year 2009 Annual Review of Ophthalmic Anti-infectives and Vote to Prior Authorize Besivance™

Oklahoma HealthCare Authority
June 2010

Current Prior Authorization Criteria

This category was initially reviewed and approved by the DUR Board in 2007. The tier structure and prior authorization criteria during Fiscal Year 2009 are as follows:

Criteria for a Tier 2 medication:

1. Approved indication/suspected infection by organism not known to be covered by Tier 1 products, or failure of a Tier 1 product.
2. Known contraindication to all indicated Tier 1 medication.
3. Prescription written by optometrists/ophthalmologists, or
4. When used for pre/post-operative prophylaxis.

Criteria for a Tier 3 medication:

1. Approved indication/suspected infection by organism not known to be covered by Tier 2 products, or failure of a Tier 2 product.
2. Known contraindication to all indicated Tier 2 medication.
3. Prescription written by optometrists/ophthalmologists, or
4. When used for pre/post-operative prophylaxis.

Ophthalmic Antibiotics: Liquids	
Tier 1	**Tier 2**
Ciloxan Solution (Ciprofloxacin)	Vigamox (Moxifloxacin)
Quixin (Levofloxacin)	Zymar (Gatifloxacin)
Ocuflox (Ofloxacin)	Azasite (Azithromycin)
Gentak (Gentamicin)	
AK-Tob (Tobramycin)	
Bleph-10, Na Sulamyd (Na Sulfacetamide)	
Polytrim (PolymyxinB/Trimethoprim)	
AK-Spore (Neo/PolyB/Gramacidin)	

Ophthalmic Antibiotics: Ointments	
Tier 1	**Tier 2**
AK-Tracin (Bacitracin)	
AK-Poly-Bac (Bacitracin/PolymyxinB)	
Ciloxan Ointment (Ciprofloxacin)	
Tobrex (Tobramycin)	
Neosporin (Neomycin/Polymyxin B/Bacitracin)	
A/T/S, Ilotycin, Roymicin (Erythromycin)	
Gentak (Gentamicin)	
Bleph-10, Sodium Sulamyd (Sodium Sulfacetamide)	

Approval Criteria for Antibiotic/Steroid Combination Products:

1. Prescription written by optometrists/ophthalmologists, or
2. When used for pre/post-operative prophylaxis

Ophthalmic Antibiotic–Steroid Combination Products	
Tier 1	**Tier 2**
	Tobradex (Tobramycin/Dexamethasone) Susp & Oint
	Zylet (Tobramycin/Loteprednol) Suspension
	Blephamide (Sulf/Prednisolone) Susp & Oint
	Pred-G (Gentamicin/Prednisolone) Susp & Oint
	Poly-Pred (Neo/Poly/Prednisolone) Susp
	Cortisporin (Neo/Poly/Hydrocortisone) Susp
	Maxitrol (Neo/Poly/Dexamethasone) Susp & Oint
	Bac/Poly/Neo/Hydrocortisone Ointment
	Neo/Poly/Bac/Hydrocortisone Ointment

Utilization of Medication or Class

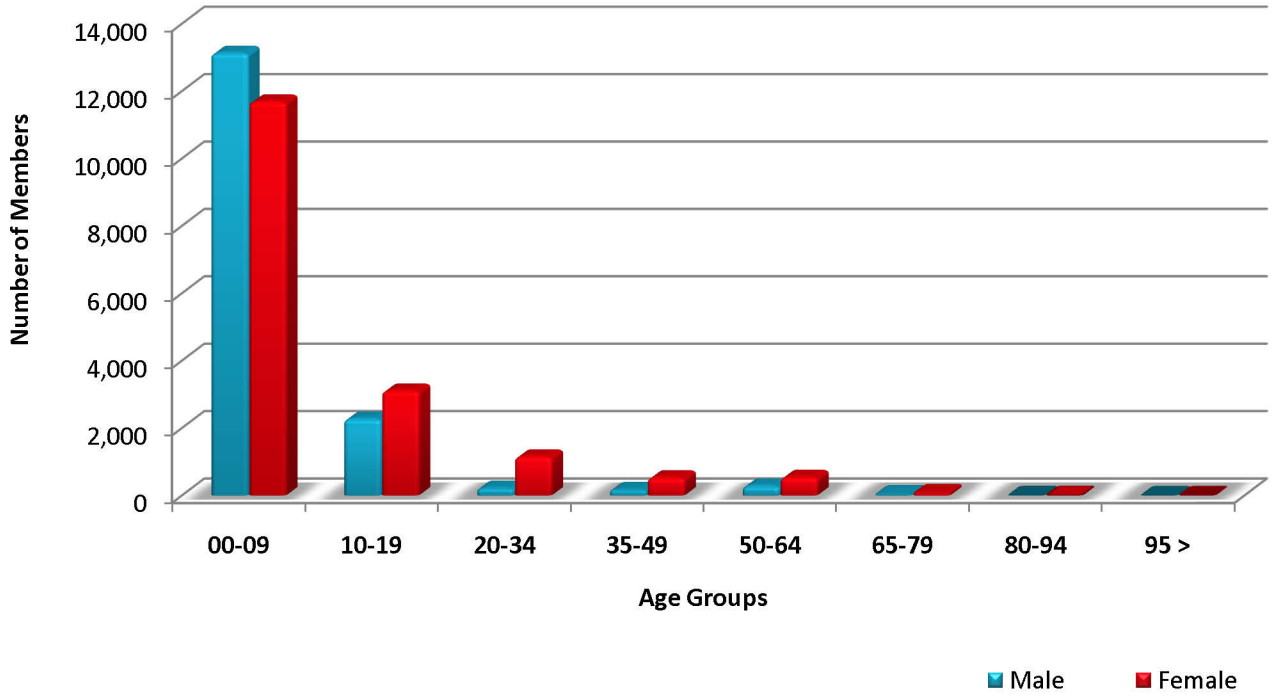
Comparison of Fiscal Years Ophthalmic Anti-infectives (no Steroids)

Fiscal Year	Members	Claims	Paid	Paid/Claim	Perdiem	Units	Days
2008	34,330	41,995	$1,049,123.75	$24.98	$2.44	253,248	429,347
2009	33,266	39,993	$1,049,599.84	$26.24	$2.56	236,150	410,284
Percent Change	-3.10%	-4.80%	0.00%	5.00%	4.90%	-6.80%	-4.40%
Change	-1,064	-2,002	$476.09	$1.26	$0.12	-17,098	-19,063

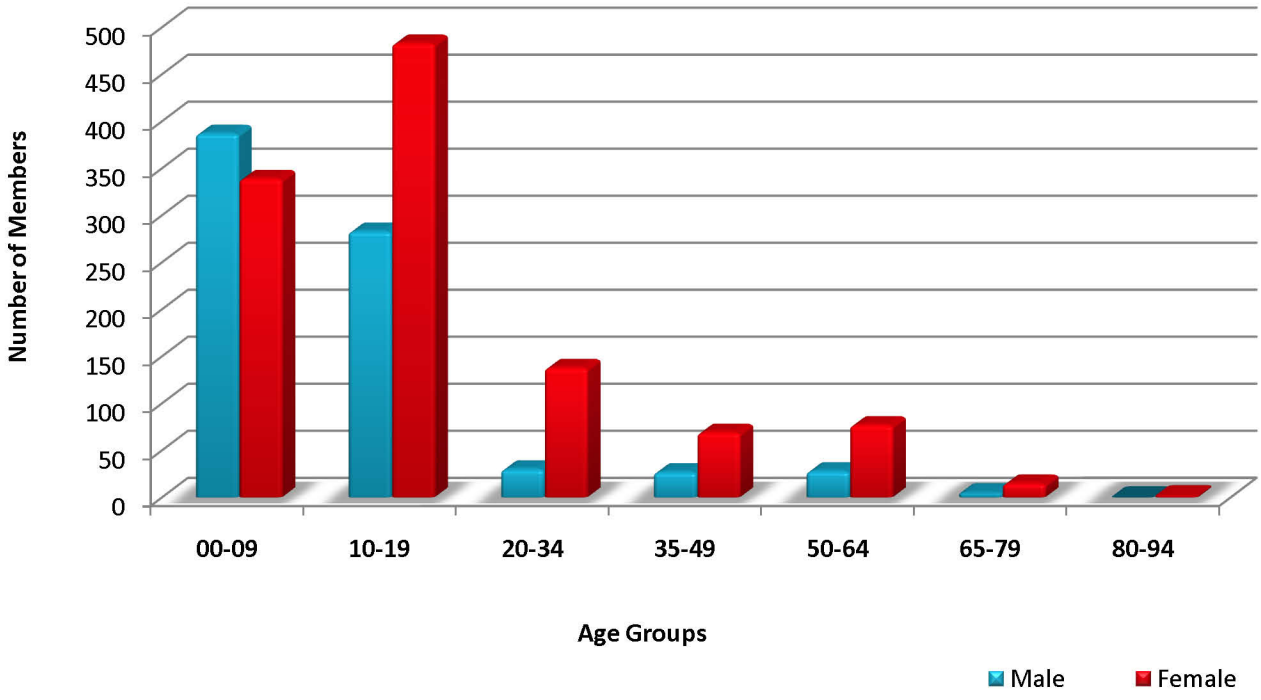
Comparison of Fiscal Years Ophthalmic Anti-infectives (with Steroids)

Fiscal Year	Members	Claims	Paid	Paid/Claim	Perdiem	Units	Days
2008	4,140	4,856	$252,272.56	$51.95	$4.58	26,741	55,051
2009	1,883	2,167	$103,305.44	$47.67	$4.26	11,378	24,258
Percent Change	-54.50%	-55.40%	-59.10%	-8.20%	-7.00%	-57.50%	-55.90%
Change	-2,257	-2,689	-$148,967.12	-$4.28	-$0.32	-15,363	-30,793

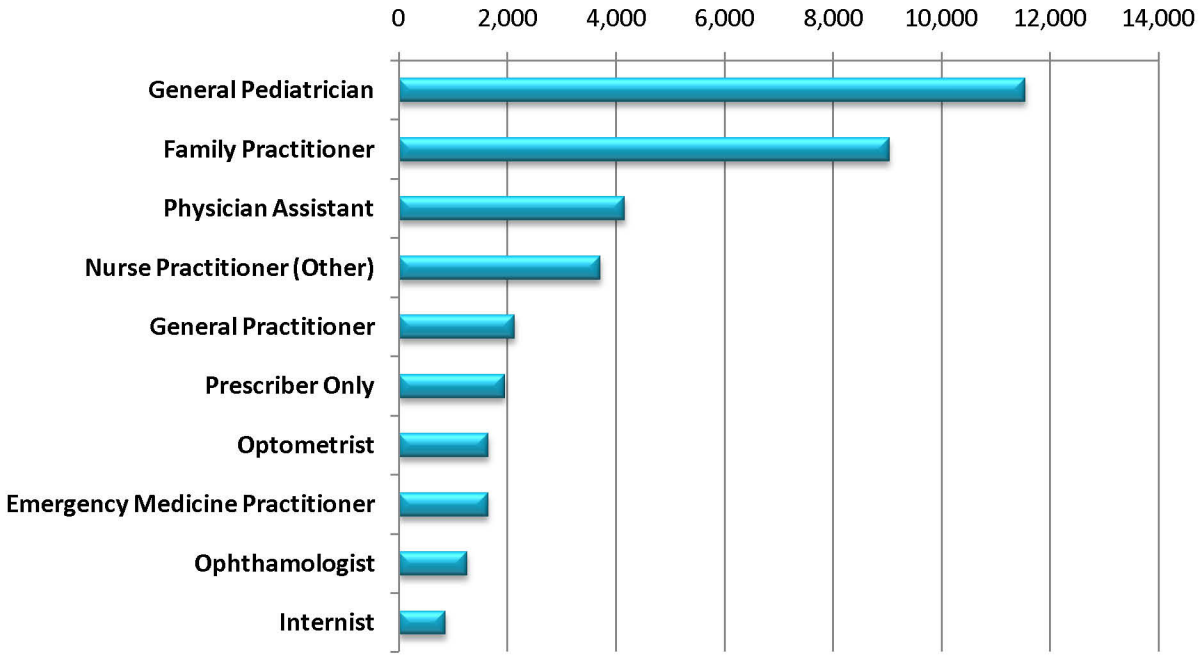
Demographics of Members Utilizing Ophthalmic Anti-infectives (no Steroids)



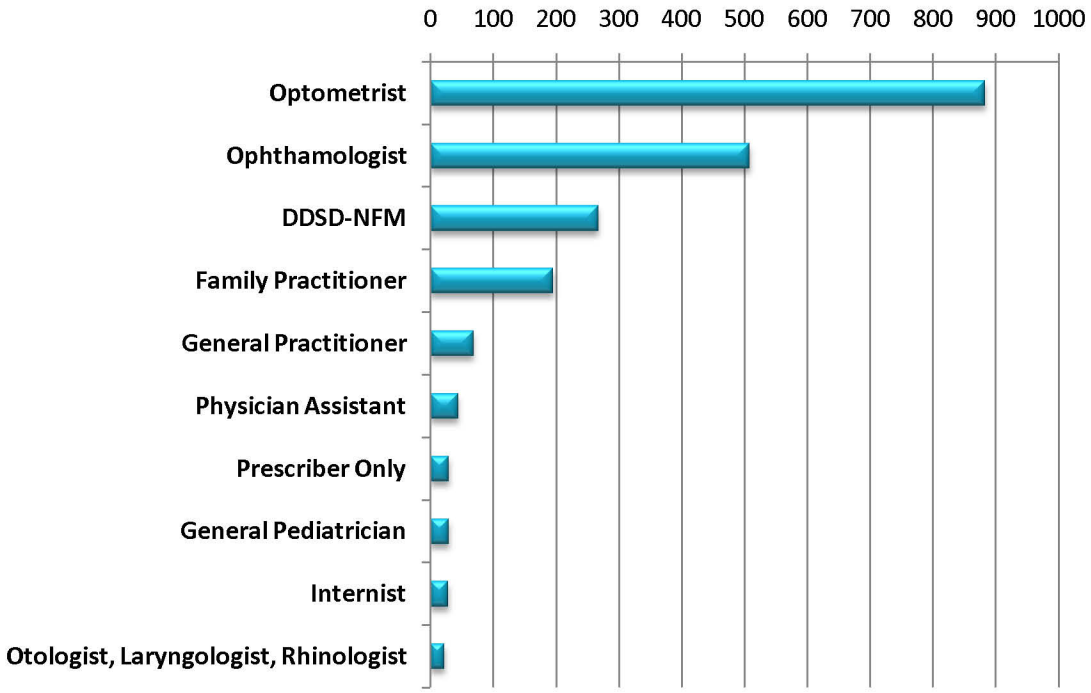
Demographics of Members Utilizing Ophthalmic Anti-infectives (with Steroids)



Prescribers of Ophthalmic Anti-infectives by Claims (no Steroids)



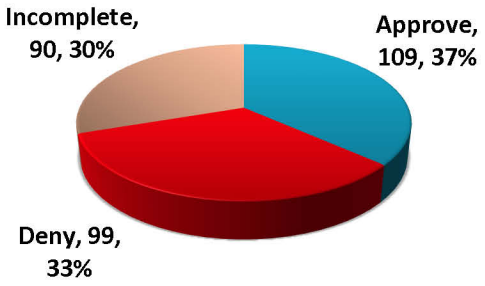
Prescribers of Ophthalmic Anti-infectives by Claims (with Steroids)



Prior Authorization of Ophthalmic Anti-infectives

There were a total of 298 petitions submitted for this PBPA category during fiscal year 2009. The following chart shows the status of the submitted petitions.

Status of Petitions for Ophthalmic Anti-infectives: FY 2009



Conclusion and Recommendations

The College of Pharmacy recommends placement of Besivance™ in Tier 3 of the Ophthalmic Antibiotic Products Product Based Prior Authorization Category. The existing criteria for this category will apply.

Ophthalmic Antibiotics: Liquids		
Tier 1	Tier 2	Tier 3
Gentak (Gentamicin)	Ciloxan Solution (Ciprofloxacin)	Vigamox (Moxifloxacin)
AK-Tob (Tobramycin)	Ocuflox (Ofloxacin)	Zymar (Gatifloxacin)
Bleph-10, Na Sulamyd (Na Sulfacetamide)		Azasite (Azithromycin)
Polytrim (PolymyxinB/Trimethoprim)		Besivance (Besifloxacin)
AK-Spore (Neo/PolyB/Gramacidin)		Quixin (Levofloxacin)

Mandatory Generic Plan applies.

Criteria for a Tier 2 medication:

1. Approved indication/suspected infection by organism not known to be covered by Tier 1 products, or failure of a Tier 1 product.
2. Known contraindication to all indicated Tier 1 medication.
3. Prescription written by optometrists/ophthalmologists, or
4. When used for pre/post-operative prophylaxis.

Criteria for a Tier 3 medication:

1. Approved indication/suspected infection by organism not known to be covered by Tier 2 products, or failure of a Tier 2 product.
2. Known contraindication to all indicated Tier 2 medication.
3. Prescription written by optometrists/ophthalmologists, or
4. When used for pre/post-operative prophylaxis.

Utilization Details of Ophthalmic Anti-infectives: Fiscal Year 2009

Ophthalmic Anti-infectives (no Steroids)

Chemical Name	Brand Name	Claims	Members	Paid	Claims/ Member	Paid/ Claim	% Cost
Moxifloxacin	VIGAMOX DRO 0.5%	9,545	8,482	$638,342.31	1.13	$66.88	60.82%
Gentamicin	GENTAMICIN SOL 0.3% OP	4,270	3,911	$27,930.79	1.09	$6.54	2.66%
Sulfacetamide Na	SOD SULFACET SOL 10% OP	3,509	3,344	$20,734.12	1.05	$5.91	1.98%
Tobramycin	TOBRAMYCIN SOL 0.3% OP	3,175	2,932	$21,741.42	1.08	$6.85	2.07%
Poly B-Trim	POLYMYXIN B/ SOL TRIMETHP	2,297	2,187	$22,798.86	1.05	$9.93	2.17%
Ciprofloxacin	CIPROFLOXACN SOL 0.3% OP	2,038	1,839	$34,971.94	1.11	$17.16	3.33%
Poly B-Trim	TRIMETHOPRIM SOL POLYMYXN	1,392	1,336	$17,347.37	1.04	$12.46	1.65%
Ofloxacin	OFLOXACIN DRO 0.3% OP	1,289	1,160	$13,878.52	1.11	$10.77	1.32%
Neo-Poly B-Gram	NEO/POLY/GRA SOL OP	1,094	1,044	$23,511.41	1.05	$21.49	2.24%
Azithromycin	AZASITE SOL 1%	1,061	932	$73,732.48	1.14	$69.49	7.02%
Gatifloxacin	ZYMAR DRO 0.3%	582	480	$40,312.33	1.21	$69.27	3.84%
Sulfacetamide Na	SULFACET SOD SOL 10% OP	542	519	$3,470.13	1.04	$6.40	0.33%
Gentamicin	GENTAK SOL 0.3% OP	204	193	$1,407.58	1.06	$6.90	0.13%
Sulfacetamide Na	BLEPH-10 SOL 10% OP	169	158	$837.02	1.07	$4.95	0.08%
Levofloxacin	QUIXIN SOL 0.5%	79	74	$5,333.16	1.07	$67.51	0.51%
Trifluridine	TRIFLURIDINE SOL 1% OP	54	44	$4,879.89	1.23	$90.37	0.46%
Levofloxacin	IQUIX SOL 1.5%	27	23	$1,776.65	1.17	$65.80	0.17%
Tobramycin	AK-TOB SOL 0.3% OP	12	11	$87.12	1.09	$7.26	0.01%
Neo-Poly B-Gram	NEOSPORIN SOL OP	1	1	$24.40	1	$24.40	0.00%
Neo-Poly B-Gram	NEOCIDIN SOL OP	1	1	$22.97	1	$22.97	0.00%
Erythromycin	ERYTHROMYCIN OIN OP	6,453	5,896	$43,741.05	1.09	$6.78	4.17%
Gentamicin	GENTAK OIN 0.3% OP	538	509	$8,788.98	1.06	$16.34	0.84%
Bac-Poly B	BACIT/POLYMY OIN OP	393	362	$5,087.91	1.09	$12.95	0.48%
Neo-Bac Zn-Poly	NEO/BAC/POLY OIN OP	325	301	$2,923.36	1.08	$8.99	0.28%
Bacitracin	BACITRACIN OIN OP	270	211	$1,799.37	1.28	$6.66	0.17%
Tobramycin	TOBREX OIN 0.3% OP	235	215	$16,284.09	1.09	$69.29	1.55%
Ciprofloxacin	CILOXAN OIN 0.3% OP	182	120	$14,727.19	1.52	$80.92	1.40%
Bac-PolyB	AK-POLY-BAC OIN OP	91	86	$1,299.49	1.06	$14.28	0.12%
Neo-Bac Zn-Poly	BAC/NEO/POLY OIN OP	74	65	$633.40	1.14	$8.56	0.06%
Gentamicin	GENTAMICIN OIN 0.3% OP	48	48	$780.88	1	$16.27	0.07%
Sulfacetamide Na	SULFACET SOD OIN 10% OP	43	40	$393.65	1.08	$9.15	0.04%
Totals		**39,993**	**33,266***	**$1,049,599.84**	**1.2**	**$26.24**	**100**

***Total number of unduplicated members**

Ophthalmic Anti-infectives (with Steroids)

Chemical Name	Brand Name	Claims	Members	Paid	Claims/ Member	Paid/ Claim	% Cost
Neo-Poly-HC	NEO/POLY/HC SUS OP	435	416	$23,264.44	1.05	$53.48	22.52%
Tobramycin- Dex	TOBRADEX SUS OP	418	375	$34,152.88	1.11	$81.71	33.06%
Neo-Poly-Dex	NEO/POLY/DEX SUS 0.1% OP	410	360	$3,419.56	1.14	$8.34	3.31%
Neo-Poly- Dex	NEO/POLY/DEX OIN 0.1% OP	380	309	$2,527.46	1.23	$6.65	2.45%
Tobramycin- Dex	TOBRAMYCIN/ SUS DEXAMETH	250	243	$18,486.83	1.03	$73.95	17.90%
Loteprednol-Tob	ZYLET SUS 0.5-0.3%	124	111	$10,423.46	1.12	$84.06	10.09%
Tob-Dex	TOBRADEX OIN OP	91	83	$8,808.14	1.1	$96.79	8.53%
Sulfacetamide Na -Pred	SULF/PRED NA SOL OP	26	21	$447.72	1.24	$17.22	0.43%
Sulfacetamide Na -Pred	BLEPHAMIDE SUS OP	21	20	$1,347.60	1.05	$64.17	1.30%
Gentamicin-Pred	PRED-G SUS OP	5	5	$150.95	1	$30.19	0.15%
Neo-Poly-Pred	POLY-PRED SUS OP	4	3	$111.32	1.33	$27.83	0.11%
Sulfacetamide Na -Pred	BLEPHAMIDE OIN S.O.P.	3	3	$165.08	1	$55.03	0.16%
Totals		**2,167**	**1,883***	**$103,305.44**	**1.15**	**$47.67**	**100.00**

***Total number of unduplicated members**

Antibacterial Coverage of Select Ophthalmic Agents

	Ciprofloxacin[i] (Ciloxan®)	**Oflaxacin**[ii] (Ocuflox®)	**Levofloxacin**[iii] (Quixin®)	**Moxifloxacin**[iv] (Vigamox®)	**Gatifloxacin**[v] (Zymar®)	**Azithromycin**[vi] (Azasite®)	**Besifloxacin**[vii] (Besivance®)
Acinetobacterium Iwoffii			√	√*			
Chlamydia trachomatis				√			
Corynebacterium species			√	√*	√*		√*
CDC coryneform group G						√*	√
Enterobacter species							
Enterobacter cloacae		√					
Escherichia coli							
Haemophilus influenza	√	√	√	√	√	√	√
Haemophilus parainfluenzae				√			
Klebsiella species							
Micrococcus luteus				√*			
Moraxella lacunata							√*
Mycoplasma pneumonia							
Neisseria gonorrhoeae							
Propionibacterium acnes		√					
Proteus mirabilis		√					
Pseudomonas aeruginosa	√	√					
Serratia marcescens	√	√*	√				
Staphylococcus aureus	√	√	√	√	√	√	√
Staphylococcus epidermidis	√	√	√	√	√		√
Staphylococcus haemolyticus				√			
Staphylococcus hominis				√			√*
Staphylococcus lugdunensis							√*
Staphylococcus warneri				√			
Streptococcus mitis					√	√	√
Streptococcus oralis							√
Streptococcus pneumonia	√	√	√	√	√	√	√
Streptococcus pyogenes							
Streptococcus salivarius							√*
Streptococcus (Group C/F)			√				
Streptococcus (Group G)			√				
Treponema pallidum							
Viridans group streptococci	√		√	√			

*Efficacy for this organism was studied in less than 10 infections.

[i] Alcon Laboratories. Ciloxan Prescribing Information. Acessed at: http://www.fda.gov/cder/foi/label/2006/019992s020lbl.pdf. September 2004.
[ii] Allergan Pharmaceuticals. Ocuflox Prescribing Information. Accessed at: http://www.fda.gov/cder/foi/nda/99/019921_S008_Ocuflox_Approval_Package.pd. August 1999.
[iii] Daiichi Pharmaceuticals. Quixin Prescribing Information. Accessed at http://www.fda.gov/cder/foi/label/2002/21199s2lbl.pdf. August 2000.
[iv] Alcon Laboratories. Vigamox Prescribing Information. Accessed at: http://www.fda.gov/cder/foi/label/2004/21598slr002_vigamox_lbl.pdf. 2004.
[v] Allergan, Inc. Zymar Prescribing Information. Accessed at: http://www.fda.gov/cder/foi/label/2005/021493s006,007lbl.pdf. August 2004.
[vi] Inspire Pharmaceuticals. Azasite Prescribing Information. Accessed at: http://www.fda.gov/cder/foi/label/2007/050810lbl.pdf April 2007.
[vii] Bausch &Lomb Pharmaceuticals. Besivance Prescribing Information. Accessed at: http://besivance.com/Besivance-Full-Prescribing-Info.pdf August 2009

Appendix I

Annual Review of Stimulants and 30 Day Notice to Prior Authorize ProCentra™

Oklahoma HealthCare Authority
June 2010

Current Prior Authorization Criteria

Stimulants		
Tier 1	**Tier 2**	**Tier 3**
methylphenidate SR (Ritalin® SR) amphetamine salt combo (Adderall®) dexmethylphenidate (Focalin®, Focalin® XR) methylphenidate ER (Concerta®) methylphenidate IR (Ritalin®, Methylin®)	atomoxetine (Strattera®) methylphenidate ER (Metadate® CD) methylphenidate ER (Metadate® ER) methylphenidate ER (Ritalin® LA) dextroamphetamine/amphetamine combo (Adderall® XR) lisdexamfetamine (Vyvanse®) guanfacine ER (Intuniv®)	armodafinil (Nuvigil®) methamphetamine (Desoxyn®) methylphenidate patch (Daytrana™) modafinil (Provigil®) dextroamphetamine (Dexedrine®, Dexedrine Spansules®) dexamphetamine (ProCentra™)

For Tier 2 Products:

- ☑ Trial with <u>one</u> Tier 1 drug (should include a longer-acting product).
  - Trial should have been within the last 30 days.
  - Dosing up to maximum or provide information regarding side effects at higher dose.
  - If trials are not in members claim history, the pharmacy profile should be submitted or detailed information regarding dates and doses should be included along with the signature from the physician.
- ☑ Diagnosis of ADHD or Narcolepsy.
- ☑ Clinical exception for non-stimulants if tics or substance abuse is present.
- ☑ Only use of one long-acting product (regardless of tier level) is allowed concurrently – except for a maximum of a two month titration period.
- ☑ An immediate release product of the same drug type may be used concurrently if an afternoon dose is required.

For Tier 3 Products:

- ☑ Trial with <u>one</u> Tier 1 drug and <u>one</u> Tier 2 drug **OR** two trials of either a Tier 1 or Tier 2.
  - Both trials should have been within the last 60 days.
  - Dosing of Tier 1 up to the FDA maximum or provide information regarding side effects at higher dose.
  - If trials are not in members claim history, the pharmacy profile should be submitted or detailed information regarding dates and doses should be included along with the signature from the physician.
- ☑ Diagnosis of ADHD or Narcolepsy.
- ☑ All other Tier 2 criteria apply.

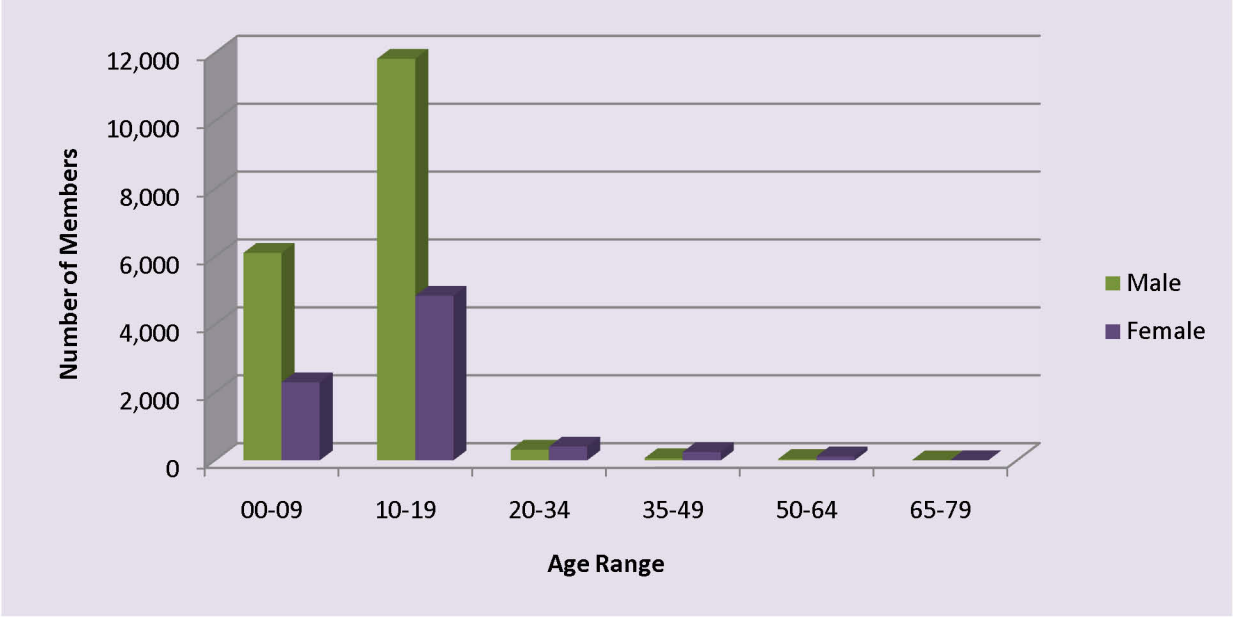
For all Tiers:

- ☑ Dosing cannot exceed 1.5 times the FDA maximum.
- ☑ Prior Authorization is required for all tiers for members greater than 20 years of age. Must have a diagnosis of ADHD or Narcolepsy.

Utilization of Stimulants

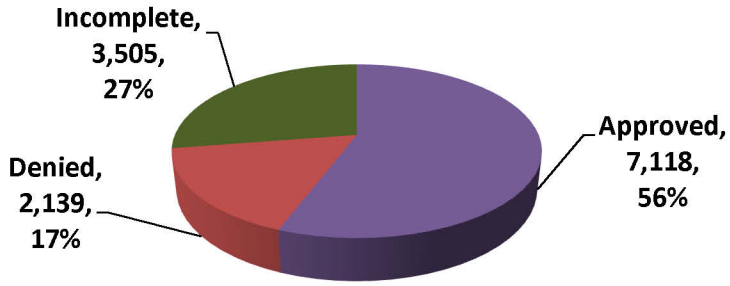
Fiscal Year	Total Members	Total Claims	Total Paid	Paid/ Claim	Paid/ Day	Total Units	Total Days
2008	24,554	182,750	$18,546,066.91	$101.48	$3.38	6,957,944	5,491,179
2009	26,295	191,446	$22,094,812.64	$115.41	$3.87	6,884,210	5,708,517
% Change	**7.10%**	**4.80%**	**19.10%**	**13.70%**	**14.50%**	**-1.10%**	**4.00%**
Change	**1,741**	**8,696**	**$3,548,745.73**	**$13.93**	**$0.49**	**-73,734**	**217,338**

Member Demographics



Prior Authorization Activity

A total of 12,762 petitions were submitted in FY 2009 for prior authorization with the following results. Step edits are in place for point-of-sale claims when tier trials have been met. The following chart shows the status of the submitted petitions.

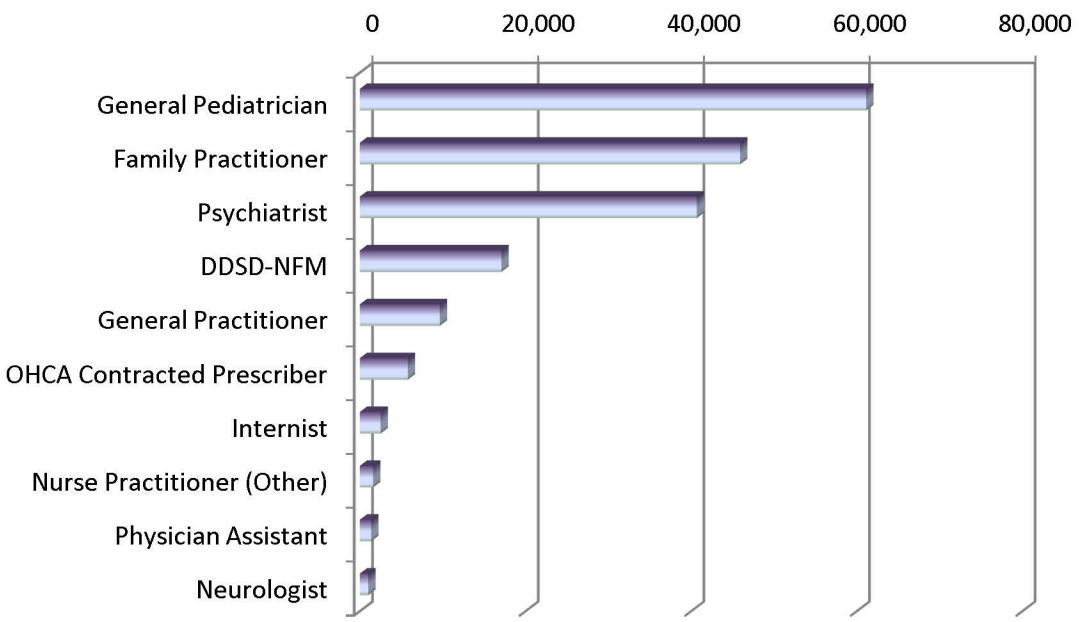


Utilization Data

GENERIC NAME	BRAND NAME(S)	CLAIMS	MEMBERS	PAID	CLAIMS/ MEMBER	PAID/ DAY	PERCENT PAID
Methylphenidate CR	METHYLPHENIDATE SR, METHYLPHENIDATE CR, METADATE ER, METHYLIN® ER,	2,391	656	48,195.14	3.6	$0.64	0.22%
Methylphenidate ER	CONCERTA®	37,838	6,949	$5,296,976.42	5.4	$4.72	23.98%
Methylphenidate ER	METADATE®CD	3,231	551	$404,397.68	5.9	$4.21	1.83%
Methylphenidate ER	RITALIN® LA	2467	460	$281,881.82	5.36	$3.82	1.28%
Methylphenidate transdermal	DAYTRANA™	2,745	509	$405,949.69	5.39	$4.96	1.84%
Methylphenidate IR	METHYLIN®, RITALIN®	13,995	3,277	$188,196.64	4.3	$0.45	0.85%
Methylphenidate IR	METHYLIN® CHEW TAB	293	82	$33,953.72	3.6	$3.89	0.16%
Methylphenidate IR	METHYLIN® SOLUTION	313	81	$61,768.01	3.9	$6.71	0.28%
Amphetamine Salt Combos	ADDERALL®,	19,270	4,277	$320,093.34	4.5	$0.55	1.44%
Amphetamine Salt combos ER	ADDERALL® XR	33,826	5,728	5,383,580.12	5.9	$5.34	24.37%
Lisdexamfetamine	VYVANSE®	34,507	6,982	$4,338,081.22	4.94	$4.24	19.63%
Dexmethylphenidate	FOCALIN®	5,145	1,200	$207,695.45	4.29	$1.36	0.94%
Dexmethylphenidate ER	FOCALIN® XR	17,233	3,503	$2,118,534.53	4.9	$4.14	9.59%
Atomoxetine	STRATTERA®	15,811	2,965	$2,460,722.41	5.33	$5.14	11.13%
Modafinil	PROVIGIL®	1,443	234	$492,745.06	6.17	$11.45	2.23%
Dextroamphetamine	DEXEDRINE ®	920	153	$44,674.64	6.01	$1.62	0.19%
Methamphetamine	DESOXYN®	15	2	$6,470.95	7.5	$14.38	0.03%
Armodafinil	NUVIGIL®	3	3	$895.80	1	$9.95	0.00%
		191,446	**26,295***	**$22,094,812.64**	**7.28**	**$3.87**	**100%**

*Total unduplicated members

Prescriber Specialty – Top 10 prescribers by number of claims



Market Changes

- Armodafinil (Nuvigil®), the R-isomer of the stimulant modafinil, was approved in 2007 but did not enter the market until April 2009. It is in Tier 3, as approved by the Board in November, 2007.
- Adderall® XR became available in generic in April 2009. After 6 months of exclusivity for the first manufacturer, the SMAC was applied in November and the cost of generic is $0.65 less than the branded product.
- The maximum approved dose of Focalin® XR was increased to 30 mg in October 2009 and that strength capsule became available in December 2009.
- Intuniv®, extended release guanfacine, was approved by the FDA in September 2009 and was moved into Tier 2 after approval by the Board in December 2009.
- ProCentra™, dextroamphetamine sulfate solution, was approved by the FDA in March 2009.

Cost comparison of alternative dosing forms

Drug	EAC	Cost of 30 day fill (10 mg)**
ProCentra™ Solution 5 mg/5 ml	$0.47/ml	$145.02
Methylin® Solution 10 mg/5ml	$0.74/ml	$115.02
Methylin® Chew tab 10 mg	$3.22	$100.62

**Include $4.02 dispensing fee

Intuniv®

Intuniv® was FDA approved in September 2009, and was moved into Tier-2 of the product based prior authorization program. Since that time, several different clinical situations have surfaced regarding the use of Intuniv® in the SoonerCare population. A clinical subcommittee was assembled to consider these questions. Here is a summary of their recommendations:

1. If a child is stabilized on immediate release guanfacine (Tenex®), should the petition for Intuniv® be approved without the required tier-1 stimulant trial?
   - Intuniv® could be approved after stabilization on guanfacine (Tenex®), but only if there had been a failed trial of a tier-1 stimulant before the guanfacine.
   - Individuals stabilized and doing well on Tenex® should remain on Tenex® rather than being allowed to move to Intuniv®.

2. If a child is stabilized on samples of Intuniv®, should the petition for Intuniv® be approved without the required tier-1 stimulant trial?
   - There should be a failed trial of a tier-1 stimulant before stabilization on samples of Intuniv®.

3. Should the petition for Intuniv® be approved concomitantly with Strattera?
   - Strattera and Intuniv® should not be used concomitantly since current literature does not support the use of them together.

4. Should the petition for Intuniv® be approved concomitantly with another stimulant medication?
   - Intuniv® could, on rare occasions, be approved in combination with a stimulant, but only after a trial of one month's duration of each medication in question.
   - If combination therapy was allowed, the stimulant should be from tier-1.

A search of publicly available information of other states' Medicaid programs was conducted to gather data on how Intuniv® is covered in relation to other stimulants. No data was found regarding coverage of Intuniv® concomitantly with stimulant medications. However, several criteria which may be of interest were noted.

- Montana – restricted to ages 6-17, established on appropriate dose of immediate release guanfacine, member must have experienced compliance issues or had inadequate response necessitating use of the extended release product.
- West Virginia – trial of all chemically unique entities of preferred stimulants (amphetamine and non-amphetamine), as well as Strattera and generic guanfacine.

Recommendations

The College of Pharmacy recommends adding ProCentra™ to tier-3 of the PBPA category. Based on the advice of the clinical subcommittee, the College of Pharmacy also recommends the DUR Board consider putting the same restrictions on Intuniv® as are on Strattera®, namely hard PA, no concomitant use with other ADHD medications, except on an individual basis, and no stabilization on immediate release guanfacine or Intuniv® samples without a tier-1 stimulant trial.

ProCentra™ Product Details[1,2]

ProCentra™ (dextroamphetamine sulfate) is a bubblegum flavored oral solution, 5 mg/5 ml, approved for children 3 years and older.

Indication

- Narcolepsy
- Attention Deficit Disorder with Hyperactivity

Dosing range

- ADHD (3-5 years) – 2.5-40 mg qd-tid
- ADHD (>6 years) – 5-40 mg qd-tid
- Narcolepsy (6-11) – 5-60 mg qd-tid
- Narcolepsy (>12 years) 5-60 mg qd-tid

Black Box Warning

- High abuse potential
- May cause sudden death and serious cardiovascular adverse events

Contraindications

- Advanced arteriosclerosis, symptomatic cardiovascular disease, moderate to severe hypertension, hyperthyroidism, known hypersensitivity or idiosyncrasy to sympathomimetic amines, glaucoma
- Agitated states
- History of drug abuse
- During or within 14 days of administration of monoamine oxidase inhibitors (may cause hypertensive crisis)

Pregnancy Risk Category: C

Precautions

- **Serious cardiovascular events**: Sudden death has occurred in children with pre-existing structural cardiac abnormalities or other serious heart problems. Sudden deaths, stroke, and myocardial infarction have been reported in adults with serious structural abnormalities, cardiomyopathy, heart rhythm abnormalities, coronary artery disease, or other serious cardiac problems.
- **Hypertension**: Blood pressure can increase by about 2-4 mmHg after dosing with stimulants so should be monitored, particularly if the patient has an underlying cardiac disease or history of a previous cardiac event
- **Psychiatric adverse events**: Patients with pre-existing psychotic disorder can have exacerbation of symptoms with stimulants.
- **Bipolar illness**: initiation of stimulant therapy can induce a mixed/manic episode in bipolar patients.

- **Emergence of new psychotic or manic symptoms**: Stimulants can cause symptoms such as hallucinations, delusional thinking, or mania in children and adolescents without history or psychotic illness or mania.
- **Aggression**: Aggressive behavior or hostility is often seen in children with ADHD, though it is not clear if it is caused by stimulant use. Children beginning treatment with stimulants should be monitored for the appearance, or worsening, of such behavior.
- **Long term suppression of growth**: stimulant use can cause slowing of growth in height and weight by as much as 2 cm of height and 2.7 kg of weight over three years, without evidence of growth rebound.
- **Seizures**: Stimulants may decrease the seizure threshold.
- **Visual disturbances**: Stimulants may cause difficulties with accommodation and blurring of vision.

Common Adverse Effects

- Palpitations
- Tachycardia
- Increase in blood pressure
- Overstimulation
- Restlessness
- Dizziness
- Insomnia
- Euphoria
- Dyskinesia
- Dysphoria
- Tremor
- Headache
- Motor/phonic tic exacerbation
- Tourette's syndrome exacerbation
- Dry mouth
- Unpleasant taste
- Diarrhea
- Constipation
- Anorexia
- Weight loss
- Urticaria
- Impotence

Drug Interactions[2]

- **Alkalinizing Agents**: May decrease the excretion of Amphetamines. *Risk D: Consider therapy modification*
- **Ammonium Chloride**: May decrease the serum concentration of Amphetamines. This effect is likely due to an enhanced excretion of amphetamines in the urine. *Risk C: Monitor therapy*
- **Analgesics (Opioid)**: Amphetamines may enhance the analgesic effect of Analgesics (Opioid). *Risk C: Monitor therapy*
- **Antacids**: May decrease the excretion of Amphetamines. *Risk C: Monitor therapy*
- **Antihistamines**: Amphetamines may diminish the sedative effect of Antihistamines. **Exceptions:** Olopatadine (Ophthalmic). *Risk C: Monitor therapy*
- **Antipsychotics:** May diminish the stimulatory effect of Amphetamines. *Risk C: Monitor therapy*
- **Atomoxetine**: May enhance the hypertensive effect of Sympathomimetics. Atomoxetine may enhance the tachycardic effect of Sympathomimetics. *Risk C: Monitor therapy*
- **Cannabinoids**: May enhance the tachycardic effect of Sympathomimetics. *Risk C: Monitor therapy*
- **Carbonic Anhydrase Inhibitors**: May decrease the excretion of Amphetamines. **Exceptions:** Brinzolamide; Dorzolamide. *Risk C: Monitor therapy*
- **Ethosuximide**: Amphetamines may diminish the therapeutic effect of Ethosuximide. Amphetamines may decrease the serum concentration of Ethosuximide. *Risk C: Monitor therapy*
- **Gastrointestinal Acidifying Agents**: May decrease the serum concentration of Amphetamines. *Risk C: Monitor therapy*
- **Iobenguane I 123**: Sympathomimetics may diminish the therapeutic effect of Iobenguane I 123. *Risk X: Avoid combination*

- **Lithium**: May diminish the stimulatory effect of Amphetamines. *Risk C: Monitor therapy*
- **MAO Inhibitors**: May enhance the hypertensive effect of Amphetamines. *Risk X: Avoid combination*
- **Methenamine**: May decrease the serum concentration of Amphetamines. This effect is likely due to an enhanced excretion of amphetamines in the urine. *Risk C: Monitor therapy*
- **Peginterferon Alfa-2b**: May decrease the serum concentration of CYP2D6 Substrates. *Risk C: Monitor therapy*
- **PHENobarbital**: Amphetamines may decrease the serum concentration of PHENobarbital. *Risk C: Monitor therapy*
- **Phenytoin**: Amphetamines may decrease the serum concentration of Phenytoin. *Risk C: Monitor therapy*
- **Sympathomimetics**: May enhance the adverse/toxic effect of other Sympathomimetics. *Risk C: Monitor therapy*
- **Tricyclic Antidepressants**: May enhance the stimulatory effect of Amphetamines. Tricyclic Antidepressants may also potentiate the cardiovascular effects of Amphetamines. *Risk C: Monitor therapy*

Other Interactions

- **Ethanol**: Avoid ethanol (may increase CNS depression).
- **Food**: Dextroamphetamine serum levels may be altered if taken with acidic food, juices, or vitamin C.
- **Herb/Nutraceutical**: Avoid ephedra (may cause hypertension or arrhythmias).

Patient information

- FDA approved Medication Guide must be dispensed with this medication at each fill.
- Take the last dose of the day about 6 hours before bedtime.
- Do not stop taking this drug abruptly.
- Contact your doctor if there any signs of heart problems such as chest pain, shortness of breath, or fainting while taking ProCentra™
- Contact your doctor if there are new or worsening mental problems, especially seeing or hearing things that are not real, believing things that are not real, or being suspicious

Reference

1. ProCentra ™ (dextroamphetamine sulfate) Product Information. Tiber Laboratories January 2009
2. LexiComp Online, available at http://online.Lexi.com

Appendix J

U.S. Food and Drug Administration

Drugs

FDA Drug Safety Communication: Possible increased risk of fractures of the hip, wrist, and spine with the use of proton pump inhibitors

Safety Announcement

[05-25-2010] The U.S. Food and Drug Administration (FDA) is revising the prescription and over-the-counter (OTC) labels for a class of drugs called proton pump inhibitors to include new safety information about a possible increased risk of fractures of the hip, wrist, and spine with the use of these medications.

Proton pump inhibitors work by reducing the amount of acid in the stomach. Nexium, Dexilant, Prilosec, Zegerid, Prevacid, Protonix, Aciphex, and Vimovo are available by prescription to treat conditions such as gastroesophageal reflux disease (GERD), stomach and small intestine ulcers, and inflammation of the esophagus. Prilosec OTC, Zegerid OTC, and Prevacid 24HR are sold over-the-counter (OTC) for the treatment of frequent heartburn.

The new safety information is based on FDA's review of several epidemiological studies that reported an increased risk of fractures of the hip, wrist, and spine with proton pump inhibitor use. Some studies found that those at greatest risk for these fractures received high doses of proton pump inhibitors or used them for one year or more (see Data Summary section).The majority of the studies evaluated individuals 50 years of age or older and the increased risk of fracture primarily was observed in this age group.

While the greatest increased risk for fractures in these studies involved people who had been taking prescription proton pump inhibitors for at least on year or who had been taking high doses of the prescription medications (not available over-the-counter), as a precaution, the "Drug Facts" label on th OTC proton pump inhibitors (indicated for 14 days of continuous use) also is being revised to include information about this risk.

Healthcare professionals and users of proton pump inhibitors should be aware of the possible increased risk of fractures of the hip, wrist, and spine with the use of proton pump inhibitors, and weigh the known benefits against the potential risks when deciding to use them.

Additional Information for Patients and Consumers

- Proton pump inhibitors are effective in treating a variety of gastrointestinal disorders. Do not stop taking your proton pump inhibitor unless tol to do so by your healthcare professional.
- Be aware that an increased risk of fractures of the hip, wrist, and spine has been reported in some studies of patients using proton pump inhibitors. The greatest increased risk for these fractures was seen in patients who receive high doses of these medications or use them longer (a year or more).
- Read and follow the directions on the OTC *Drug Facts* label, when considering use of OTC proton pump inhibitors.
- Be aware that the OTC proton pump inhibitors should only be used as directed for 14 days for the treatment of frequent heartburn. If your heartburn continues, talk to your healthcare professional. No more than three 14-day treatment courses should be used in one year.
- Talk to your healthcare professional about any concerns you may have about using proton pump inhibitors.
- Report any side effects with proton pump inhibitors to FDA's MedWatch program using the information at the bottom of the page in the "Contact Us" box.

Additional Information for Healthcare Professionals

- Proton pump inhibitors provide important benefits for many patients in treating or preventing conditions such as erosive esophagitis, nonsteroidal anti-inflammatory drug-induced ulcers and gastroesophageal reflux disease.
- Be aware of the increased risk of fractures of the hip, wrist, and spine seen in some observational studies in patients using proton pump inhibitors.
- When prescribing proton pump inhibitors, consider whether a lower dose or shorter duration of therapy would adequately treat the patient's condition.
- Follow the recommendations in the product labeling when prescribing proton pump inhibitors.
- Individuals at risk for osteoporosis should have their bone status managed according to current clinical practice, and should take adequate vitamin D and calcium supplementation.
- Report any adverse events with proton pump inhibitors to FDA's MedWatch program using the information at the bottom of the page in the "Contact Us" box.

Data Summary

To date, randomized clinical trials of proton pump inhibitors have not found an increased risk of fractures of the hip, wrist, or spine. These studies are generally six months in duration and there is limited information on effects of higher than recommended doses.

The decision to revise the *Warnings and Precautions* section of the prescription labeling as well as the OTC *Drug Facts* label for proton pump inhibitors is based on FDA's review of the findings from seven published epidemiological studies.[1-7] These studies used claims data from computerized

administrative databases to evaluate the risk of fractures of the hip, wrist, and spine in patients treated with proton pump inhibitors compared to individuals who were not using proton pump inhibitors (The findings from these studies are found in the Table below).

In these studies:

- Six reported an increased risk of fractures with the use of proton pump inhibitors [1,2,3,5,6,7].
- Exposure to proton pump inhibitors ranged from a period of 1 to 12 years, depending on the study.
- The emergence of fractures varied among studies; with one study reporting an increase in fractures with use of proton pump inhibitors in the previous year [2] and another study finding an increase after 5 to 7 years of proton pump inhibitor use[3].
- The increased risk of fractures was primarily observed in older individuals.
- Two studies reported an increase in fractures with higher doses of proton pump inhibitors [2,5].
- Two studies reported an increase in fractures with longer duration of use [2,3].
- One study did not find a relationship between proton pump inhibitor use and fractures [4]. This study limited the study population to those without major risk factors for fracture.

FDA does not have access to the data or the protocols for these studies, so our ability to verify that the studies were conducted as described in the original publications is limited. Based on our review of the published articles, the key strengths of these studies are that they appear well-designed, considered the effects of both dose and duration of use of proton pump inhibitors on fracture risk, and used appropriate statistical methods to reduce bias by adjusting for potential factors that are known to be associated with the occurrence of fractures such as age, gender, presence of co-existing conditions and use of co-prescribed medications.

Several study limitations, however, make understanding the clinical relevance of the reported findings difficult to determine. Administrative claims databases do not typically contain information on all potential factors that could influence the relationship between proton pump inhibitors use and fracture risk. These studies were not able to account for missing or incomplete information on family history of osteoporosis, smoking history, weight and height measurements, alcohol use, history of dietary and supplement use (calcium and vitamin D), OTC medication use, presence of digestive diseases, such as ulcers, reasons for proton pump inhibitor use, and recent history of immobility, dizziness, or falls. In addition, in most studies where a possible link with osteoporotic fracture was reported, no information was collected about the timing of proton pump inhibitor use in relation to onset or worsening of osteoporosis.

However, the exact mechanisms for an increased risk of fractures with proton pump inhibitor use are not known. Three epidemiologic studies found no consistent association between chronic proton pump inhibitor use and bone mineral density [6,7,8].

Based on the available data, at this time it is not clear if the use of proton pump inhibitors is the cause of the increased risk of fractures seen in some epidemiologic studies.

To further investigate this issue, the FDA plans to analyze data from several large, long-term, placebo-controlled clinical trials of bisphosphonates (drugs used to prevent fractures) to assess the risk of fractures in women at risk for osteoporosis-related fractures who used or did not use proton pump inhibitors.

FDA is also working with the manufacturers of these products to further study this possible risk. For example, as part of the Dexilant (dexlansoprazole) approval, (January 2009), the manufacturer was required to perform a postmarketing clinical trial to evaluate the effects of dexlansoprazole and esomeprazole on bone homeostasis, including changes in biomarkers of bone formation and bone resorption.The results from this trial are expected at the end of 2011.

In summary, the available data, including findings from several epidemiological studies, suggest a possible increased risk of fractures of the hip, wrist, and spine in patients using proton pump inhibitors. The data suggest that the increased risk may be dependent upon dose, duration of use, or both. At the present time, there is uncertainty about the magnitude of this risk. In light of this uncertainty, when prescribing proton pump inhibitors, healthcare professionals should consider whether a lower dose or shorter duration of therapy would adequately treat the patient's condition.

Table of epidemiological studies evaluating fracture risk with proton pump inhibitors

Study	Study Time Period	Study Population	Findings related to Proton Pump Inhibitors (PPIs)
Vestergaard 2006	1/1/2000 – 12/31/2000	• 124,655 cases with fractures • 373,962 matched controls • All ages Data source: Denmark health database[1]	PPI use within the last year • Overall fracture risk, Odds Ratio (OR) = 1.18 (95% CI, 1.12–1.43) • Risk of hip fracture, OR = 1.45 (95% CI, 1.28–1.65) • Risk of spine fracture, OR = 1.60 (95% CI, 1.25–2.04) • Risk of forearm fracture, OR = 0.95 (0.82-1.11) • No dose-response relationship seen with PPIs and fracture risk: *(DDD [defined daily doses] were the number of doses in a year)*
Yang 2006	1987 - 2003	• 13,556 cases with fractures • 135,386 matched controls • Ages ≥ 50 years • Data source: U.K./GPRD[2]	• Risk of hip fracture, PPI use > 1 year adjusted Odds Ratio (aOR)± = 1.44 (95% CI, 1.30–1.59) • Risk of hip fracture increased with high-dose PPI use > 1 year: *(dose defined as dose/day, >1.75 doses/day)* aOR = 2.65 (95% CI, 1.80-3.90) • Risk of hip fracture increased with longer duration of PPI use ◦ 1 yr, aOR = 1.22 (95% CI, 1.15-1.30) ◦ 4 yr, aOR = 1.59 (95% CI, 1.39-1.80)
Targownik 2008	1996 - 2004	• 15,792 cases with fractures • 47,289 matched controls • Ages ≥ 50 years • Data source: PHRDR/[3] Manitoba, Canada	• Risk of hip, wrist, spine fractures with PPI use ≥ 7 years adjusted Odds Ratio (aOR) ¥ = 1.92 (95% CI, 1.16–3.18) • Risk of hip fracture increased with longer duration of use ◦ PPI use ≥ 5 years, aOR = 1.62 (95% CI, 1.02–2.58) ◦ PPI use ≥ 6 years, aOR = 2.49 (95% CI, 1.33-4.67) ◦ PPI use ≥ 7 years, aOR = 4.55 (95% CI, 1.68–12.29)
Kaye 2008	1995 - 2005	• 1,098 cases with fractures • 10,923 matched controls • Ages 50 – 70 years	• Estimated Relative Risk (RR) of hip fracture = 0.9 (95% CI, 0.7–1.11) *(Patients at risk for fracture were excluded from the analysis)* • Risk of hip fracture not detected with increased number of PPI prescriptions

Corley 2010	1995-2007	• Data source: U.K/GPRD[2] • 33,752 cases with fractures • 130,471 matched controls • Ages ≥ 18 years • Data source: KPNC/[4] California, USA	• Risk of fracture with ≥ 2 years of PPI use and 1 other risk factor Odds Ratio (OR) = 1.30 (95% CI, 1.21–1.39) ◦ Risk factors: alcohol abuse, arthritis, diabetes, kidney disease, glucocorticoids, cerebrovascular disease, dementia, epilepsy, gait disorder, hemiplegia, psychoses, smoking, visual impairment, anxiolytic use • Risk of fracture increased with higher PPI dose: *(dose = number of pills per day >1.5)* OR = 1.41 (95% CI, 1.21-1.64) • Risk of fracture did not consistently increase with longer duration of use
Yu 2008	Women: 7.6 years mean follow-up Men: 5.6 years mean follow-up	• Women (4,574 non-PPI users and 234 PPI users) • Men (4,920 non-PPI users and 487 PPI users) Ages ≥ 65 years • Data source: MrOS/SOF[5]	• Risk of hip fracture ◦ Women: adjusted Relative Hazard (aRH)£ = 1.16 (95% CI, 0.80-1.67) ◦ Men: aRH = 0.62 (95% CI, 0.26-1.44) • Risk of nonspine fracture ◦ Women: aRH = 1.34 (95% CI, 1.10-1.64) ◦ Men: aRH = 1.21 (95% CI, 0.91-1.62)
Gray 2010	7.8 years, mean follow-up	• 2,831 PPIs users • 127,756 non-PPIs users • Post-menopausal women ages 50 – 79 years • Data source: WHI OS/WHI CT[6]	• Risk of total fractures adjusted Hazard Ratio (aHR) ≠ = 1.25 (95% CI, 1.15-1.36) • Risk of hip fracture, aHR = 1.00 (95% CI, 0.71-1.40) • Risk of spine fracture, aHR = 1.47 (95% CI, 1.18-1.82) • Risk of wrist fracture, aHR = 1.26 (95% CI, 1.05-1.51) • No consistent trend for fracture risk with duration of use

Data Source: 1. Denmark Health Database; 2. United Kingdom, General Practice Research Database; 3. Population Health Research Data Repository (Manitoba, Canada); 4. Kaiser Permanente Northern California; 5. Osteoporosis fractures in Men Study/Study of Osteoporotic Fractures; 6. Women's Health Initiative Observation Study/Women's Health Initiative Clinical Trials

± Adjusted for sex, age, body mass index, medication use (anxiolytics, antidepressants, NSAID/aspirin, thiazide diuretic, antipsychotic, antiparkinsonian, antiseizure, hormone therapy, corticosteroid, thyroxine), health condition (alcoholism, arthritis, stroke, asthma or COPD, dementia, diabetes mellitus, congestive heart failure, impaired mobility, myocardial infarction, peptic ulcer disease, seizure disorder, peripheral vascular disease, visual impairment, current smoker, prior fractures).

¥ Adjusted for income, region of residence, diagnoses (short or long-term diabetes, epilepsy, ischemic heart disease, myocardial infarction, hypertension, arthritis, solid organ transplant, chronic obstructive pulmonary disease, substance use, depression, schizophrenia, dementia), home care use and multiple medications.

£ Adjusted for age, clinic, race, body mass index, alcohol use, exercise, oral or inhaled corticosteroid use, NSAID use, calcium supplement use, osteoporosis medication use, and self-reported health, concurrent weight change, and initial total hip bone mineral density. SOF group is also adjusted for caffeine intake and estrogen use. MrOS group is also adjusted for smoking and history of stomach surgery.

≠Adjusted for age, race/ethnicity, body mass index, enrollment in clinical trial status, indicator for cohort, smoking, physical activity (metabolic equivalent tasks), self-reported health, having a parent who broke a hip after age 40 years, treated diabetes mellitus, history of fracture at 55 years o older, and corticosteroid use, physical function score, history of myocardial infarction or angina, asthma or emphysema, arthritis, stomach or duodenal ulcer, moderate or severe heartburn, osteoporosis, number of psychoactive medications, and use of hormone therapy and bisphosphonates.

References:

1. Vestergaard P, Rejnmark L, Mosekilde L. Proton pump inhibitors, histamine H2 receptor antagonists, and other antacid medications and the risk of fracture. *Calcif Tissue Int.* 2006;79:76-83.

2. Yang YX, Lewis JD, Epstein S, Metz DC. Long-term proton pump inhibitor therapy and risk of hip fracture. *JAMA* 2006;296:2947-53.

3. Targownik LE, Lix LM, Metge CJ, Prior HJ, Leung S, Leslie WD. Use of proton pump inhibitors and risk of osteoporosis-related fractures. *CMAJ* 2008 Aug 12;179(4):319-26.

4. Kaye JA, Jick H. Proton pump inhibitor use and risk of hip fractures in patients without major risk factors. *Pharmacotherapy* 2008;28:951-59.

5. Corley, D.A., Kubo, A., Zhao, W., Quesenberry, C., Proton Pump Inhibitors and Histamine-2 Receptor Antagonists are Associated with Hip Fractures among At-Risk Patients, *Gastroenterology* (2009), doi:10.1053/j.gastro.2010.03.055.

6. Gray SL, LaCroix AZ, Larson J, Robbins J, Cauley JA, Manson JE, Chen Z. Proton Pump Inhibitor Use, Hip Fracture, and Change in Bone Mineral Density in Postmenopausal Women. *Arch Intern Med* 2010;170 (9):765-771.

7. Yu EW, Blackwell T, Ensrud KE, Hillier TA, Lane NE, Orwoll E, Bauer DC, et al. Acid-Suppressive Medications and Risk of Bone Loss and Fracture in Older Adults. *Calcif Tissue Int.* 2008;83(4):251-259.

8. Targownik LE, Lix LM, Leung S, Leslie WD. Proton-pump inhibitor use is not associated with osteoporosis or accelerated bone mineral density loss. *Gastroenterology* 2010;138:896-904.

Related Information

- FDA: Possible Fracture Risk with High Dose, Long-term Use of Proton Pump Inhibitors[1]
  FDA press release (5/25/2010)
- Possible Increased Risk of Bone Fractures With Certain Antacid Drugs[2]
  FDA Consumer Update

Contact Us

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

MedWatch Online[3]

Regular Mail: Use postage-paid FDA Form 3500[4]
Mail to: MedWatch 5600 Fishers Lane
Rockville, MD 20852-9787

Links on this page:

1. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm213377.htm
2. http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm213240.htm
3. http://www.fda.govhttps://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm
4. http://www.fda.gov/downloads/Safety/MedWatch/DownloadForms/UCM082725.pdf

U.S. Food and Drug Administration

Safety

Orlistat (marketed as Alli and Xenical): Labeling Change

Audience: Family Practice healthcare professionals, patients/consumers

[Posted 05/26/2010] FDA notified healthcare professionals and patients that it has approved a revised label for Xenical to include new safety information about cases of severe liver injury that have been reported rarely with the use of this medication. The agency is also adding a new warning about rare reports of severe liver injury to the OTC Drug Facts label for Alli.

Xenical and Alli are medications used for weight-loss that contain different strengths of the same active ingredient, orlistat. Xenical (orlistat 120 mg) is available by prescription and Alli (orlistat 60 mg) is sold over-the-counter without a prescription. This new safety information, originally announced in August 2009, is based on FDA's completed review of orlistat.

Healthcare professionals should weigh the benefits of weight-loss with the potential risks associated with Xenical and Alli before prescribing or recommending these medications to their patients; patients should stop use of orlistat and contact their healthcare professional if they develop the signs and symptoms of liver injury, including itching, yellow eyes or skin, dark urine, light-colored stools, or loss of appetite.

[05/26/2010 - Drug Safety Communication [1] - FDA]

[05/26/2010 - Questions and Answers: Orlistat and Severe Liver Injury [2] - FDA]

Previous MedWatch alert:

[08/24/2009 - Early Communication About an Ongoing Safety Review [3] - FDA]

Links on this page:

1. http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm213038.htm
2. http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm213040.htm
3. http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm180025.htm

U.S. Food and Drug Administration

Safety

Ultram (tramadol hydrochloride), Ultracet (tramadol hydrochloride/acetaminophen): Label Change

Audience: Pain management healthcare professionals

[Posted 05/25/2010] Ortho-McNeil-Janssen and FDA notified healthcare professionals of changes to the Warnings section of the prescribing informatio for tramadol, a centrally acting synthetic opioid analgesic indicated for the management of moderate to moderately severe chronic pain. The strengthened Warnings information emphasizes the risk of suicide for patients who are addiction-prone, taking tranquilizers or antidepressant drugs and also warns of the risk of overdosage. Tramadol-related deaths have occurred in patients with previous histories of emotional disturbances or suicidal ideation or attempts, as well as histories of misuse of tranquilizers, alcohol, and other CNS-active drugs. Tramadol may be expected to have additive effects when used in conjunction with alcohol, other opioids or illicit drugs that cause central nervous system depression. Serious potential consequences of overdosage with tramadol are central nervous system depression, respiratory depression and death. Tramadol has mu-opioid agonist activity, can be abused and may be subject to criminal diversion.

[April 2010 - Dear Healthcare Professional Letter[1]: Ultram - Ortho-McNeil-Janssen]

[April 2010 - Dear Healthcare Professional Letter[2]: Ultracet - Ortho-McNeil-Janssen]

Links on this page:

1. http://www.fda.gov/downloads/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/UCM213265.pdf
2. http://www.fda.gov/downloads/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/UCM213266.pdf

U.S. Food and Drug Administration

News & Events

FDA NEWS RELEASE

For Immediate Release: June 1, 2010
Media Inquiries: Elaine Gansz Bobo, 301.796.7567, elaine.bobo@fda.hhs.gov
Consumer Inquiries: 888-INFO-FDA

FDA Approves New Injectable Osteoporosis Treatment for Postmenopausal Women

The U.S. Food and Drug Administration today approved Prolia, an injectable treatment for postmenopausal women with osteoporosis who are at high risk for fractures.

Osteoporosis is a disease in which the bones become weak and are more likely to break. According to the National Institute of Arthritis and Musculoskeletal and Skin Diseases, 80 percent of the people in the United States with osteoporosis are women. One out of every two women over age 50 will break a bone in their lifetime due to osteoporosis.

People with osteoporosis at high risk for fracture include those that have had an osteoporotic fracture, or have multiple risk factors for fracture; or those who have failed or are intolerant to other available osteoporosis therapy. Prolia works to decrease the destruction of bone and increase bone mass and strength. An injection of Prolia is recommended once every six months.

"Due to its prevalence, osteoporosis is a serious concern to public health," said Julie Beitz, M.D., director of the FDA's Office of Drug Evaluation III. "The approval of Prolia provides another treatment option for postmenopausal women with osteoporosis who are susceptible to fractures."

The safety and efficacy of Prolia in the treatment of postmenopausal osteoporosis was demonstrated in a three-year, randomized, double-blind, placebo-controlled trial of 7,808 postmenopausal women ages 60 to 91 years. In the study, Prolia reduced the incidence of vertebral, non-vertebral, and hip fractures in postmenopausal women with osteoporosis.

The most common side effects reported with Prolia include back pain, pain in the extremities, musculoskeletal pain, high cholesterol levels, and urinary bladder infections. Serious adverse reactions include hypocalcaemia (low calcium levels in the blood), serious infections, including infections of the skin, and dermatologic reactions such as dermatitis, rashes, and eczema.

Prolia causes significant suppression of bone turnover and this suppression may contribute to the occurrence of osteonecrosis of the jaw, a severe bon disease that affects the jaw, atypical fractures, and delayed fracture healing.

Prolia was approved with a risk evaluation and mitigation strategy (REMS) that includes a Medication Guide for patients and communications to health care providers that explains the risks and benefits of the drug.

Prolia is manufactured by Amgen Manufacturing Limited, a subsidiary of Thousand Oaks, Calif.-based Amgen Inc.

For more information

Fast Facts on Osteoporosis – National Institute of Arthritis and Musculoskeletal and Skin Diseases [1]

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RSS Feed for FDA News Releases [2] [what is RSS? [3]]

Links on this page:

1. http://www.niams.nih.gov/Health_Info/Bone/Osteoporosis/osteoporosis_ff.asp
2. http://www.fda.gov/AboutFDA/ContactFDA/StayInformed/RSSFeeds/PressReleases/rss.xml
3. http://www.fda.gov/AboutFDA/ContactFDA/StayInformed/RSSFeeds/ucm144575.htm

U.S. Food and Drug Administration

Drugs

FDA Public Health Alert: Healthcare Professionals Warned Not To Use Certain Intravenous Metronidazole, Ondansetron, and Ciprofloxacin Due To Potential Contamination

Updated June 1, 2010

On May 29, 2010, the U.S. Food and Drug Administration (FDA) alerted healthcare professionals not to use certain intravenous bags of metronidazole, ondansetron, and ciprofloxacin because of potential contamination. FDA has received reports of floating matter in IV bags manufactured by Claris Lifesciences Limited, in Ahmedabad, India. Foreign matter should not be present in a sterile injectable product. Potentially affected products are sold under the Claris, Sagent Pharmaceuticals, Pfizer, and West-Ward Pharmaceuticals labels.

Healthcare professionals should NOT use and should immediately remove from their pharmacy inventories any of the following intravenous (IV) bag products manufactured by Claris and sold under the following labels:

- **Claris – metronidazole, ciprofloxacin, ondansetron**
- **Pfizer – metronidazole, ciprofloxacin, ondansetron**
- **Sagent Pharmaceuticals – metronidazole, ondansetron**
- **West–Ward Pharmaceuticals – metronidazole, ondansetron**

Patients who have received these products should be observed for signs or symptoms of illness and treated appropriately.

Metronidazole and ciprofloxacin are antibiotics used to treat a variety of infections. Ondansetron is an antiemetic used to treat nausea and vomiting associated with chemotherapy or surgery.

A Claris customer received a complaint of white matter in a bag of metronidazole, and subsequent microbiological analysis identified the matter as a *Cladosporium* mold. Molds of this type can cause infections in susceptible patients, such as immunocompromised individuals. Another customer complaint of white matter in a bag of ondansetron was received, and that bag is currently under analysis. At this time, FDA is not aware of any reports of injuries due to administration of these products.

Claris is initiating a recall of all lots of these two products, as well as all lots of ciprofloxacin. These products were all manufactured on the same manufacturing line. FDA is investigating the situation and will notify the public when new information becomes available.

Only metronidazole, ciprofloxacin, and ondansetron in IV bags made by Claris and sold under the Claris, Sagent, Pfizer, and West-Ward Pharmaceuticals labels are affected. Sagent does sell IV bags of ciprofloxacin, but they are not made by Claris and are NOT subject to this recall. West Ward does not sell an intravenous bag formulation of ciprofloxacin.

Links on this page:

U.S. Food and Drug Administration

Drugs

FDA Drug Safety Communication: Drug labels now contain updated recommendations on the appropriate use of long-acting inhaled asthma medications called Long-Acting Beta-Agonists (LABAs)

Safety Announcement

[06/02/2010]Long-Acting Beta-Agonists (LABAs), a class of medications used for the treatment of asthma and chronic obstructive pulmonary disease (COPD), now have new recommendations in their drug label intended to promote their safe use in the treatment of asthma. The new recommendations do not apply to the use of LABAs for the treatment of COPD.

In February 2010, the agency announced it was requiring manufacturers to revise their drug labels because of an increased risk of severe exacerbation of asthma symptoms, leading to hospitalizations, in pediatric and adult patients, as well as death in some patients using LABAs for the treatment of asthma (see February 2010 LABA Drug Safety Communication[1]).

The new recommendations in the updated labels state:

- Use of a LABA alone without use of a long-term asthma control medication, such as an inhaled corticosteroid, is contraindicated (absolutely advised against) in the treatment of asthma.
- LABAs should not be used in patients whose asthma is adequately controlled on low or medium dose inhaled corticosteroids.
- LABAs should only be used as additional therapy for patients with asthma who are currently taking but are not adequately controlled on a long-term asthma control medication, such as an inhaled corticosteroid.
- Once asthma control is achieved and maintained, patients should be assessed at regular intervals and step down therapy should begin (e.g., discontinue LABA), if possible without loss of asthma control, and the patient should continue to be treated with a long-term asthma control medication, such as an inhaled corticosteroid.
- Pediatric and adolescent patients who require the addition of a LABA to an inhaled corticosteroid should use a combination product containing both an inhaled corticosteroid and a LABA, to ensure adherence with both medications.

FDA believes that when LABAs are used according to the recommendations outlined above and in the approved drug labels, the benefits of LABAs in improving asthma symptoms outweigh their risks of increasing severe asthma exacerbations and deaths from asthma.

Additional Information for Patients

- Long-Acting Beta Agonists (LABAs) do not relieve sudden-onset asthma symptoms. You should always have a rescue inhaler, such as an albuterol inhaler, to treat sudden onset asthma symptoms.
- LABAs must never be taken alone for the treatment of asthma.
- If you need a LABA plus a long-term asthma control medication that is not available as a combination product, you should work with your healthcare professional to ensure that each medication is taken correctly.
- You should read the *Medication Guide* for LABAs and talk to your healthcare professional about any questions you may have about the use of LABAs.

Additional Information for Healthcare Professionals

- Long-Acting Beta Agonists (LABAs) should not be started in patients with acutely deteriorating asthma.
- Discuss with patients and families the warning signs of worsening asthma and advise them to seek immediate medical attention should their condition deteriorate.
- LABAs do not relieve sudden-onset asthma symptoms. A rescue inhaler, such as an albuterol inhaler, should be prescribed to treat sudden asthma symptoms.
- Encourage patients, families, and caregivers to read the *Medication Guide* that accompanies LABA prescriptions.
- In pediatric and adolescent patients who need the addition of a LABA to an inhaled corticosteroid, prescribe a combination inhaled corticosteroid – LABA product. Using a combination product will help ensure adherence with both of these medications.

FDA Approved Long-Acting Beta Agonists

Brand Name	LABA active ingredient	Corticosteroid active ingredient	FDA Approved Uses
Serevent Diskus	Salmeterol	None	Asthma, COPD, exercise-induced bronchospasm
Foradil Aerolizer	Formoterol	None	Asthma, COPD, exercise-induced bronchospasm
Foradil Certihaler*	Formoterol	None	Asthma
Advair Diskus	Salmeterol	Fluticasone	Asthma, COPD
Advair HFA	Salmeterol	Fluticasone	Asthma
Symbicort	Formoterol	Budesonide	Asthma, COPD
Brovana	Arformoterol	None	COPD
Perforomist	Formoterol	None	COPD

* not currently marketed in the U.S.

Related Information