Drug Utilization Review Board

Oklahoma Health Care Authority
2401 N.W. 23rd Street, Suite 1A
Oklahoma City, Oklahoma 73107
Ponca Room

Wednesday
October 12, 2011
6:00 p.m.

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

MEMORANDUM

TO: Drug Utilization Review Board Members

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

SUBJECT: Packet Contents for Board Meeting – October 12, 2011

DATE: October 6, 2011

NOTE: THE DUR BOARD WILL MEET AT 6:00 P.M. THE MEETING WILL BE HELD IN THE PONCA ROOM AT THE OKLAHOMA HEALTH CARE AUTHORITY OFFICES IN SHEPHERD MALL. (NORTH ENTRANCE)

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

Call to Order

Public Comment Forum

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

Update on DUR / MCAU Program – See Appendix B.

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

60 Day Notice to Prior Authorize Multiple Sclerosis Medications – See Appendix D.

30 Day Notice to Prior Authorize Biologic Products for the Treatment of Rheumatoid Arthritis, Crohn's Disease, Plaque Psoriasis, and Ankylosing Spondylitis – See Appendix E.

Action Item – Annual Review of Pediculicides and 30 Day Notice to Prior Authorize Natroba™ – See Appendix F.

Action Item – Annual Review of Ocular Antibiotics and 30 Day Notice to Prior Authorize Moxeza™ – See Appendix G.

Action Item – Annual Review of Antihypertensives and 30 Day Notice to Prior Authorize Amturnide™ and Edarbi™ – See Appendix H.

Action Item – Annual Review of Antidepressants and 30 Day Notice to Prior Authorize Viibryd® – See Appendix I.

FDA and DEA Updates – See Appendix J.

Future Business

Adjournment

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Oklahoma Health Care Authority
Drug Utilization Review Board
(DUR Board)
Meeting – October 12, 2011 @ 6:00 p.m.

Oklahoma Health Care Authority
2401 N.W. 23rd Street, Suite 1-A
Oklahoma City, Oklahoma 73107
Ponca Room (North Entrance)

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

1. Call To Order
- A. Roll Call – Dr. Graham

Items to be presented by Dr. Muchmore, Chairman:

2. Public Comment Forum
- A. Acknowledgment of Speakers and Agenda Items

Items to be presented by Dr. Muchmore, Chairman:

3. Action Item – Approval of DUR Board Meeting Minutes – See Appendix A.
- A. September 14, 2011 DUR Minutes – Vote
- B. September 15, 2011 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 July 2011
- B. Retrospective Drug Utilization Review Response for May 2011
- C. Medication Coverage Activity Audit for September 2011
- D. Pharmacy Help Desk Activity Audit for September 2011

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

5. Action Item – Vote to Prior Authorize Firazyr® – See Appendix C.
- A. COP Recommendations

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

6. 60 Day Notice to Prior Authorize Multiple Sclerosis Medications – See Appendix D.
- A. Member Demographics
- B. Market Share
- C. Cost Comparison
- D. Safety and Efficacy
- E. Economic Impact
- F. COP Recommendations

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

7. 30 Day Notice to Prior Authorize Biologic Products for the Treatment of Rheumatoid Arthritis, Crohn's Disease, Plaque Psoriasis, and Ankylosing Spondylitis – See Appendix E.

A. COP Recommendations

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

8. Action Item – Annual Review of Pediculicides and 30 Day Notice to Prior Authorize Natroba™ – See Appendix F.

A. Current Authorization Criteria
B. Utilization Review
C. Prior Authorization Review
D. Market News and Update
E. COP Recommendations
F. Utilization Details
G. Natroba™ Product Details

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

9. Action Item – Annual Review of Ocular Antibiotics and 30 Day Notice to Prior Authorize Moxeza™ – See Appendix G.

A. Current Authorization Criteria
B. Utilization Review
C. Prior Authorization Review
D. Market News and Update
E. COP Recommendations
F. Moxeza™ Product Details

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

10. Action Item – Annual Review of Antihypertensives and 30 Day Notice to Prior Authorize Amturnide™ and Edarbi™ – See Appendix H.

A. Current Authorization Criteria
B. Utilization Review
C. Prior Authorization Review
D. Market News and Update
E. COP Recommendations
F. Amturnide™ and Edarbi™ Product Details

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

11. Action Item – Annual Review of Antidepressants and 30 Day notice to Prior Authorize Viibryd® – See Appendix I.

A. Current Authorization Criteria
B. Utilization Review
C. Prior Authorization Review
D. Market News and Update
E. COP Recommendations
F. Utilization Details
G. Viibryd® Product Details

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

12. FDA and DEA Updates – See Appendix J.

13. Future Business

A. Annual Review of Statins
B. Annual Review of Narcotics
C. New Product Reviews
D. Medical Product Reviews

14. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES of MEETING of SEPTEMBER 14, 2011

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): Jo Nel Speegle, Manish Mittal, Amany Hassan	X	

OKLAHOMA HEALTH CARE AUTHORITY STAFF:	PRESENT	ABSENT
Mike Fogarty, J.D., M.S.W.; Chief Executive Officer		X
Garth Splinter, M.D., M.B.A.; Director of Medicaid/Medical Services		X
Rebecca Pasternik-Ikard, Deputy State Medicaid Director	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
Carter Kimble, MPH/Public Affairs- Information Rep.	X	
Jill Ratterman, D.Ph.; Pharmacy Specialist	X	
Rodney Ramsey; Drug Reference Coordinator	X	
Kerri Wade, Senior Pharmacy Financial Analyst	X	

OTHERS PRESENT:		
Don Kempin, Novo Nordisk	Vanessa Papion, UCB	Tom Arnhart, MedImmune
Brett Brewer, EMD Serono	Melanie Eads, Novartis	Richard Ponder, J&J
Brad Burgstahler, Elan	Toby Thompson, Pfizer	Carol A. Curtis, AZ
Charlene Kaiser, Amgen	Brent Clarkson, Pfizer	Mark DeClerk, Lilly
Felicia Hill, Biogen	John Omick, NPC`	Donna Erwin, BMS
Stephen Brammer, BMS	Jeff Frye, BMS	Brian Maves, Pfizer
Warren Tayes, Merck	Russ Wilson, JJHCS	Renee Parks, JJHCS
Janie Huff, Takeda	Jim Chapman, Abbott	Holly Turner, Merck

	PRESENT FOR PUBLIC COMMENT:	
Agenda Item No. 5	Russ Rainwater, Bristol-Myers Squibb	
Agenda Item No. 9	Brad Clay, Amgen	Vanessa Papion, UCB
Agenda Item No. 10	Carol Gaines, EMD Serono	Dr. Chaouki Khoury
	Dr. Gabriel Pardo	
Agenda Item No. 11	Sam Smothers, MedImmune	

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 acknowledged the speakers for public comment:

Agenda Item No. 5	Russ Rainwater, Bristol-Myers Squibb	
Agenda Item No. 9	Brad Clay, Amgen	Vanessa Papion, UCB
Agenda Item No. 10	Carol Gaines, EMD Serono	Dr. Chaouki Khoury
	Dr. Gabriel Pardo	
Agenda Item No. 11	Sam Smothers, MedImmune	

ACTION: NONE REQUIRED

AGENDA ITEM NO. 3: APPROVAL OF DUR BOARD MINUTES

3A: August 10, 2011 DUR Minutes

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

ACTION: MOTION CARRIED

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

4A: Retrospective Drug Utilization Review: May 2011

4B: Retrospective Drug Utilization Review Response: April 2011

4C: Medication Coverage Activity Audit: August 2011

4D: Pharmacy Help Desk Activity Audit: August 2011

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: VOTE TO PRIOR AUTHORIZE DIABETES MEDICATIONS

For Public Comment; Russ Rainwater: Good evening. It's good to see you again. I was here last month to testify on behalf of Onglyza or Saxagliptin and tonight I just want to make some brief comments on the challenges in treating Type II diabetes. In selecting appropriate drugs for Type II the clinicians are always having to balance the efficacy and risk, especially hypoglycemia and weight gain and patients who often present with comorbidities and that can include cardiovascular disease, renal insufficiency and obesity. Pharmacoeconomic data related to hypoglycemia and diabetes has revealed that diabetic patients who experience hypoglycemia are more likely to have increased emergency room visits, hospitalizations and ambulatory care, all of which lead to increased costs to the healthcare system. It's well appreciated that certain classes of oral antidiabetic agents are associated with risk of hypoglycemia. In fact in recent data that was published in JAMA last year, they took a look at sulfonylureas and in the glinides and found that there was a four to seven-fold increase in increase in relative risk of patients experiencing hypoglycemia with those agents. Correspondingly when they took a look at DPP-4 inhibitors they found that there was a 26% reduction in relative risk of hypoglycemia with those agents. Onglyza as you know is a DPP-4 inhibitor; it's been available now for over two years and has an extensive clinical trial program in Phase 3 which included over 4,000 patients in that database. The overall safety profile for Onglyza as we mentioned to you last month is comparable to placebo. Due to the mechanism of action for Onglyza which is a glucose dependent stimulation of the beta cell-produced insulin response to meals, the overall hypoglycemia rate for Onglyza is very low. When Onglyza is either, is added to Metformin as either initial combination therapy for treatment naive patients or added on to Metformin, it's been found to be similar to placebo in the clinical trials as far as the rates of hypoglycemia. If you look at the data that's included in our package insert and in our clinical package, there's a 52-week non-inferiority trial where Onglyza was added to Metformin and compared to Glipizide in that form of combination. Onglyza achieved the overall efficacy endpoint in terms of A1-C reduction but did it without any marked increase in terms of hypoglycemia and weight gain as compared to sulfonylurea therapy. The overall rates for hypoglycemia were 3% for the Onglyza side on the study, compared to 36.3% in sulfonylurea, the glipizide. Confirmed hypoglycemia defined in the study as signs and symptoms of hypoglycemia along with a finger stick blood glucose of less than 50 mg/dL was 8% in the glipizide arm compared to zero with Onglyza. And also, patients that were on the glipizide arm gained on average 1.1 kg, whereas patients that were on Onglyza and Metformin combination lost on the average 1.1 kg in the study. The other aspect too is to think about renal, using agents, oral agents that are available for use in renal patients who have Type II diabetes. Onglyza has been proven safe in this area, regardless of the degree of renal compromise. In the 12-week trial, Onglyza given at a dose of 2.5 mg once a day in patients who had a creatinine clearance of 50 mg/mL effectively reduced the A1C did not change the overall renal functions. And so with that, I would just conclude that Onglyza with its' clinical profile has been proven safe in various patients, especially patients with renal insufficiency and can be used in place of sulfonylurea. Thank you.

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

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: VOTE TO PRIOR AUTHORIZE XIAFLEX®
Materials included in agenda packet; presented by Dr. Le.
Ms. Varalli-Claypool moved to approve as submitted; seconded by Dr. Rhymer.
ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: VOTE TO PRIOR AUTHORIZE BERINERT®, CINRYZE® AND KALBITOR®
Materials included in agenda packet; presented by Dr. Moore.
Dr. Harrell moved to approve as submitted; seconded by Dr. Feightner.
ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: 30-DAY NOTICE TO PRIOR AUTHORIZE FIRAZYR®
Materials included in agenda packet; presented by Dr. Moore.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 9: 60-DAY NOTICE TO PRIOR AUTHORIZE BIOLOGIC PRODUCTS FOR THE TREATMENT OF RHEUMATOID ARTHRITIS, CROHN'S DISEASE, PLAQUE PSORIASIS, AND ANKYLOSING SPONDYLITIS

For Public Comment; Brad Clay: Hello, good evening. My name is Brad Clay. I'm an outcomes and economics medical liaison in Amgen scientific affairs. I'm here to discuss briefly Enbrel or etanercept. The first think I want to do is make this committee and its' advisors aware that in the last ten days or so a new label has been issued for this product and across the class for the anti-TNF agents, and this makes it version 45 now for Enbrel which is not surprising when you think about a molecule that's been on the market since 1998, has over 19 years of clinical experience and 2.5 million patient years of post-marketing experience. So most of these updates are due to post-marketing safety concerns. This past one dealt primarily with the warning to be aware of opportunistic infections. And so briefly I just want to share three things that I would ask the committee to keep in mind when you're considering this class over the next few minutes and the next couple of months. The first is that although there's, according to a publication in February of this year in The Annals of Rheumatic Diseases which was an updated expert consensus statement for the treatment of rheumatic diseases, just like your DUR packet states, although there's no head-to-head evidence that would suggest that one anti-TNF agent is more effective than the other, this expert panel did make three statements. The first was that based on meta-analyses that etanercept may be safer than adalimumab and anakinra and infliximab, that auto-antibodies significantly decreased the effectiveness of Adalimumab and Infliximab, but not Enbrel; and that based upon European registries that the reactivation rates of tuberculosis as well as the rates of opportunistic infections may be significantly increased when patients receive these monoclonal antibodies compared to those who received Etanercept. Now I don't mean to suggest that monoclonal antibodies cause rampant TB or anything like that. The rates are still very low but I think the lesson is, in a certain population over a certain time frame you see statistically significant differences in adverse event rates. The second point I'd like to make has to do with dosing. There is another publication in May of this year in The Journal of Clinical and Experimental Rheumatology and there was a poster presentation or an oral presentation at ISPOR this year. Both of these projects were sponsored by Amgen, by the way, and the first looked at retrospectively, 44 clinics in five European countries. The second project looked at the Janus data from the years 2005 to 2009. And they looked at the incidence of dose increases among these three agents with respect to rheumatoid arthritis. And the European retrospective look over these clinics where they did chart reviews, looking at two different definitions of dose increase, they found that Etanercept had significantly less dose increase than the two monoclonal antibodies. The same thing occurred in the look at the Ingenix data where they used three different definitions of dose increase. And then finally I'd just like to point out that Enbrel has the indication to treat juvenile idiopathic arthritis in patients as young as two years old, which is the lowest age among this class of agents. So I know it's very easy to treat this as a commodity market. This class has grown significantly over the past few years, but I would challenge you, one could simply look at the generic names of the products and you can see that Enbrel may be a little bit different and offer a little more differential value to Oklahoma Medicaid members, and just respectfully would ask you to keep those thoughts in mind. Thank you very much.

For Public Comment; Vanessa Papion: Thank you. First I'll make apologies that our medical science liaison had a family emergency so I'm a regional account executive and not a medical science liaison, but I am very familiar with our data. I'm going to go with the three point theme as well. Cimzia is a PEGylated antibody fragment and it is indicated for both rheumatoid arthritis as well as Crohn's Disease. The first point in Crohn's Disease is that Crohn's is a waxing and waning disease, so for many patients they won't flare. Cimzia, you can recapture remission with just one extra dose which doesn't increase the long-term dosing or the cost of the drug. In our precise fourth study 49 patients were reinduced and 41% remained in remission after one year. The second point that I wanted to make in rheumatoid arthritis is that Cimzia can be used as monotherapy or with Methotrexate and will produce clinical responses in some patients as soon as one week. So Cimzia has a very rapid onset and long-term maintenance of efficacy with stated dosing which I know is important to you. Post hoc analysis revealed that patients who didn't achieve a minimal improvement at about 12 weeks had only a 1% chance of achieving low disease activity at one year, so what that means to you is that it makes it very possible for an early 12-week decision on whether to move on to another therapy rather than spending time on ineffective therapy. The third point is in safety and the gentleman from Amgen did mention the changes that the FDA made to the package insert across the class. In summary, Cimzia provides fast and last clinical improvements in Crohn's Disease and RA with an acceptable safety profile, dosing is stable, you can make a 12-

week decision with Cimzia. It can be used in combination of monotherapy and efficacy is seen in both anti-TNF naïve patients as well as experienced patients.
Materials included in agenda packet; presented by Dr. Sipols.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 10: DRUG UTILIZATION REVIEW OF MULTIPLE SCLEROSIS MEDICATIONS

For Public Comment; Carol Gaines: Thank you for having me speak today. I am the representing EMD Serono and the drug Rebif, and my background is I'm a neurologist, practiced in Wisconsin, so whenever I'm given the opportunity to speak about MS I like to frame it around patients and one of the hardest things is to, I think all my competitors in the room would agree is multiple sclerosis is a big disease. It's not like treating a staph infection. It's probably a group of diseases. That's why every article starts by describing it as a heterogeneous disease. And that literally means multiple scars. We don't have biomarkers right now, we don't have a way to stage the immunological disease, we don't have a way to say the drug is working or not. So from my vantage point, speaking for clinicians and patients I think that you would agree choice and DMD's in our first line drugs is really essential to find drugs that work for patients. Having said that, I am speaking for the drug Rebif and I don't want to take too much of your time but I do want to point out an important part of why Rebif is even on the market and that is a head-to-head trial. There are very few head-to-head trials in the MS field, but of the ones that brought Rebif to market is a head-to-head trial with Avonex and it's a Class I evidenced randomized controlled trial. It's a comparative phase and a transition phase or where patients in the second phase transition from Avonex to Rebif, so in the initial phase of this head-to-head trial which was the basis for Rebif's approval there was a 30% reduction compared Rebif to Avonex. In the transition phase, 605 patients transitioned to the second phase of this trial. Of 605 patients, 73% of Avonex and 91% of Rebif patients went to the transition phase. Avonex to Rebif resulted in a 50% reduction in relapse rates whereas the transition from Rebif to Rebif was only a transition of .46 to .34. Both statistically significant P value .001 were for Avonex to Rebif and .028 all in the med guides and prescribing information that I can leave with you today. So there is a head-to-head trial that you can refer to so that you're limiting the class. That's not my recommendation but there are, at least when you're thinking of doing so, there are head-to-head trials. Compared to Avonex the adverse effects were similar, that's that they're in balance. There are some differences which I can point to, injection site disorders, 85 vs. 33, hepatic function disorders 18 vs. 10, blood disorders 14 vs. 5, and for Avonex there were more flu-like symptoms, 55 vs. 43. But what I'm really here to say today, as this is a very difficult disease for clinicians and their patients, and I hope that you think or talk seriously about continuing to provide Rebif unrestricted to your Medicaid patients, and I'd like to leave these in case you'd like to look at the Avonex trial or anything else that's …..

For Public Comment; Dr. Chaouki Khoury: I'm Chaouki Khoury. I'm a neurologist at OU. I do the MS clinic for the private patients, but I'm also director of the neurology residents clinic. So basically I'm going to be seeing almost all MS patients on Medicaid in the Oklahoma City metro area and even farther out because not a whole lot of people do see Medicaid. So we deal with all of the Medicaid patients and I was asked by Novartis to come and talk but I'm not employed by any company it's just because I see the Medicaid patient. And I agree with the first speaker. The main thing that we want as neurologists is choice because MS is a very heterogeneous disease and it's hard to say everybody needs to get on this drug as first line and then if you fail there's something else. It's going to be very hard to decide on that and the only head-to-head trial that you can rely on if you want to look at head-to-head trial, are usually against Avonex which we all know it's the weakest of them all and then the young doctors know head-to-head trial, you've proved that because no companies will put their drug on the line and say let's try this against that and then ending up failing, so we're not going to get head-to-head trials on (unintelligible) something like that, so the companies would not sponsor head-to-head trial, so that's not going to get there. So basically we need to go by clinical efficacy and side effect profile, and with them having difference side effect profiles we'd like to have all of them available because my depressed patient who is having bad depression with psychosis I'm probably not going to start them on the Interferon which typically start off as the first line agent. And then more importantly is patient preferences in terms of compliance with injections. Now that we have an oral medication on the market it's hard to say we're going to put you on the injections, sorry because you don't have insurance because you have Medicaid, you have to suffer through the injections when many of them might not be compliant. On the other hand I don't want this to come across as if all patients are getting on the fingolimod, the Gilenya because that's not the case. So what usually happens in the clinic or we teach the residents to do as when a patient comes in with a new diagnosis of MS they sit them down and they go over the list of the medication. They say this is Avonex, this is what the side effect profile is, this is Rebif, this is what the side effect profile is, this is Betaseron, this is Gilenya and this is Copaxone. We cover the side effect profiles, we cover how long they've been on the market, what we know about their efficacy and then we decide with the patient. Now if somebody with very active disease we'd probably not even present Avonex as an option to that but to present all the others, not having any head-to-head trial, we can give them all of them and then based on their co-morbid condition and then what the side effect profile of that medication, might choose one over the other. So I don't know what specifically I can answer in terms of questions because in my mind I don't have one that is by far this is the best, that's what we need to use all the time, and then when they fail this we go on to the other. And looking at cost difference, it's really not that huge. There is a little bit of difference in cost, I'm not saying that, but there's not that much difference in costs, so I don't see how you guys (unintelligible) in the position you have to decide which one should be first line and which one should not be first line, so my opinion as being a neurologist treating this patient is to leave all of them available except for Tysabri of course being second line based on the side effect profile that would be my recommendation, but all the others being first line agents to see what goes for these patients.

Dr. Muchmore: We recognize this is an area that is art of medicine because there just aren't hard endpoints and that's always a problem for us on any area where art is very important in choosing the drug.

Dr. Khoury: There are some endpoints, it's not like there is no endpoints. We always go by disease activity so somebody who comes to me and is having monthly or every two month relapses and I put them on a drug and now they go a whole year with no relapse, it's hard to argue that the drug is not working for them. Yes there is no test I can do in terms of taking a blood level or something like that but a clinical history plus the MRI disease activity, again we can go to the debate as what measure is the all important thing is that grey matter, stuff like that, but we can go by MRI to say here, this is (unintelligible). The best story I have is a patient of mine who recently (that's why he's still on my mind) comes in had tons of attacks we start him on a certain drug, Tysabri in this case because it had tried tons of other ones and he stabilizes on Tysabri better and doesn't show any new lesions. Clinically he's not had any more attacks, got off the Tysabri for personal reasons, has two attacks in the time he's off, gets

back on Tysabri, stabilized again. So yes, true, there is no blood level we can go by or a specific endpoint per se, but it's hard to argue this patient is not responding to Tysabri when you have such success story like that, so we always try to go by MRI and by clinical history on these patients. But if you need hard data in terms of comparing which one to choose over the other, yes we don't have that.

Dr. Graham: Doctor, if you did see there was a significant difference in cost on one of the agents, would that make a difference in your thinking?

Dr. Khoury: If they have a similar side effect profiles, yes. So if you take for example Extavia and Betaseron which aren't the same drug, if there is significant cost differences, yes I would go with the cheaper one and then it's justifiable to say you know what, we don't know which one is better but this one is similar to this one, yet much less expensive, then yes, it's justifiable to put that as a Tier 1, that as a Tier 2.

Dr. Graham: And if you had a methodology where you could report that side effect that you didn't want for that particular patient and get it approved, would that be satisfactory?

Dr. Khoury: Totally fine. If all I have to do is put, discuss with patient based on the fact that patient has this based on the patient has that, that's why we're choosing this with the caveat of having the option of patient does not want injections for example, I think that's justifiable if I develop MS, hopefully not never, I would definitely want to be on a pill not on an injection where I inject myself, but that's a personal preference. I have tons of my patients why I give that option, to say you know what, the pill has been on the market very recently, I don't have that kind of risk. I saw my grandmother who got on fen-phen and she's dead because of it and I don't want to take any of this, I want it to be on the market for twenty years before I try it. I have almost half of new diagnoses who do that. They don't want to get on the pill, even most recently a 15-year old girl, her and her mother discussed it and I thought it's a young girl, of course she's not going to do injections and they chose the injection over the pill. But I want to be able to give them that option.

Dr. Feightner: Chose injections over the pill?

Dr. Khoury: Yep, a 15-year old girl just because she's like, you know what, I don't want to take any risks because her grandma had had some complication with one of these medications in the past, so she saw that.

Dr. Feightner: That's difficult for me to swallow.

Dr. Muchmore: Have you run into any severe bradycardia with the fingolimod?

Dr. Khoury: We've had one patient who had severe bradycardia on initial administration.

Dr. Muchmore: Do you do your initial administration in the hospital or in clinic?

Dr. Khoury: That is Consta… what's the name of the company that you use? Concentra? So I have my nurse do that. Yes, Concentra was administering all of these with monitoring further for six hours.

Dr. Muchmore: So they monitor for the six hours?

Dr. Khoury: Occasionally we do put them out. They come in for six hours and then they go home after that.

Dr. Muchmore: But your experience has been it's not been a real high rate of bradycardia? I've been interested in that.

Dr. Khoury: Dr. Pardo probably can, have much more experience than me in that field because he has a much larger patient population, his incidence might be much greater.

For Public Comment; Dr. Gabriel Pardo: I appreciate the opportunity to address you all. I to verify that I am here on behalf of the patients primarily and my colleagues. I am the director of the Oklahoma Medical Research Foundation Multiple Sclerosis Center of Excellence. We take care of over 2,500 MS patients at that facility, of the estimated 3,500 patients with MS in the state of Oklahoma. So we certainly have the bulk of the patients and we've been taking care of them for the last ten years or so. So I am representing the patients and of course the physicians that take care of multiple sclerosis patients. I hope that the committee will not hold against me the fact that I'm not wearing a black suit, that's fine with you all? And of course I'm very impressed to be talking about the fact that you are reviewing the this category. I cannot more what has been said here before and that is that multiple sclerosis is a very complex disease to take care of. If there's a disease that's challenging not only in diagnosis but in being able to study lots of patients and follow them successfully over time, I think that MS is the primary example of that. That being said, the heterogeneous presentation also requires a very individualized management of these patients, so when we approach the management of these patients we always think from two perspectives. One is including this many patients on a disease-modifying therapy that will alter the course of the disease that is the purpose. We know that across the board these medications as a category have made a huge difference since they were introduced some eighteen years ago. In the long-term outcomes for these patients, we are seeing patients that are remaining healthier without significant disability many years down the road. Something that we were not seeing when we were not treating these patients. And the second aspect of course is the management of symptoms and comprehensive approach to the management of MS quite complex. The decision making as Dr. Khoury mentioned before is very individualized. We cannot really approach these with categories of medications but with specific medications that go with specific characteristics of the presentation of the disease in a given patient. And that is not only the disease activity, the disability the patient might have, but also extends into the support group that they have, how accessible it is for them to self-inject or help other people inject them. And a whole host of other characteristics that we make a decision in the sanctity of the examination room along with the patient as a combined decision based on all these factors. So certainly the thought of having to restrict the access to certain medications based on other factors like medicoeconomics that we understand are extremely important really will hamper our ability to guarantee a good long-term outcome for these patients. When I think of medicoeconomics of course, I have two things in mind. One is how can we save some money and resources now and that is extremely important, but what is more important in my mind is how can I save resources and money long-term by keeping a given patient functional without disability, able to remain engaged in the workforce or being able to continue to study or be a good family member long-term. By making a decision now, what's going to be the best option for that. I'm not going to say that one medication is better than another because it's better than another for a given patient and if we are restricting the access I think that's going to hamper our ability to really provide this very comprehensive care that we're trying to provide. I can assure you that when we make that decision with a patient, it is a very thoughtful process. It is not something that we do just because it's the fad of the moment. It is something that we really do with great care and that we believe this is the best decision for a given patient at a given time. And it's a dynamic process and of course things might change. But I just want to say that to allow the committee to think about restricting access in any way to any of these medications and guarantee to you that the physicians who are involved in taking care of these patients go through a very careful, thoughtful process of deciding what's best for a given patient.

Dr. Feightner: Why is Copaxone number one? Why is it used the most? It seems to be a good market share. Why is that your first choice?

Dr. Pardo: It's not my first choice, but certainly when you look at market share nationwide Copaxone is number one, but it's not historically what has been the case. Other agents have been number one over time. Copaxone has become number one based on many different factors. One,

perhaps the side effect profile that makes it more appealing for physicians and patients to some degree. The fact that there have been some trials especially in the recent years that have shown equivalent efficacy compared to the interferons or to some of the interferons. Studies that were not done specifically to check efficacy but that have been what's rated that as one of the secondary outcomes. And the fact that I think perhaps of course, it's been in the market for some time and there is good confidence in the long-term safety data of the medication. Now that can be said also for the interferons as a category. So you have four different interferons so they are going to have to share their market portion, but if you take the interferons as a category and Copaxone as the only agent in its' own category, then perhaps they are quite equivalent and I do not know the numbers.

Dr. Feightner: Okay, we have 508 claims on Copaxone versus Betaseron of 165 claims, so just look at that, you know, coming to the clinic it just looks like that Copaxone is where the first choice out of …… instead of …… the presentation was that you know, we look at each of them equivalently, each of them were equal, now but it looks like, the data's showing me that Copaxone is number one, so ……

Dr. Pardo: Right, if you were to add the prescriptions for Betaseron, for Rebif, and for Avonex perhaps you will be equivalent to Copaxone . I do not know, but so interferons as a group perhaps are equivalent to Copaxone.

Dr. Muchmore: And the interferons as a group are about the same numbers as Copaxone.

Dr. Pardo: And all of these agents, the interferons, Copaxone and the Fingolimod, Gilenya, the augmentation are all FDA approved as first line therapy and of course we would like to have that ability to decide on using them first line in any given patient if we see fit. But Tysabri is the only one that is approved with second line therapy, rightfully so despite being extremely efficacious in controlling inflammatory disease activity. It does have a more significant side effect profile and is to be taken into consideration, and that's how we approach it clinically anyway.

Dr. Feightner: We looked at the side effect profile …… one last question. If we look at the side effect profile of interferons and come up with a method to allow use of those if you have that on a petition like Dr. Graham was saying, that would be something that you'd find acceptable as well?

Dr. Pardo: Certainly. That being said, I would have to obviously state that the side effect profile of interferons is quite benign as well. So what we're doing here is the decision, an initial decision from a patient understanding that as a category, interferons are going to give you some flu-like symptoms associated with the injection, but we know and it has been demonstrated that those are temporary. They tend to go away after the patient has been using the medication for a while. We do take measures to minimize those side effects by escalating the therapy. We start lower doses and over a period of one month we go up. We tend to premedicate our patients with nonsteroidals and acetaminophen and with that being said, it's a very manageable side effect profile. I do not want to leave the impression that it's a difficult one to handle. The only other requirement is monitoring fever, enzymes and white count for the interferons on a regular basis. But we very uncommonly see side effects in that regard that would require change in therapy.

There was some discussion among the Board members as to whether or not these medications need prior authorization and if there is an advantage to the Health Care Authority to require prior authorization.

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 11: ANNUAL REVIEW OF SYNAGIS®

For Public Comment; Sam Smothers: I promise you this will probably be the shortest talk from MedImmune you've seen in the past few years. But I would like to say thank you to the Board for allowing us to speak tonight and most importantly to say that we support the recommendation from the College of Pharmacy that are being proposed tonight and to let you know that we are, as a company, really trying to address the concerns that the committee's had in the past with regards to compliance as well as from appropriate candidates to be submitted for prior authorization. So some of the things that we're doing is working with the State to identify what those appropriate kids are, as they are outlined by the criteria, and then also working on the compliance with Marlene's group and the care coordination department and making sure that that information is available to NICU's as well as practitioners, that this service is available through the State, that if you identify a child or family that may be at risk for being non-compliant then getting those kids referred into the State so that follow-up phone calls can be made, identify why they may be being non-compliant and trying to address that. So again I'd just like to say thanks for all that you guys do to protect these high risk kids throughout the State and we're here to help address the concerns that you have with problem compliance as well as appropriateness of therapy. I'd be happy to answer any questions. I also have Tom Arnhart who's our medical science director, if you have any questions clinically for him. One thing to note that in 2012 there will be a new set of redbook recommendations that will be published so that may be time to ……

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

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: Utilization Review of Pediculicides
B: Annual Review of Ophthalmic Antibiotics
C: New Product Reviews
D: Medical Product Reviews

ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: ADJOURNMENT: The meeting was adjourned at 7:45 p.m.

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

Memorandum

Date: September 15, 2011

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

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

Subject: DUR Board Recommendations from Meeting of September 14, 2011

Recommendation 1: Vote to Prior Authorize Type 2 Diabetes Medications

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends prior authorization of Type 2 Diabetes Medications with the following criteria:

1. To qualify for a Tier 2 medication, the member must have a trial of a Tier 1 medication (must include a trial of metformin titrated up to maximum dose), or a clinical reason why a Tier 1 medication is not appropriate.
2. For initiation with dual or triple therapy, additional Tier 2 medications can be approved based on current AACE or ADA guidelines.
3. To qualify for a Tier 3 medication, the member must have tried a Tier 2 medication in the same category and have a documented clinical reason why the Tier 2 medication is not appropriate.
4. To qualify for a Special Prior Authorized medication, the member must be currently stabilized on the requested product or have attempted at least 3 other categories of

Tier 2 or Tier 3 medications, or have a documented clinical reason why the requested product is necessary for the member.

a. For members with steatohepatitis, pioglitazone can be approved after a trial of a Tier 1 medication (must include a trial of metformin titrated up to maximum dose), or a clinical reason why a Tier 1 medication is not appropriate.

Tier 1	Tier 2†	Tier 3	Special PA
Biaguanides Metformin Metformin SR Metformin-Glyburide Metformin-Glipizide Sulfonylureas Glyburide Glyburide Micronized Glipizide Glipizide SR Glimepiride Miscellaneous Chlorpropamide Tolbutamide	Supplementally rebated or best net price product from each class in Tier 3.	DPP-4 Inhibitors Saxagliptin Saxagliptin-Metformin Sitagliptin Sitagliptin-Metformin Linagliptin Glinides Repaglinide-Metformin Repaglinide Nateglinide GLP-1 Agonists Exenatide Liraglutide Alpha-Glucosidase Inhibitors Acarbose Miglitol	Biaguanides Riomet Soln* Metformin Long-Acting‡ Thiazolidinediones Rosiglitazone Pioglitazone Rosiglitazone-Metformin Rosiglitazone-Glimepiride Pioglitazone-Metformin Pioglitazone-Glimepiride Amylinomimetic Pramlintide‡

*No prior authorization required for member 12 and under.
†At least one Tier 2 from each Tier 3 category will be determined based on supplemental rebate or best federal rebate.
‡Special criteria currently apply.

Recommendation 2: Vote to Prior Authorize Xiaflex®

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends medical prior authorization of Xiaflex® with the following approval criteria:

1. FDA approved indication of Dupuytren's contracture with palpable cord, functional impairment and fixed-flexion contractures of the metacarpophalangeal (MP) joint or proximal interphalangeal (PIP) joint of 30 degrees or more.
2. Must be 18 years or older.
3. Not a candidate for needle aponeurotomy.
4. Physician must be trained in treatment of Dupuytren's contracture and injections of the hand.
5. Quantity limit of 3 doses (one dose per 4 weeks) per cord.

Recommendation 3: Vote to Prior Authorize Berinet®, Cinryze®, and Kalbitor®

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends medical prior authorization of Berinet®, Cinryze®, and Kalbitor® with the following approval criteria:

Criteria for Approval for Cinryze® (C1 esterase inhibitor)

1. Documented diagnosis of Hereditary Angioedema
2. For prophylaxis of Hereditary Angioedema
3. History of at least one or more abdominal or respiratory HAE attacks per month, or history of laryngeal attacks, or three or more emergency medical treatments per year
4. Documented intolerance, insufficient response, or contraindication to
    a. attenuated androgens (e.g. danazol, stanozolol, oxandrolone, methyltestosterone) AND
    b. antifibrinolytic agents (e.g. ε – aminocaproic acid, tranexamic acid) OR
    c. recent hospitalization for severe episode of angioedema
5. Not currently taking an angiotensin converting enzyme (ACE) inhibitor or estrogen replacement therapy.
6. Dosing:
    a. The recommended dose of Cinryze® is 1000 units IV every 3 to 4 days, approximately 2 times per week, to be infused at a rate of 1 ml/min.
    b. Initial doses to be administered in outpatient setting by healthcare provider. Patients can be taught by their healthcare provider to self-administer Cinryze® intravenously.
    c. Quantity limit of 8000 units per month will apply, i.e. 2 treatment per week, or 8 treatments per month.

Criteria for Approval of Berinert® (C1 esterase inhibitor):

1. Documented diagnosis of Hereditary Angioedema
2. For acute attacks of Hereditary Angioedema

Criteria for Approval of Kalbitor® (ecallentide):

1. Documented diagnosis of Hereditary Angioedema
2. For acute attacks of Hereditary Angioedema

Recommendation 4: Annual Review of Synagis®

NO ACTION REQUIRED.

The College of Pharmacy does not recommend changes to the current criteria.

Appendix B

RETROSPECTIVE DRUG UTILIZATION REVIEW REPORT
July 2011

MODULE	DRUG INTERACTION	DUPLICATION OF THERAPY	DRUG-DISEASE PRECAUTIONS	DOSING & DURATION
Total # of messages	46,817	57,394	961,429	24,863
Limits applied	Established, Major, Males and Females, Age 0-18	Duplication of Acetaminophen Products, Males and Females, Age 21-25	Contraindicated, Asthma, Males and Females, Age 0-12	High Dose Only, SSRIs & SSNRIs, Males and Females, 0-150
Total # of messages after limits were applied	23	128	122	128
Total # of members reviewed	23	115	98	128

LETTERS

Category	Prescribers	Pharmacies	Total Letters
Drug Interaction	0	0	0
Duplication of Therapy	51	16	67
Drug-Disease Precautions	13	0	13
Dosing & Duration	28	2	30
Total Letters Sent	92	18	110

Retrospective Drug Utilization Review Report

Claims Reviewed for May 2011

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 25-26	Contraindicated, Renal Failure, Males and Females, Age 0-150	High Dose and Duration, Oxazolidinones (Zyvox), Males and Females, Age 0-150

Response Summary (Prescriber)
Letters Sent: 84
Response Forms Returned: 34

The response forms returned yielded the following results:

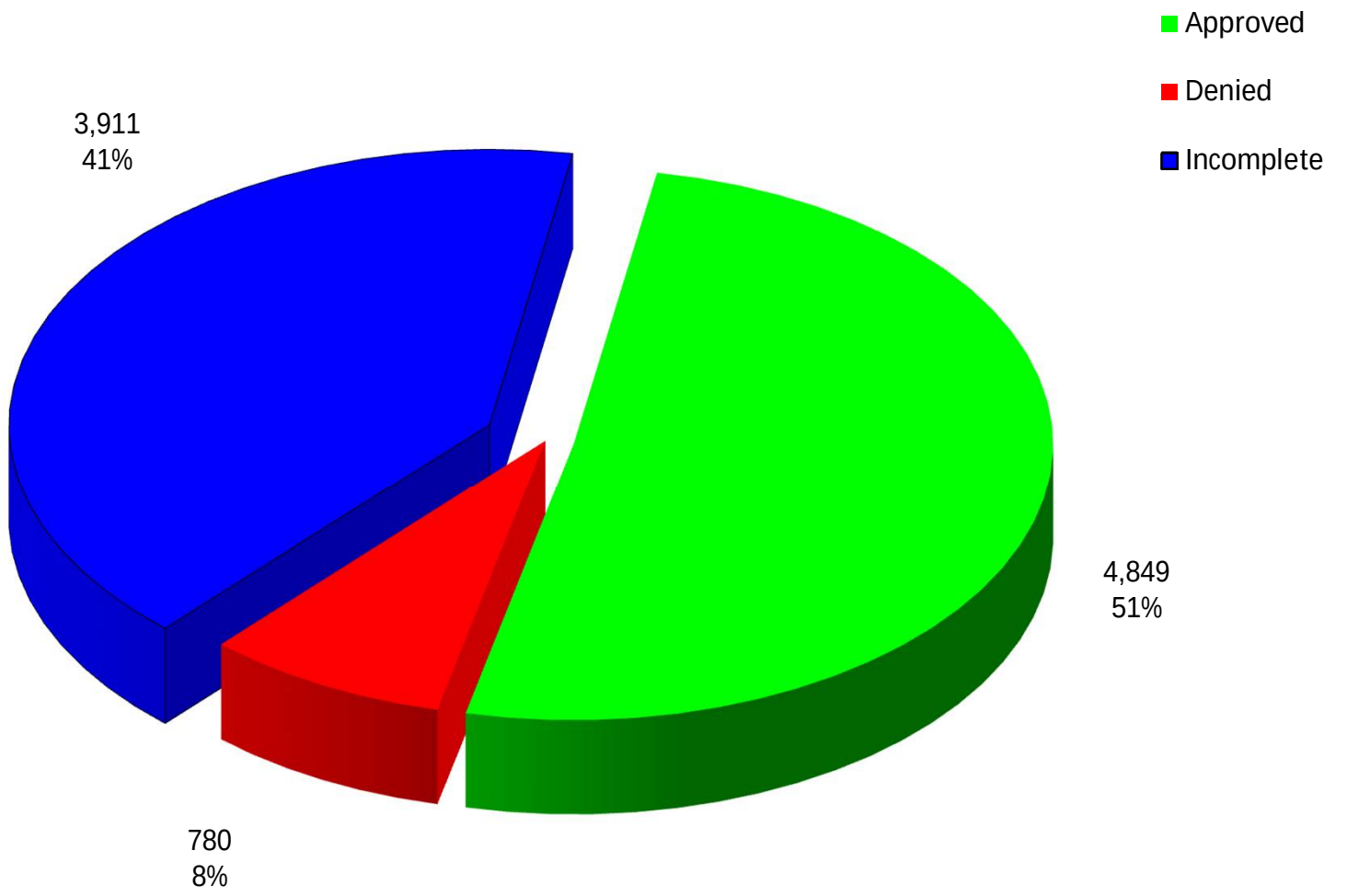
4 (12%)	*Record Error—Not my patient.*
7 (21%)	*No longer my patient.*
0 (0%)	*Medication has been changed prior to date of review letter.*
11 (32%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
10 (29%)	*I am aware of this situation and will plan to continue monitoring therapy.*
2 (6%)	*Other*

Response Summary (Pharmacy)
Letters Sent: 2
Response Forms Returned: 2

The response forms returned yielded the following results:

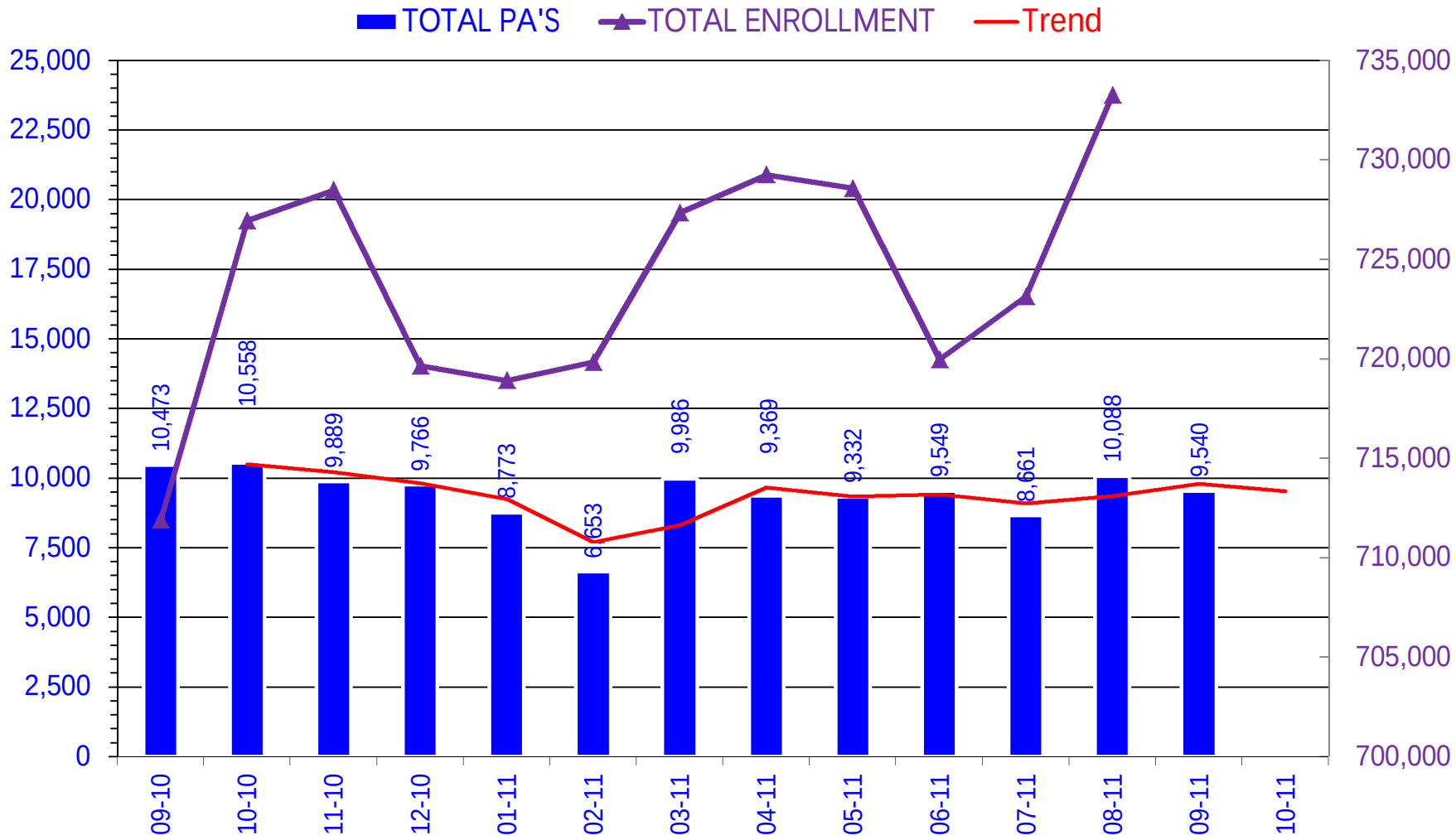
0 (0%)	*Record Error—Not my patient.*
0 (0%)	*No longer my patient.*
0 (0%)	*Medication has been changed prior to date of review letter.*
1 (50%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
1 (50%)	*I am aware of this situation and will plan to continue monitoring therapy.*
0 (0%)	*Other*

PRIOR AUTHORIZATION ACTIVITY REPORT: September 2011



PA totals include overrides

PRIOR AUTHORIZATION REPORT: September 2010 – September 2011



PA totals include overrides

Prior Authorization Activity

9/1/2011 Through 9/30/2011

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort	379	148	24	207	359
Amitiza	27	6	3	18	272
Anti-Ulcer	512	237	87	188	98
Antidepressant	313	110	22	181	344
Antihistamine	231	144	8	79	340
Antihypertensives	85	27	4	54	339
Antimigraine	102	22	16	64	282
Atypical Antipsychotics	665	348	21	296	350
Benign Prostatic Hypertrophy	6	1	0	5	361
Benzodiazepines	69	40	3	26	221
Bladder Control	61	11	7	43	363
Brovana (Arformoterol)	2	1	0	1	365
Byetta	17	7	0	10	363
Elidel/Protopic	39	22	3	14	97
ESA	111	87	2	22	109
Fibric Acid Derivatives	4	0	1	3	0
Fibromyalgia	135	35	16	84	361
Fortamet/Glumetza	1	0	1	0	0
Forteo	3	2	0	1	363
Glaucoma	31	8	0	23	321
Growth Hormones	54	38	4	12	171
HFA Rescue Inhalers	69	25	5	39	315
Insomnia	89	21	10	58	169
Misc Analgesics	42	4	34	4	249
Muscle Relaxant	179	41	82	56	76
Nasal Allergy	255	60	47	148	138
NSAIDS	171	33	23	115	301
Ocular Allergy	65	12	4	49	88
Ocular Antibiotics	50	14	4	32	10
Opioid Analgesic	296	147	21	128	242
Other	837	296	86	455	269
Otic Antibiotic	72	18	2	52	20
Pediculicides	124	60	9	55	15
Plavix	225	152	0	73	321
Singulair	978	538	55	385	263
Smoking Cessation	54	16	5	33	28
Statins	142	67	5	70	355
Stimulant	893	433	63	397	313
Suboxone/Subutex	153	114	8	31	80
Symlin	3	1	0	2	362
Synagis	2	0	0	2	0
Topical Antibiotics	12	3	1	8	16
Topical Antifungals	24	5	3	16	82
Ultram ER and ODT	6	1	0	5	365
Xolair	10	1	4	5	361
Xopenex Nebs	31	16	1	14	334
Zetia (Ezetimibe)	29	13	3	13	362
Emergency PAs	4	4	0	0	
Total	**7,662**	**3,389**	**697**	**3,576**	

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Overrides					
Brand	37	22	2	13	267
Dosage Change	525	503	3	19	11
High Dose	9	6	0	3	113
IHS-Brand	8	6	0	2	67
Ingredient Duplication	9	9	0	0	17
Lost/Broken Rx	113	108	1	4	9
NDC vs Age	3	3	0	0	271
Nursing Home Issue	108	99	3	6	9
Other	39	34	0	5	12
Quantity vs. Days Supply	1,023	668	73	282	269
Stolen	4	2	1	1	4
Overrides Total	**1,878**	**1,460**	**83**	**335**	
Total Regular PAs + Overrides	**9,540**	**4,849**	**780**	**3,911**	

Denial Reasons

Unable to verify required trials.	3,194
Does not meet established criteria.	749
Lack required information to process request.	719

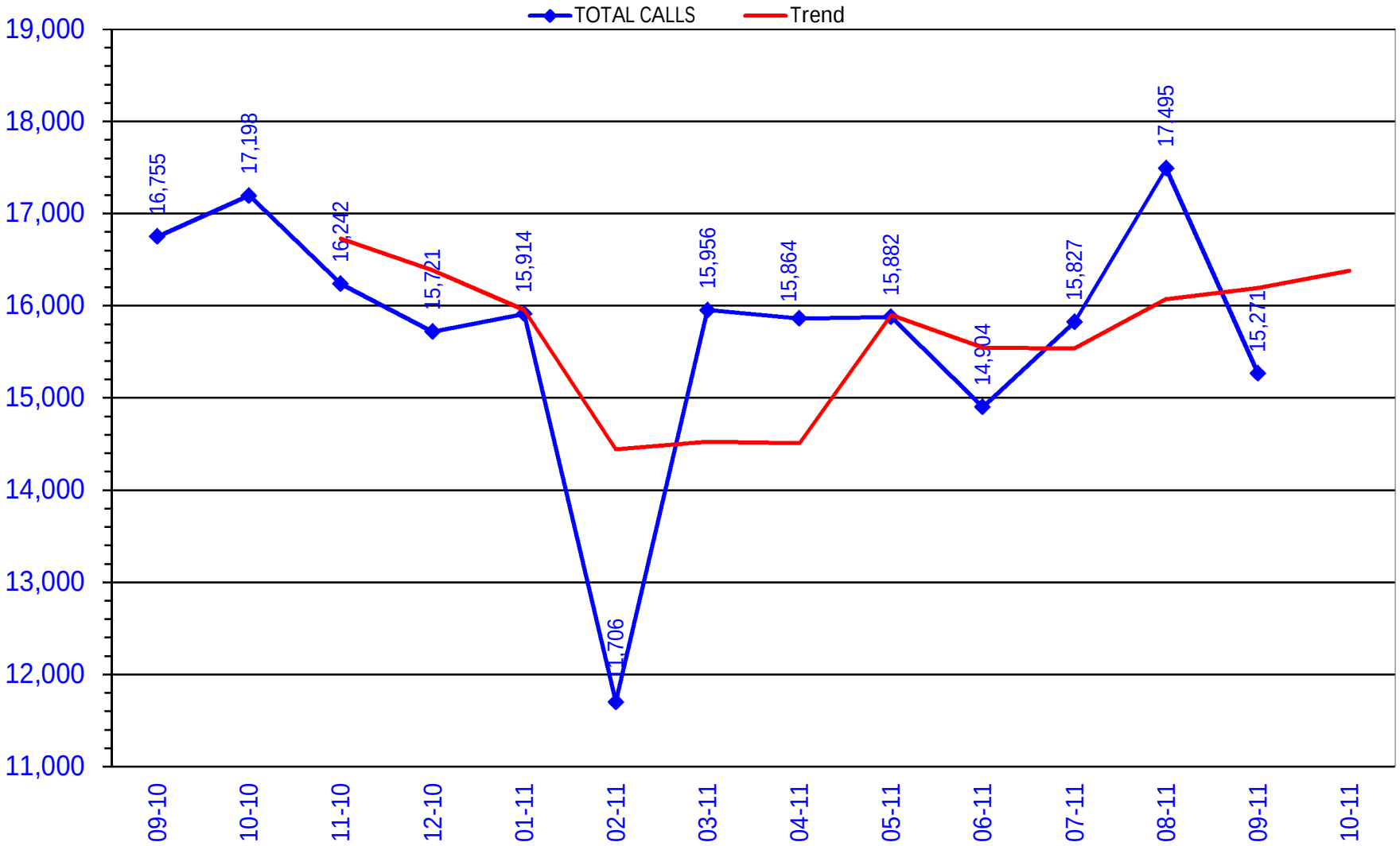
Duplicate Requests: 576

Letters: 1,525

No Process: 354

Changes to existing PAs: 507

CALL VOLUME MONTHLY REPORT:
September 2010 – September 2011



Appendix C

Vote to Prior Authorize Firazyr® (Icatibant)

Oklahoma Health Care Authority, October 2011

Under Oklahoma state law, the OHCA DUR Board must review and make recommendations for any drug subject to prior authorization, whether covered under the pharmacy benefit, the medical benefit, or both. Accordingly, physician administered drugs are brought through the same DUR process as those dispensed by pharmacies.

Recommendations

The College of Pharmacy recommends placing a prior authorization on Firazyr® (icatibant) with the following criteria:

1. Documented diagnosis of Hereditary Angioedema (HAE)
2. For acute attacks of Hereditary Angioedema (HAE)

Appendix D

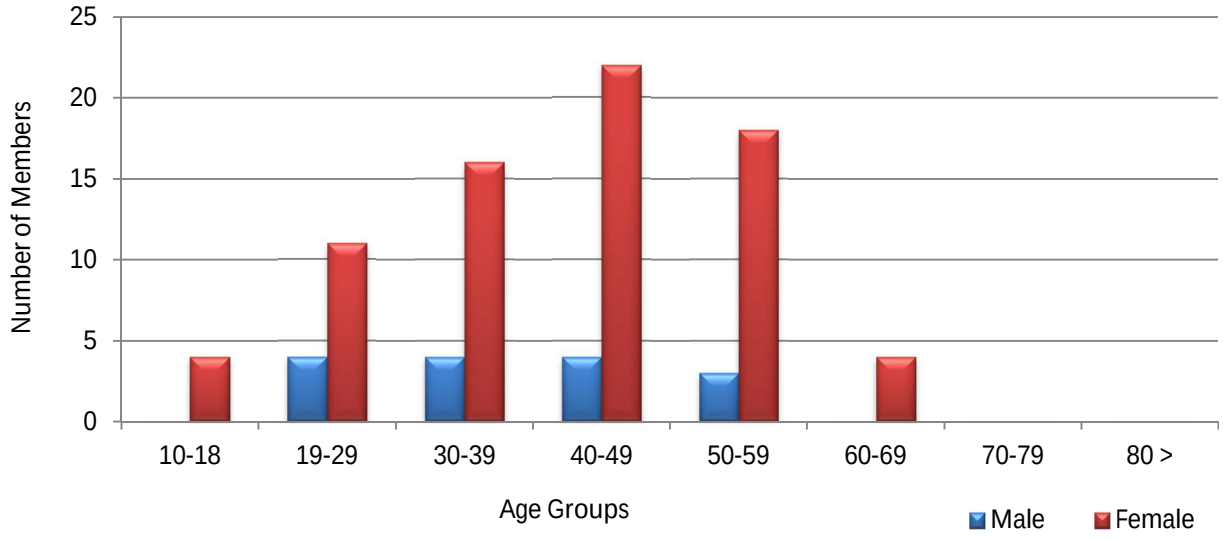
60 Day Notice to Prior Authorize Multiple Sclerosis Medications

Oklahoma Health Care Authority
October 2011

This category was introduced for possible inclusion in the Product Based Prior Authorization program in September 2011. See the September DUR packet for a more complete discussion of the category. This notice and statement of potential economic impact are presented to meet the statutory requirements of 63 O.S. Sec. 5030.5.

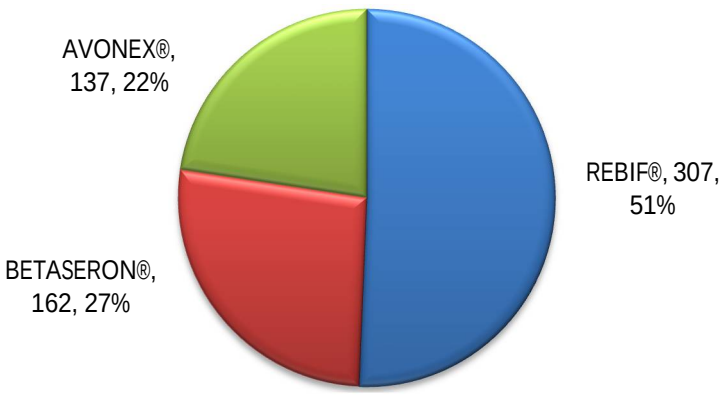
Member Demographics of Interferons

In fiscal year 2011, there were a total of 90 members utilizing the interferon class of medications through the pharmacy benefit. Within this population there were 19 waiver patients.



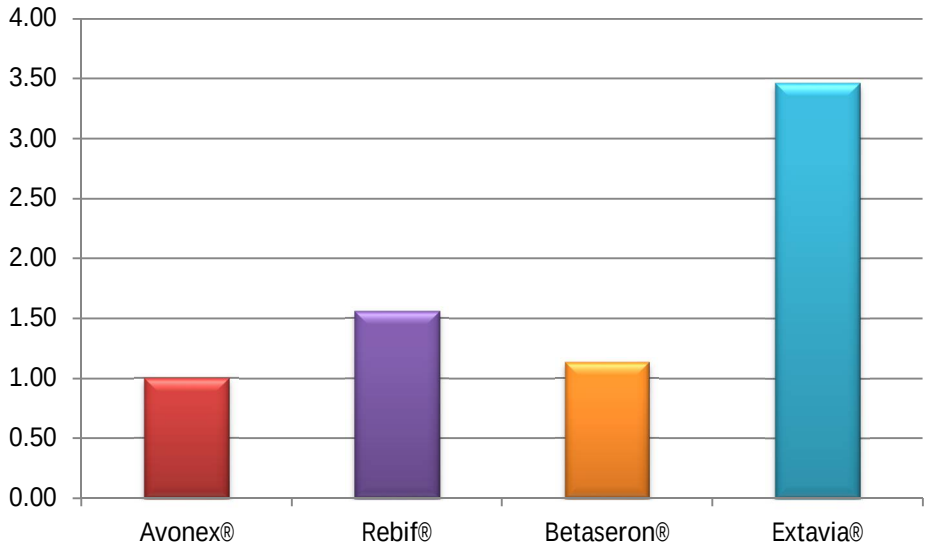
Market Share of Interferons

During fiscal year 2011, there were a total of 606 claims for the interferon class of medications.



Cost Comparison of Interferons

The chart below shows a comparison of net costs based on cost per month. The costs of the interferons are compared as a ratio to the medication with the lowest monthly cost.



Comparison of Safety and Efficacy of Interferons

Studies to date comparing the efficacy of the interferon formulations have found no clear significant differences on clinical measures. One head to head study[i] comparing interferon beta-1b (Rebif) dosed TIW vs. the interferon beta-1a (Avonex) dose once weekly showed TIW dosing had higher rates of relapse free patients (74.9% vs 63.3%) and fewer active MRI lesions. However, the patients in the TIW dosing group experienced higher rates of injection site reactions ((83% vs 28%), higher rates of asymptomatic abnormalities of liver enzymes (18% vs 9%), higher rates of altered leukocyte counts (11% vs 5%), and development of neutralizing antibodies (25% vs 2%). These results were also demonstrated in another study[ii] comparing interferon beta-1b dosed every other day vs interferon beta-1a dosed once weekly which showed the QOD dosing resulted in higher rates of relapse free patients (51% vs 36%).

The results of clinical trials often times may not reflect real world outcomes, especially in patients with MS where there may be large differences in baseline patient populations in addition to the variable clinical course of the disease. The Quality Assessment in Multiple Sclerosis Therapy trial (QUASIMS)[iii], a large, open label observational study, including 510 treatment sites in Europe showed no significant differences among interferon beta products when used as initial or follow-up therapy on all outcomes measured.

Economic Impact

Potential Secondary Costs

Overall efficacy is considered to be similar across the products in this class, but drug selection requires individual patient history which includes, but is not limited to: other illnesses, disease risk factors, and current symptoms.

Potential Administrative Costs

The potential number of petitions which might be required if a Tier 2 product was not chosen initially by the prescriber is estimated to be approximately 100. The total number of members who will be affected by this change is unknown until the final Tier 2 selection has been made. Previously, it has been theorized that the total cost per petition to the healthcare system (includes cost to physicians, pharmacists, and program) is between $7.63 and $14.82. Total cost for prior authorization to the healthcare system is estimated to be between $1,000 and $1,500 annually. Anticipated actual administrative cost to the program is projected to be less than $1,500.

Potential Program Savings

Because this category will be grandfathered, early savings will be possible for new starts or therapy changes only, and will depend on the final Tier 1 product selection. Potential net ingredient savings to the program after rebates based on the recommended tiers and a potential shift of 50% of market share from Tier 2 to Tier 1 is estimated to be 6% of the FY11 total reimbursement to pharmacies for this category of drugs. The maximum first year saving would be 11% of the FY11 total reimbursement. Increased future saving might be incurred with increased use of the Tier 1 product.

Recommendations

The College of Pharmacy recommends the following for the Multiple Sclerosis Category of Medications:

Tier 1	Tier 2
Interferon β - 1a (Avonex®)	Interferon β - 1a (Rebif®)
Lowest Supplemental Rebated Medication	Interferon β - 1b (Extavia®)
	Interferon β - 1b (Betaseron®)

Interferon Prior Authorization Criteria:

1. Documented diagnosis of relapsing remitting MS.
2. Tier-2 medications require failure of the preferred Tier-1 product defined as:
    a. Occurrence of an exacerbation after 6 months.
    b. Significant increase in MRI lesions after 6 months.
    c. Adverse reactions or intolerable side effects.
3. No concurrent use with other therapies.
4. Compliance will be checked for continued approval every 6 months.

Glatiramer Acetate (Copaxone®) Prior Authorization Criteria:

1. FDA approved diagnosis.
2. No concurrent use with other therapies.
3. Compliance will be checked for continued approval every 6 months.

Fingolimod (Gilenya®) Prior Authorization Criteria:

1. Documented diagnosis of relapsing remitting MS with at least one relapse in the previous 12 months.
2. No concurrent use with other therapies.
3. Compliance will be checked for continued approval every 6 months.

[i] Panitch H, Goodin DS, Francis G, et al. Randomized, comparative study of interferon beta-1a treatment regimens in MS: the EVIDENCE trial. Neurology. 2002;59:1496-1506.

[ii] Durelli L, Verdun E, Barbero P, et al. Every-other-day interferon beta-1b versus once-weekly interferon beta-1a for multiple sclerosis: results of a 2-year prospective randomised multicentre study (INCOMIN). Lancet. 2002;359:1453-1460.

[iii] Limmroth V, Malessa R, Zettl UK, Koehler J, Japp G. Quality Assessment in Multiple Sclerosis Therapy (QUASIMS): a comparison of interferon beta therapies for relapsing-remitting multiple sclerosis. J Neurol. 2007;254:67-77.

Appendix E

30 DAY NOTICE TO PRIOR AUTHORIZE BIOLOGIC PRODUCTS FOR THE TREATMENT OF RHEUMATOID ARTHRITIS, CROHN'S DISEASE, PLAQUE PSORIASIS, AND ANKYLOSING SPONDYLITIS

OKLAHOMA HEALTH CARE AUTHORITY
OCTOBER 2011

This category was introduced for possible inclusion in the Product Based Prior Authorization program in August 2011. See the August and September DUR packets for a more complete discussion of the category. This notice is presented to meet the statutory requirements of 63 O.S. Sec. 5030.5.

Several medications in this category are given by intravenous (IV) infusion. Giving a medication by IV infusion rather than by a self-administered method can increase the annual cost. The Medicaid reimbursement rates for the most commonly listed codes used in conjunction with these products are listed below:

1. First hour of infusion: $131.59
2. Each additional hour of infusion: $28.41
3. Office visit: $37.99-$127.30 (depends on level of complexity of patient care)

So, for example, the annual cost would be about $1850 for a medication that was infused over an hour for 14 doses (3 loading doses then monthly), plus additional charges for the office visit which can vary. Other variable costs could include charges for IV normal saline and other supplies.

RECOMMENDATIONS

The College of Pharmacy recommends pharmacy and medical prior authorization of this class of medications with the following criteria and tier structure :

Tier 2 authorization criteria:

1. FDA approved diagnosis
2. A trial of at least one Tier 1 product in the last 90 days that did not yield adequate relief of symptoms or resulted in intolerable adverse effects.
3. Prior stabilization on the Tier 2 medication documented within the last 100 days.

Tier 3 authorization criteria:

1. FDA approved diagnosis
2. Recent trials of one Tier 1 product and all available Tier 2 medications that did not yield adequate relief of symptoms or resulted in intolerable adverse effects.
3. Prior stabilization on the Tier 3 medication documented within the last 100 days.
4. A unique FDA-approved indication not covered by Tier 2 products.

Biologic Medications		
Tier 1	**Tier 2**	**Tier 3**
DMARDs appropriate to disease state:	Supplemental rebated medications	Abatacept (Orencia®)
Methotrexate		Adalimumab (Humira®)
Hydroxychloroquine		Alefacept (Amevive®)
Sulfasalazine		Anakinra (Kineret®)
Minocycline		Certolizumab pegol (Cimzia®)
Oral Corticosteroids		Etanercept (Enbrel®)
Leflunomide		Golimumab (Simponi®)
Mesalamine		Infliximab (Remicade®)
6-Mercaptopurine		Rituximab (Rituxan®)
Azathioprine		Tocilizumab (Actemra®)
NSAIDs		Ustekinumab (Stelara®)

Appendix F

Annual Review of Pediculicides - Fiscal Year 2011
30 Day to PA Natroba™ (spinosad) Topical Suspension

Oklahoma Health Care Authority
October 2011

Current Prior Authorization Criteria

OTC treatments for lice are a covered benefit for all members. A prescription is required for coverage, and fills are limited to one individual package size for a seven day supply.

Currently, the following OTC products are covered:

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

Approval Criteria:

- **Approval of Tier 2 medication** requires a trial with one Tier 1 medication with inadequate response or adverse effect.
- **Approval of Tier 3 medication** requires trials with all available Tier 2 medication(s) with inadequate response or adverse effect.

Tier 1	Tier 2	Tier 3
Covered OTC Lice Products Generics with SMAC Pricing	Supplemental Rebate	Lindane Lotion & Shampoo Crotamiton (Eurax®) Lotion Benzoyl Alcohol (Ulesfia™) Lotion Malathion (Ovide®)

The following restrictions also apply for each individual product based on FDA approval information:

Malathion lotion (Ovide®)

- Member must be at least 6 years old (stated on package label)
- Quantity limit of 60ml for 7 day supply; may be repeated once if needed for current infestation after 7 days from original fill date

Crotamiton lotion (Eurax®)

- Member must be at least 18 years of age
- Quantity limit of 60 grams or milliliters for 30 day supply

Lindane lotion & shampoo

- Member must be at least 13 years old or weigh at least 110 pounds
- Quantity limit of 60ml for 7 day supply
- One 7 day supply per 30 days maximum

Ulesfia™ (benzoyl alcohol) Lotion

- Available only after first-line treatment with an OTC product has failed
- Member must be at least 6 months old
- Due to mechanism of action, requires retreatment after 7 days
- Hair length would be required in order to approve the appropriate number of bottles if requesting more than 2 bottles per treatment (4 bottles for both treatments)

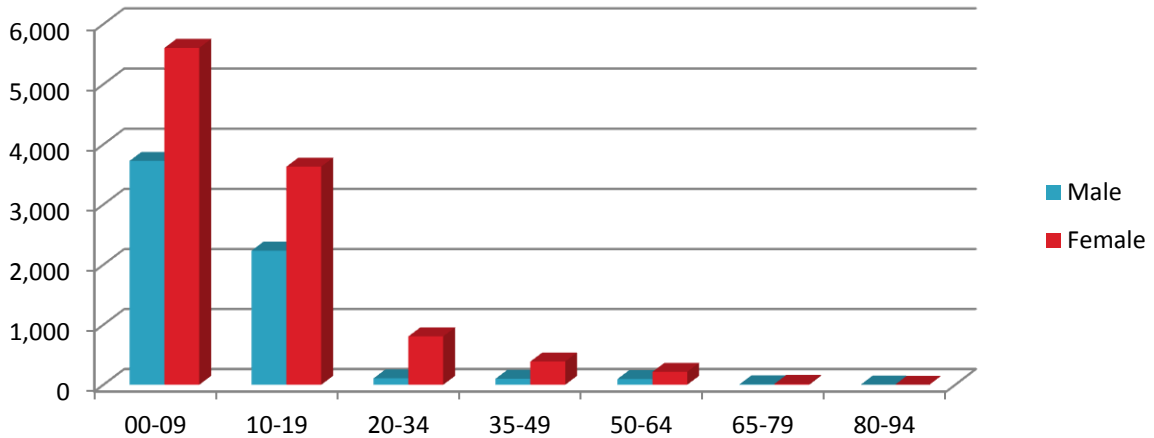
Clinical exception if known resistance to OTC Permethrin and Pyrethrin.

Utilization of Pediculicides: Fiscal Year 2011

Comparison of Fiscal Years

Fiscal Year	Members	Claims	Cost	Cost/Claim	Cost/Day	Units	Days
2010	15,016	21,134	$562,532.47	$26.62	$2.44	1,499,622	230,644
2011	16,924	26,404	$474,668.07	$17.98	$1.52	1,848,487	312,940
Percent Change	**12.7%**	**24.9%**	**-15.60%**	**-26.6%**	**-37.7%**	**23.3%**	**35.7%**
Change	**1,908**	**5,270**	**-$87,864.40**	**-$8.64**	**-$0.92**	**348,865**	**82,296**

Demographics of Members Utilizing Medication or Class: FY 2011

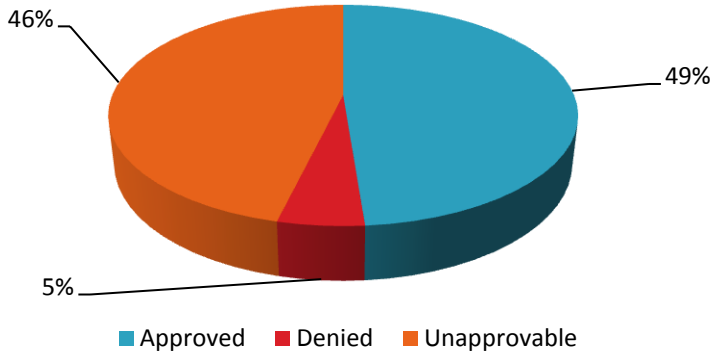


Top 10 Prescribers of Pediculicides by Number of Claims: FY 2011

Specialty	Claims	Cost
General Pediatrician	6,095	$129,996.13
Family Practitioner	5,108	$92,061.18
Physician Assistant	3,619	$62,968.11
Nurse Practitioner (Other)	3,259	$61,866.70
Unknown	2,978	$38,812.13
Non-Contracted Prescriber	1,551	$24,872.02
General Practitioner	1,378	$23,924.78
Emergency Medicine Practitioner	639	$10,083.87
Internist	452	$7,514.22
DDSD-NFM	381	$7,882.11

Prior Authorizations

There were a total of 1,456 petitions submitted for this PBPA category during fiscal year 2011. The following chart shows the status of the submitted petitions.



Market News and Update

Natroba™ (spinosad) Topical Suspension 0.9% - Approved January 2011 for the topical treatment of head lice infestation in patients 4 years of age and older. Natroba™ causes a neuronal excitation in insects and lice, periods of hyperexcitation are followed by paralysis and death.

Conclusion and Recommendations

The College of Pharmacy recommends continuation of the current Product Based Prior Authorization criteria. Additionally, the College recommends placement of Natroba™ (spinosad) in Tier 3 of the current structure. An age restriction of 4 years or older and a quantity limit of 240 mL every 30 days will also apply.

Utilization Details of Pediculicides: Fiscal Year 2011

Chemical Name	Brand Name	Claims	Units	Days	Members	Cost	Cost/ Day	% Cost
Permethrin	PERMETHRIN CRE 5%	12,816	767,596	134,753	9,440	$197,246.13	$1.46	41.55%
Permethrin	PERMETHRIN LOT 1%	10,390	747,005	136,082	6,497	$124,226.11	$0.91	26.17%
Permethrin	SM LICE LOT TREATMNT	1,564	118,636	19,923	1,020	$22,337.30	$1.12	4.71%
Permethrin	ACTICIN CRE 5%	394	23,581	4,012	305	$6,052.82	$1.51	1.28%
Permethrin	LICE TREATME LIQ 1%	190	21,959	3,505	114	$2,889.32	$0.82	0.61%
Malathion	MALATHION LOT 0.5%	633	37,465	6,441	496	$83,274.34	$12.99	17.54%
Benzyl Alcohol	ULESFIA LOT 5%	332	127,145	6,848	232	$29,964.10	$4.38	6.31%
Lindane	LINDANE SHA 1%	39	2,340	452	31	$4,439.99	$9.82	0.94%
Lindane	LINDANE LOT 1%	21	1,260	204	16	$2,415.90	$11.84	0.51%
Crotamiton	EURAX CRE 10%	20	1,200	600	17	$1,416.66	$2.36	0.30%
Crotamiton	EURAX LOT 10%	5	300	150	5	$405.40	$2.70	0.09%
	Totals	**26,404**	**1,848,487**	**312,940**	**16,924***	**$474,668.07**	**$1.52**	

***Total number of unduplicated members**

PRODUCT DETAILS OF NATROBA™ (SPINOSAD) TOPICAL SUSPENSION

FDA-APPROVED JANUARY 18, 2011

INDICATIONS: Natroba™ Topical Suspension (spinosad) is indicated for the topical treatment of head lice infestation in patients four (4) years of age and older.

DOSAGE FORMS:

- 0.9%, viscous, slightly opaque, light orange-colored suspension.

ADMINISTRATION:

- For topical use only. Natroba™ Topical Suspension is not for oral, ophthalmic, or intravaginal use.
- Shake bottle well. Apply sufficient Natroba™ Topical Suspension to cover dry scalp, then apply to dry hair. Depending on hair length, apply up to 120 mL (one bottle) to adequately cover scalp and hair.
- Leave on for 10 minutes, then thoroughly rinse off Natroba™ Topical Suspension with warm water.
- If live lice are seen 7 days after the first treatment, a second treatment should be applied.
- Avoid contact with eyes.

CONTRAINDICATIONS: None

SPECIAL POPULATIONS:

- **Pregnancy Category B**: There are no adequate and well-controlled studies with Natroba™ Topical Suspension in pregnant women. Studies in humans did not assess for the absorption of benzyl alcohol contained in Natroba™ Topical Suspension. Reproduction studies conducted in rats and rabbits were negative for teratogenic effects. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed. No comparisons of animal exposure with human exposure are provided in this labeling due to the low systemic exposure noted in the clinical pharmacokinetic study which did not allow for the determination of human AUC values that could be used for this calculation. Systemic embryofetal development studies were conducted in rats and rabbits. Oral doses of 10, 50 and 200 mg/kg/day spinosad were administered during the period of organogenesis (gestational days 6 – 15) to pregnant female rats. No teratogenic effects were noted at any dose. Maternal toxicity occurred at 200 mg/kg/day. Oral doses of 2.5, 10, and 50 mg/kg/day spinosad were administered during the period of organogenesis (gestational days 7 – 19) to pregnant female rabbits. No teratogenic effects were noted at any dose. Maternal toxicity occurred at 50 mg/kg/day. A two-generation dietary reproduction study was conducted in rats. Oral doses of 3, 10, and 100 mg/kg/day spinosad were administered to male and female rats from 10-12 weeks prior to mating and throughout mating, parturition, and lactation. No reproductive/developmental toxicity was noted at doses up to 10 mg/kg/day. In the presence of maternal toxicity, increased dystocia in parturition, decreased gestation survival, decreased litter size, decreased pup body weight, and decreased neonatal survival occurred at a dose of 100 mg/kg/day.
- **Nursing Mothers:** Spinosad, the active ingredient in Natroba™ Topical Suspension is not systemically absorbed; and therefore, will not be present in human milk. However, Natroba™ Topical Suspension contains benzyl alcohol, which may be systemically absorbed through the

skin, and the amount of benzyl alcohol excreted in human milk with use of Natroba™ Topical Suspension is unknown. Caution should be exercised when Natroba™ Topical Suspension is administered to a lactating woman. A lactating woman may choose to pump and discard breast milk for 8 hours (5 half-lives of benzyl alcohol) after use to avoid infant ingestion of benzyl alcohol.

- **Pediatric Use:** The safety and effectiveness of Natroba™ Topical Suspension have been established in pediatric patients 4 years of age and older with active head lice infestation. Safety in pediatric patients below the age of 4 years has not been established. Natroba™ Topical Suspension is not recommended in pediatric patients below the age of 6 months because of the potential for increased systemic absorption due to a high ratio of skin surface area to body mass and the potential for an immature skin barrier. Natroba™ Topical Suspension contains benzyl alcohol which has been associated with serious adverse reactions and death in neonates and low birth-weight infants. The "gasping syndrome" (characterized by central nervous system depression, metabolic acidosis, gasping respirations, and high levels of benzyl alcohol and its metabolites found in the blood and urine) has been associated with benzyl alcohol dosages >99 mg/kg/day in neonates and low-birth weight infants. Additional symptoms may include gradual neurological deterioration, seizures, intracranial hemorrhage, hematologic abnormalities, skin breakdown, hepatic and renal failure, hypotension, bradycardia, and cardiovascular collapse. The minimum amount of benzyl alcohol at which toxicity may occur is not known. Premature and low-birth weight infants, as well as patients receiving high dosages, may be more likely to develop toxicity
- **Geriatric Use:** Clinical studies of Natroba™ Topical Suspension did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

WARNINGS & PRECAUTIONS:

- **Benzyl Alcohol Toxicity:** Natroba™ Topical Suspension contains benzyl alcohol and is not recommended for use in neonates and infants below the age of 6 months. Systemic exposure to benzyl alcohol has been associated with serious adverse reactions and death in neonates and low birth-weight infants.
- **Overdosage:** If oral ingestion occurs, seek medical advice immediately.

ADVERSE REACTIONS REPORTED AT >1%:

- Application site erythema
- Ocular erythema
- Application site irritation

ADVERSE REACTIONS REPORTED AT <1 %:

- Application site dryness, application site exfoliation, alopecia, and dry skin.

DRUG INTERACTIONS: There are no known significant interactions.

PATIENT INFORMATION:

- Use Natroba™ Topical Suspension exactly as prescribed. Your healthcare provider will prescribe the treatment that is right for you. Do not change your treatment unless you talk to your healthcare provider.
- Use Natroba™ Topical Suspension in one or two treatments that are one week apart. If live lice are seen one week (7 days) after you first used Natroba™ Topical Suspension you will need to use Natroba™ Topical Suspension again.
- Shake bottle well right before use.
- Use Natroba™ Topical Suspension when your hair is dry. Do not wet your hair before applying Natroba™ Topical Suspension.
- It is important to use enough Natroba™ Topical Suspension to coat completely every single louse and to leave it on your scalp for the full 10 minutes.
- Because you need to completely cover all of the lice with Natroba™ Topical Suspension, you may need help in applying Natroba™ Topical Suspension to your scalp and hair. Make sure that you and anyone who helps you apply Natroba™ Topical Suspension reads and understand this leaflet and the Patient Instructions for Use.
- Children will need an adult to apply Natroba™ Topical Suspension for them.
- Do not swallow Natroba™ Topical Suspension. If swallowed, call your healthcare provider right away.
- Do not get into eyes. If Natroba™ Topical Suspension gets in the eye, flush with water right away.
- Wash your hands after you apply Natroba™ Topical Suspension.

REFERENCES

Natroba™Label Information. AstraZeneca Pharmaceuticals, Inc. Available online at: **http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?id=43749**. Last revised May 2011.

Appendix G

Annual Review of Ocular Antibiotics and 30-day Notice to Prior Authorize Moxeza™ (moxifloxacin hydrochloride ophthalmic solution)
Oklahoma HealthCare Authority
October 2011

Current Prior Authorization Criteria

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	Tier 3
Gentak (Gentamicin)	Ciloxan Solution (Ciprofloxacin)	Vigamox (Moxifloxacin)
AK-Tob (Tobramycin)	Ocuflox (Ofloxacin)	Azasite (Azithromycin)
Bleph-10, Na Sulamyd (Na Sulfacetamide)		Besivance (besifloxacin HCL)
Polytrim (PolymyxinB/Trimethoprim)		Iquix (Levofloxacin)
AK-Spore (Neo/PolyB/Gramacidin)		Quixin (Levofloxacin)
		Zymar (Gatifloxacin)
		Zymaxid (Gatifloxacin)

Ophthalmic Antibiotics: Ointments	
Tier 1	Tier 2
AK-Tracin (Bacitracin)	Ciloxan Ointment (Ciprofloxacin)
AK-Poly-Bac (Bacitracin/PolymyxinB)	
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

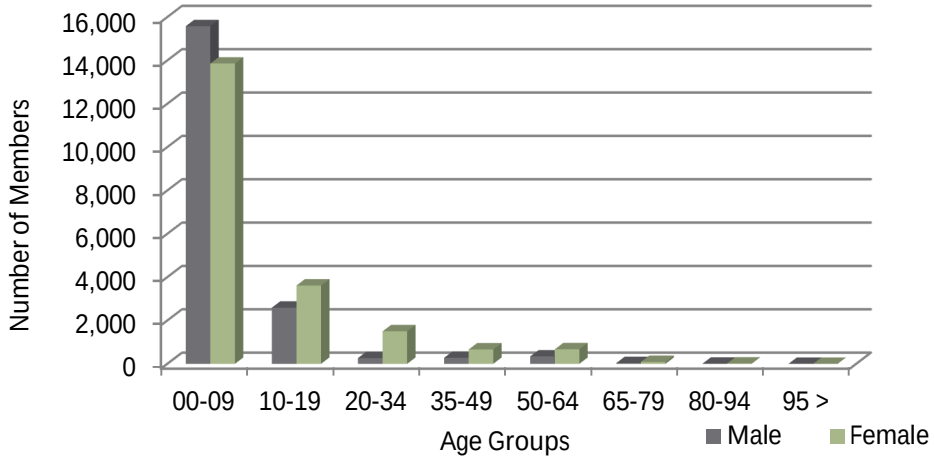
Ophthalmic Antibiotic–Steroid Combination Products	
Tier 1	Tier 2
	Tobradex (Tobramycin/Dexamethasone) Susp & Oint
	Zylet (Tobramycin/Loteprednol) Suspension
	Blephamide (Sulf/Prednisolone) Susp & Oint
	Pred-G (Gentamicin/Prednisolone) Susp & Oint
	Poly-Pred (Neo/Poly/Prednisolone) Susp
	Cortisporin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

Utilization of Ocular Antibiotics

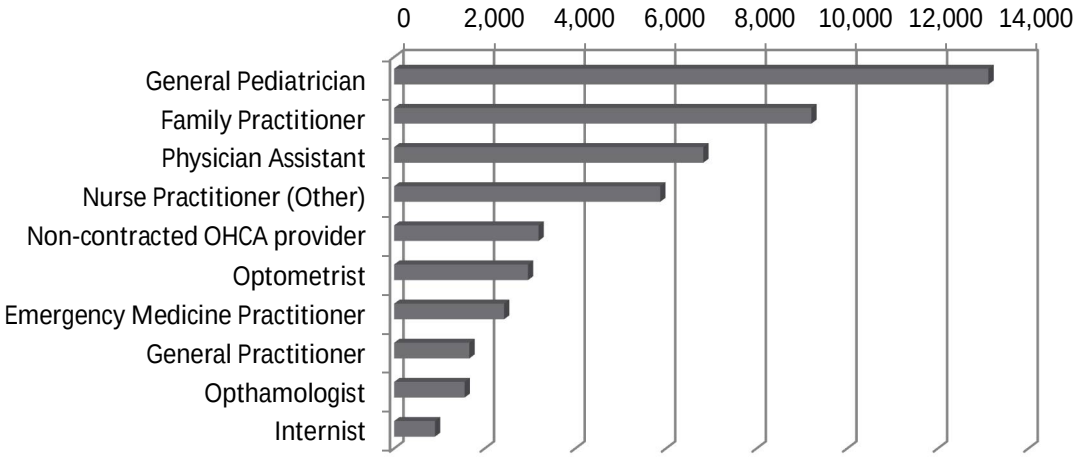
Comparison of Fiscal Years

Fiscal Year	Members	Claims	Cost	Cost/Claim	Perdiem	Units	Days
2010	36,894	43,465	$1,136,172.99	$26.14	$2.49	273,932	455,809
2011	39,489	50,398	$838,768.72	$16.64	$1.54	372,339	544,539
Percent Change	7.00%	16.00%	-26.20%	-36.30%	-38.20%	35.90%	19.50%
Change	2,595	6,933	-$297,404.27	-$9.50	-$0.95	98,407	88,730

Demographics of Members Utilizing Ocular Antibiotics: FY 2011



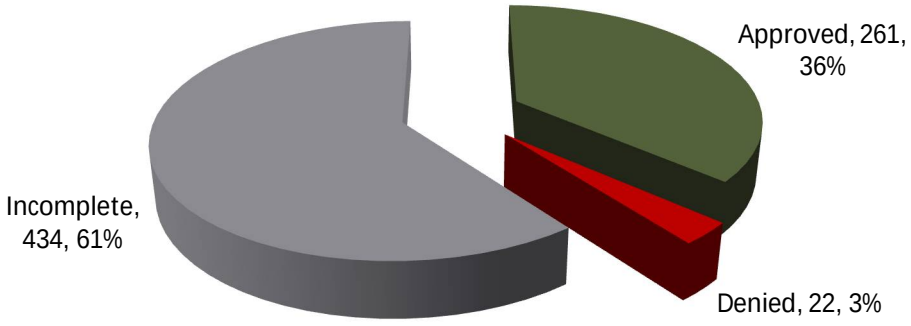
Prescribers of Ocular Antibiotics by Number of Claims: FY 2011



Prior Authorization of Ocular Antibiotics

There were a total of 717 petitions submitted for this PBPA category during fiscal year 2011. Please note that for this PBPA category the system will automatically search Tier 1 medications in member's claims history within a certain timeframe and if detected, the member can automatically get the Tier 2 medication without submitting a prior authorization form. The following chart shows the status of the submitted petitions.

Status of Petitions for Ocular Antibiotics: FY 2011



Market News and Updates

Upcoming patent expirations:

- Azasite®- March 2019
- Zymar®- February 2020
- Zymaxid®- February 2020
- Vigamox®- March 2020
- Besivance®- June 2021

New approvals:

- Moxeza™ (moxifloxacin hydrochloride ophthalmic solution)
  - Entered the market 01/15/2011.
  - Indicated for the treatment of bacterial conjunctivitis caused by susceptible strains of organisms.
  - Clinical trials showed that Moxeza™ was superior to its vehicle for both clinical and microbiological outcomes.
  - Cost of Moxeza™ is $85.59 for a 3 mL bottle. In contrast, the cost of a 10 mL bottle of polymyxin B sulfate/trimethoprim ophthalmic solution is $9.66, and 5 mL of ciprofloxacin 0.3% ophthalmic drops is $6.78.

Conclusion and Recommendations

The College of Pharmacy recommends changing the current 3 tiered structure of this PBPA category into 2 tiers, and the placement of Moxeza™ into Tier 2, with the following criteria:

Criteria for a Tier 2 medication:

3. Approved indication/suspected infection by organism not known to be covered by Tier 1 products, or failure of at least TWO Tier 1 products, one of which must be from the fluoroquinolones category.
4. Known contraindication to all indicated Tier 1 medication.
5. Prescription written by optometrists/ophthalmologists, or
6. When used for pre/post-operative prophylaxis.

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

Utilization Details of Ocular Antibiotics: Fiscal Year 2011

BRAND NAME	CLAIMS	UNITS	DAYS	MEMBERS	COST	UNITS/ DAY	CLAIMS/ MEMBER	PER DIEM	PERCENT COST
GENTAMICIN SOL 0.3% OP	9,296	51,928	92,601	7,798	$102,262.53	0.56	1.19	$1.10	12.19%
TOBRAMYCIN SOL 0.3% OP	7,340	38,173	74,473	6,282	$54,295.95	0.51	1.17	$0.73	6.47%
POLYMYXIN B/ SOL TRIMETHP	7,098	71,109	90,959	6,141	$74,653.18	0.78	1.16	$0.82	8.90%
TRIMETHOPRIM SOL POLYMYXN	3,816	38,128	44,612	3,349	$48,260.77	0.85	1.14	$1.08	5.75%
SOD SULFACET SOL 10% OP	3,791	56,664	65,087	3,329	$36,501.52	0.87	1.14	$0.56	4.35%
SULFACET SOD SOL 10% OP	3,125	46,765	30,284	2,771	$45,860.78	1.54	1.13	$1.51	5.47%
NEO/POLY/GRA SOL OP	1,422	14,194	16,732	1,241	$26,383.47	0.85	1.15	$1.58	3.15%
TOBRAMYCIN/ SUS DEXAMETH	913	4,583	10,371	778	$66,733.12	0.44	1.17	$6.43	7.96%
VIGAMOX DRO 0.5%	787	2,462	10,046	571	$65,599.54	0.25	1.38	$6.53	7.82%
CIPROFLOXACN SOL 0.3% OP	278	1,383	3,349	230	$3,028.50	0.41	1.21	$0.90	0.36%
BLEPH-10 SOL 10% OP	249	1,325	1,950	228	$1,893.08	0.68	1.09	$0.97	0.23%
OFLOXACIN DRO 0.3% OP	232	1,420	2,868	190	$2,843.35	0.5	1.22	$0.99	0.34%
AZASITE SOL 1%	144	447	2,432	116	$14,536.50	0.18	1.24	$5.98	1.73%
ZYMAR DRO 0.3%	115	575	1,680	102	$8,723.64	0.34	1.13	$5.19	1.04%
ZYLET SUS 0.5-0.3%	94	455	1,213	83	$9,698.67	0.38	1.13	$8.00	1.16%
ZYMAXID SOL 0.5%	83	208	1,082	63	$6,291.16	0.19	1.32	$5.81	0.75%
TOBRADEX SUS OP	65	318	665	52	$6,031.51	0.48	1.25	$9.07	0.72%
BESIVANCE SUS 0.6%	58	290	951	43	$4,429.36	0.3	1.35	$4.66	0.53%
GENTAK SOL 0.3% OP	48	264	780	38	$521.26	0.34	1.26	$0.67	0.06%
AK-TOB SOL 0.3% OP	27	135	199	27	$311.06	0.68	1	$1.56	0.04%
BLEPHAMIDE SUS OP	17	105	208	15	$1,166.09	0.5	1.13	$5.61	0.14%
PRED-G SUS OP	15	75	129	12	$452.39	0.58	1.25	$3.51	0.05%
TOBRADEX ST SUS OP	11	60	130	10	$1,183.04	0.46	1.1	$9.10	0.14%
QUIXIN SOL 0.5%	8	40	151	3	$588.62	0.26	2.67	$3.90	0.07%
SULF/PRED NA SOL OP	6	40	52	4	$103.09	0.77	1.5	$1.98	0.01%
MOXEZA SOL 0.5%	2	6	30	2	$166.00	0.2	1	$5.53	0.02%
NEOSPORIN SOL OP	1	10	10	1	$18.91	1	1	$1.89	0.00%
ERYTHROMYCIN OIN OP	8,737	31,719	69,655	7,603	$148,684.28	0.46	1.15	$2.13	17.73%
GENTAK OIN 0.3% OP	958	3,395	7,424	854	$17,916.44	0.46	1.12	$2.41	2.14%
BACIT/POLYMY OIN OP	532	1,869	4,527	417	$9,338.14	0.41	1.28	$2.06	1.11%
TOBREX OIN 0.3% OP	333	1,209	2,693	303	$25,121.27	0.45	1.1	$9.33	3.00%
BACITRACIN OIN OP	278	1,050	2,687	234	$14,819.11	0.39	1.19	$5.52	1.77%
TOBRADEX OIN OP	218	767	1,923	177	$26,291.02	0.4	1.23	$13.67	3.13%
NEO/BAC/POLY OIN OP	158	585	1,398	137	$6,510.43	0.42	1.15	$4.66	0.78%

BRAND NAME	CLAIMS	UNITS	DAYS	MEMBERS	COST	UNITS/ DAY	CLAIMS/ MEMBER	PER DIEM	PERCENT COST
AK-POLY-BAC OIN OP	85	297	581	68	$1,516.04	0.51	1.25	$2.61	0.18%
CILOXAN OIN 0.3% OP	41	224	407	15	$5,557.82	0.55	2.73	$13.66	0.66%
GENTAMICIN OIN 0.3% OP	7	25	51	7	$130.09	0.48	1	$2.55	0.02%
BAC/NEO/POLY OIN OP	4	14	27	4	$30.28	0.52	1	$1.12	0.00%
BLEPHAMIDE OIN S.O.P.	3	14	96	3	$230.40	0.15	1	$2.40	0.03%
ILOTYCIN OIN OP	1	4	10	1	$47.77	0.35	1	$4.78	0.01%
NEOCIDIN OIN OP	1	4	6	1	$19.61	0.67	1	$3.27	0.00%
GARAMYCIN OIN 0.3% OP	1	4	10	1	$18.93	0.35	1	$1.89	0.00%
TOTALS:	50,398	372,342	544,539	39,489*	$838,768.72	0.68	1.28	$1.54	100.00%

*Total unduplicated number of members

Product Details of Moxeza™ (moxifloxacin hydrochloride ophthalmic solution)

Alcon Laboratories, Inc.

INDICATIONS:

- Treatment of bacterial conjunctivitis caused by susceptible strains of the following organisms: Aerococcus viridans*, Corynebacterium macginleyi*, Enterococcus faecalis*, Micrococcus luteus*, Staphylococcus arlettae*, Staphylococcus aureus, Staphylococcus capitis, Staphylococcus epidermidis, Staphylococcus haemolyticus, Staphylococcus hominis, Staphylococcus saprophyticus*, Staphylococcus warneri*, Streptococcus mitis*, Streptococcus pneumoniae, Streptococcus parasanguinis*, Escherichia coli*, Haemophilus influenzae, Klebsiella pneumoniae*, Propionibacterium acnes, Chlamydia trachomatis*
  *Efficacy for this organism was studied in fewer than 10 infections.

DOSAGE FORMS: 4 mL bottle filled with 3 mL sterile ophthalmic solution of moxifloxacin hydrochloride, 0.5% as base.

DOSING & ADMINISTRATION:

- Instill 1 drop in the affected eye(s) 2 times daily for 7 days.

CONTRAINDICATIONS:

- None.

SPECIAL POPULATIONS:

- Pregnancy Category C: Based on animal data, may cause fetal harm.
- Nursing Mothers: Caution should be exercised when administered to a nursing woman.
- Pediatric Use: The safety and effectiveness in infants below 4 months of age has not been established.

- Geriatric Use: No overall differences in safety and effectiveness have been observed between elderly and younger patients.

WARNINGS & PRECAUTIONS:

- Topical ophthalmic use only
  - NOT FOR INJECTION, for topical use only and should not be injected subconjunctivally or introduced directly into the anterior chamber of the eye.
- Hypersensitivity reactions
  - In patients receiving systemically administered quinolones, including moxifloxacin, serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported, some following the first dose.
- Growth of resistant organisms with prolonged use
  - As with other anti-infectives, prolonged use may result in overgrowth of non-susceptible organisms, including fungi. If superinfection occurs, discontinue use and institute alternative therapy. Whenever clinical judgment dictates, the patient should be examined with the aid of magnification, such as slit-lamp biomicroscopy, and, where appropriate, fluorescein staining.
- Avoidance of contact lens wear
  - Patients should be advised not to wear contact lenses if they have signs or symptoms of bacterial conjunctivitis.

ADVERSE REACTIONS (Events Reported in 1-2% of Patients Treated)

- Eye irritation
- Pyrexia
- Conjunctivitis

DRUG INTERACTIONS:

- None reported.

INFORMATION FOR PATIENTS:

- Advise patients not to touch the dropper tip to any surface to avoid contaminating the contents.
- Advise patients not to wear contact lenses if they have signs and symptoms of bacterial conjunctivitis.
- Systematically administered quinolones, including moxifloxacin, have been associated with hypersensitivity reactions, even following a single dose. Patients should be told to discontinue use immediately and contact their physician at the first sign of a rash or allergic reaction.

References:

Moxeza™ Label Information. Alcon Laboratories, Inc. Available online at: http://ecatalog.alcon.com/PI/Moxeza_us_en.pdf Last revised 2010.

Appendix H

Fiscal Year 2011 Annual Review of Antihypertensives
30 Day Notice to Prior Authorize Amturnide® (aliskiren/amlodipine besylate/HCTZ) and Edarbi® (azilsartan medoxomil)

Oklahoma HealthCare Authority
October 2011

Current Prior Authorization Criteria

There are 7 categories of antihypertensive medications currently included in the Product Based Prior Authorization program, as well as two specialty products:

1. Calcium Channel Blockers (**CCBs**)
2. Angiotensin I Converting Enzyme Inhibitors (**ACEIs**)
3. **ACE/CCBs** Combination Products
4. ACE inhibitor and hydrochlorothiazide combination products (**ACEI/HCTZs**)
5. Angiotensin II Receptor Blockers (**ARBs**)
6. ARB combination products (**ARB Combinations**)
7. Direct Renin Inhibitors (**DRIs**) and DRI Combination products
8. Clonidine extended release products (Nexiclon® XR) and clonidine transdermal patches (Catapres TTS®)

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

1. documented inadequate response to two Tier 1 medications, (trials must include medication from all available classes where applicable), or
1. adverse drug reaction to all Tier 1 class of medications, or
2. previous stabilization on the Tier 2 medication, or
3. a unique indication for which the Tier 1 antihypertensives lack

To qualify for a Tier 3 antihypertensive medication there must be

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

Criteria for DRIs Authorization

1. FDA approved indication.
2. Recent trial, within the previous 6 months and at least 4 weeks in duration, of an ACE Inhibitor (or an ARB if previous trial of an ACEI) and a diuretic, used concomitantly at recommended doses, that did not yield adequate blood pressure control.
3. May be used in either monotherapy or combination therapy.

Criteria for Authorization of clonidine special formulations

Prior Authorization of **Nexiclon XR® (clonidine extended release) and Catapres TTS® Patch** (clonidine) with the following criteria:

a. FDA-approved indication of hypertension in adults.
b. Must provide a clinically significant reason why the member cannot take clonidine immediate release tablets.

Calcium Channel Blockers (CCB medications)		
Tier-1	**Tier-2**	**Tier-3**
amlodipine (Norvasc®)	diltiazem (Cardizem® LA)	
diltiazem (Cardizem®)	nicardipine (Cardene® SR)	
diltiazem (Tiazac®, Taztia XT®)	verapamil (Covera-HS®)	
diltiazem CD (Cardizem® CD)	nisoldipine (Sular®)	
diltiazem ER (Cartia XT®, Diltia XT®)	amlodipine/atorvastatin (Caduet®)	
diltiazem SR (Cardizem® SR)		
diltiazem XR (Dilacor® XR)		
felodipine (Plendil®)		
isradipine (Dynacirc®, Dynacirc CR®)		
nicardipine (Cardene®)		
nifedipine (Adalat®, Procardia®)		
nifedipine CC (Adalat® CC)		
nifedipine ER		
nifedipine XL (Nifedical XL®, Procardia XL®)		
nimodipine (Nimotop®)		
verapamil (Calan®, Isoptin®, Verelan®)		
verapamil SR		

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

Angiotensin Converting Enzyme Inhibitors (ACE Inhibitors)		
Tier-1	**Tier-2**	**Tier-3**
benazepril (Lotensin®)		perindopril erbumine (Aceon®)
captopril (Capoten®)		
enalapril (Vasotec®)		
enalaprilat (Vasotec® IV)		
fosinopril (Monopril®)		
lisinopril (Prinivil®, Zestril®)		
moexipril (Univasc®)		
quinapril (Accupril®)		
trandolapril (Mavik®)		
ramipril (Altace®)		
ACE Inhibitor / Calcium Channel Blocker Combinations		
Tier-1 ACE + Tier 1 CCB	trandolapril / verapamil (Tarka®)	
	benazepril / amlodipine (Lotrel®)	
	enalapril / felodipine (Lexxel®)	
ACE Inhibitor / HCTZ Combinations		
benazepril/HCTZ (Lotensin® HCT)		
captopril/HCTZ (Capozide®)		
enalapril/HCTZ (Vasoretic®)		
fosinopril/HCTZ (Monopril-HCT®)		
lisinopril/HCTZ (Prinzide®,Zestoretic®)		
moexipril/HCTZ (Uniretic®)		

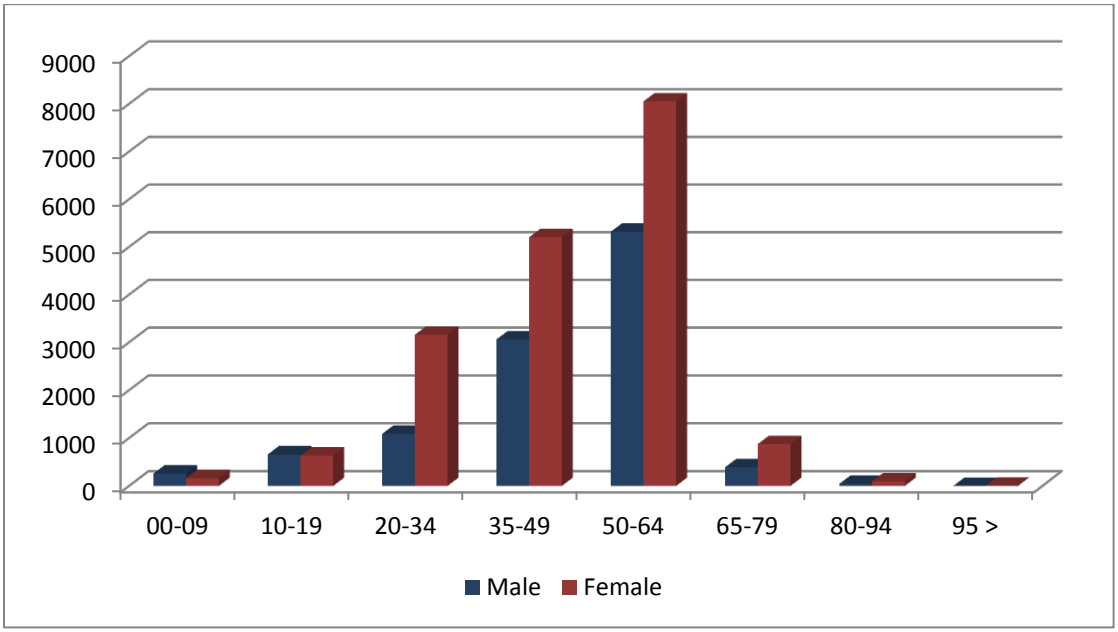
Direct Renin inhibitors		
Tier-1	**Tier-2**	**Tier-3**
Tier-1 ACE Inhibitor + Diuretic	ARB + Diuretic	Aliskiren (Tekturna®)
		Aliskiren/HCTZ (Tekturna HCT®)
		Aliskiren/valsartan (Valturna®)
		Aliskiren/amlodipine (Tekamlo®)

Utilization of Antihypertensives

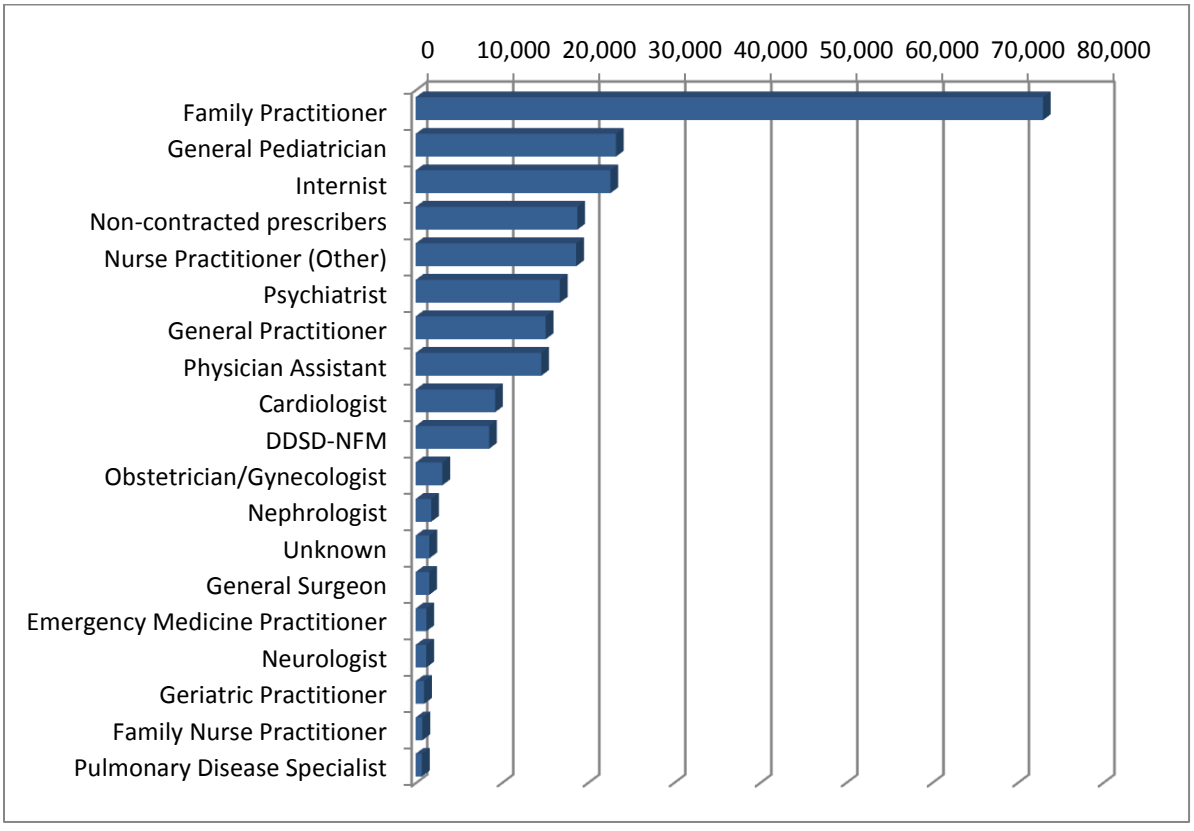
Comparison of Fiscal Years

Fiscal Year	Members	Claims	Cost	Cost/Claim	Perdiem	Units	Days
2010	26,112	130,247	$3,373,162.64	$25.90	$0.67	6,587,291	5,021,208
2011	29,030	147,376	$3,256,825.19	$22.10	$0.57	7,365,496	5,736,939
Percent Change	11.2%	13.2%	-3.4%	-14.7%	-14.9%	11.8%	14.3%
Change	2,918	17,129	-$116,337.45	-$3.80	-$0.10	778,205	715,731

Demographics of Members Utilizing Antihypertensives for FY 2011



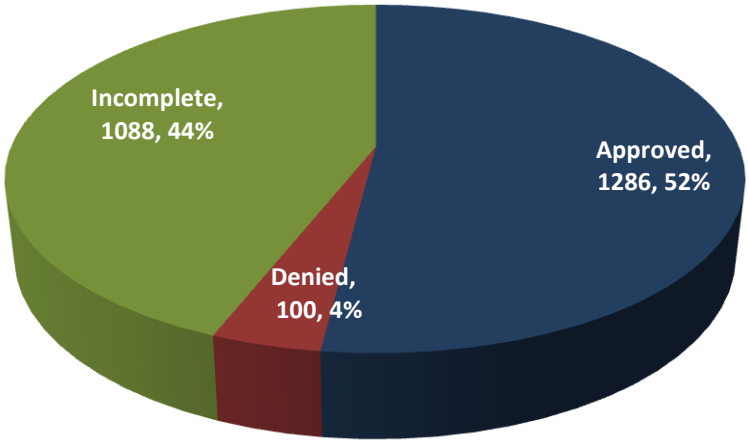
Top 20 Prescribers of Antihypertensives by Number of Claims for FY 2011



Prior Authorization of Antihypertensives

There were a total of 2,474 petitions submitted for this category during fiscal year 2011. Computer edits are in place to detect tier-1 medications in member's recent claims history and generate automated prior authorization where possible. The following chart shows the status of the submitted petitions.

Status of Petitions for Antihypertensives: FY 2011



Market News and Update

- **Amturnide®** (aliskiren / amlodipine besylate / hydrochlorothiazide) was approved in December 2010.
  - Available as 150 mg/5 mg/12.5 mg, 300 mg/5 mg/12.5 mg, 300 mg/5 mg/25 mg, 300 mg/10 mg/12.5 mg, and 300 mg/10 mg/25 mg tablets.
  - Cost of therapy is approximately $82-$103 per 30 tablets depending on the dose.

- **Edarbi™** (azilsartan medoxomil) was approved in February 2011.
  - Available as 40 mg and 80 mg tablets.
  - Cost of therapy is $82 per 30 tablets, regardless of dose.

- **New generic approvals**:
  - Matzim™ LA from Watson Laboratories, Inc., the AB rated generic of Cardizem LA was approved in March 2011. It is now available as multi-source product and has a State Maximum Allowable Cost (SMAC) designation.
  - Mylan Pharmaceuticals launched nisoldipine extended release, the generic version of Shinogi Pharma's Sular® in January 2011.
  - Ranbaxy is expected to bring out a generic of Caduet (amlodipine/atorvastatin) in November 2011. Pfizer and Ranbaxy entered into a settlement agreement restricting Ranbaxy from bringing their product to market prior to that date. The first patent for Caduet expired in March 2010.

- **Patent Expirations**
  - Irbesartan September 2011
  - Valsartan March 2012
  - Candesartan June 2012
  - Telmistartan January 2014
  - Eprosartan August 2014
  - Olmesartan April 2016

Conclusion and Recommendations

The College of Pharmacy recommends the following changes to the Antihypertensives PBPA category:

1. Placement of Amturnide® (aliskirin/amlodipine/HCTZ) in Tier 3 of the DRI category.
2. Placement of Edarbi™ (azilsartan) into Tier 3 of the ARB category.
3. As ARB patents expire, move generic ARB's to Tier 1 once exclusivity lapses and SMAC is applied.

ARBs (Angiotensin Receptor Blockers) and ARB Combination Products		
Tier-1	**Tier-2**	**Tier-3**
ACE Inhibitor:	amlodopine / valsartan (Exforge®)	candesartan (Atacand®)
benazepril (Lotensin®)	amlodopine / valsartan (Exforge® HCT)	candesartan / HCTZ (Atacand® HCT)
captopril (Capoten®)	amlodipine / olmesartan (Azor™)	eprosartan (Teveten®)
enalapril (Vasotec®)	irbesartan (Avapro®)	eprosartan / HCTZ (Teveten® HCT)
enalaprilat (Vasotec® IV)	irbesartan / HCTZ (Avalide®)	telmisartan/amlodipine (Twynsta)
fosinopril (Monopril®)	valsartan (Diovan®)	telmisartan (Micardis®)
lisinopril (Prinivil®, Zestril®)	valsartan / HCTZ (Diovan HCT®)	telmisartan / HCTZ (Micardis® HCT)
moexipril (Univasc®)	olmesartan (Benicar®)	olmesarten/amlodipine/HCTZ (Tribenzor®)
quinapril (Accupril®)	olmesartan / HCTZ (Benicar HCT®)	**azilsartan (Edarbi™)**
trandolapril (Mavik®)		
ramipril (Altace®)		
ARBs:		
losartan (Cozaar®)		
losartan / HCTZ (Hyzaar®)		

Direct Renin inhibitors (Tekturna®)		
Tier-1	**Tier-2**	**Tier-3**
Tier-1 ACE Inhibitor + Diuretic	ARB + Diuretic	Aliskiren (Tekturna®)
		Aliskiren/HCTZ (Tekturna HCT®)
		Aliskiren/valsartan (Valturna®)
		Aliskiren/amlodipine (Tekamlo®)
		Aliskiren/amlodipine/HCTZ (Amturnide™)

Utilization Details of Antihypertensives for Fiscal Year 2011

BRAND NAME	CLAIMS	UNITS	DAYS	MEMBERS	PAID	UNITS / DAY	CLAIMS / CLIENT	PER DIEM	PERCENT PAID
CALCIUM CHANNEL BLOCKERS	39,617	1,742,797	1,486,888	9,707	$925,174.32	1.17	4.08	$0.62	29.05%
CCB/ACE INHIBITOR COMBOS	1,455	71,112	63,135	266	$159,049.00	1.13	5.47	$2.52	4.88%
ACE INHIBITORS	73,758	4,149,173	2,886,884	17,673	$522,401.10	1.44	4.17	0.18	16.04%
ACE/HCTZ COMBOS	18,891	874,013	770,817	5074	$148,056.44	1.13	3.72	$0.19	4.63%
ARB/ ARB COMBOS	11,496	473,761	454,572	2,423	$1,181,047.40	1.04	4.74	$2.60	36.86%
DIRECT RENIN INHIBITORS	246	11,917	11,717	63	$37,762.03	1.02	3.9	$3.22	1.16%
CLONIDINE EXTENDED RELEASE PRODUCTS	1,207	5,030	34,787	290	$240,731.06	0.14	4.13	$6.92	7.37%
CATEGORY TOTALS	147,376	7,365,496	5,736,939	29,030*	$3,256,825.19	1.28	5.08	$0.57	100%

Total unduplicated number of members

PRODUCT DETAILS OF AMTURNIDE™ (ALISKIREN, AMLODIPINE, HCTZ)[i]

INDICATIONS:
Amturnide™ is a combination of a direct renin inhibitor, a dihydropyridine calcium channel blocker, and a thiazide diuretic indicated for the treatment of hypertension. Amturnide® is not indicated for initial therapy.

WARNING: AVOID USE IN PREGNANCY
When pregnancy is detected, discontinue Edarbi as soon as possible. Drugs that act directly on the renin-angiotensin system can cause injury and death to the developing fetus *[see Warnings and Precautions]*

DOSAGE FORMS: Tablets of aliskiren/amlodipine/hydrochlorothiazide:

- 150/5/12.5 mg
- 300/5/12.5 mg
- 300/5/25 mg
- 300/10/12.5 mg
- 300/10/25 mg

ADMINISTRATION:

- Amturnide™ may be substituted for its individually titrated components for patients on aliskiren, amlodipine, and hydrochlorothiazide.
- Amturnide may be used as add-on/switch therapy for patients not adequately controlled on any two of the following: aliskiren, dihydropyridine calcium channel blockers, and thiazide diuretics.
- Amturnide may be substituted for its individually titrated aliskiren, amlodipine and HCTZ.

CONTRAINDICATIONS: Anuria; Hypersensitivity to sulfonamide-derived drugs

SPECIAL POPULATIONS:

- **Pregnancy Category D**: Avoid use in pregnancy.
- Nursing mothers: Avoid use while nursing; discontinue either nursing or the drug.
- Geriatric patients: No overall differences in the efficacy or safety of Amturnide® were observed in this patient population, but greater sensitivity of some older individuals cannot be ruled out.

WARNINGS & PRECAUTIONS:

- Avoid fetal or neonatal exposure
- Head and neck angioedema: Discontinue Amturnide.
- Hypotension in volume- or salt-depleted patients with treatment initiation may occur: Correct volume-depletion prior to administration
- Increased angina or myocardial infarction with calcium channel blockers may occur upon dosage initiation or increase in amlodipine
- Avoid in patients with severely impaired renal function (creatinine clearance ≤30 mL/min)
- Uptitrate HCTZ slowly: in patients with renal disease, thiazides may precipitate azotemia. Cumulative effects of the drug may develop in patients with impaired renal function.
- Titrate gradually in patients with hepatic impairment
- Thiazide diuretics may cause an exacerbation or activation of systemic lupus erythematosus
- Acute myopia and secondary angle closure glaucoma: Discontinue HCTZ

ADVERSE REACTIONS (reported in ≥ 2% of patients treated):

- Dizziness
- Peripheral edema
- Headache
- Nasopharyngitis

DRUG INTERACTIONS:

- **Aliskiren**
  - Cyclosporine: Avoid concomitant use
  - Itraconazole: Avoid concomitant use
- **HCTZ**
  - Alcohol, barbiturates, narcotics: Potentiation of orthostatic hypotension.
  - Anti-diabetic drugs: Dosage adjustment of antidiabetic may be required.
  - Cholestyramine and colestipol: Reduced absorption of thiazides.
  - Corticosteroids, ACTH: Electrolyte depletion, hypokalemia.
  - Lithium: Reduced renal clearance and high risk of lithium toxicity when used with diuretics. Should not be given with diuretics.
  - NSAIDs: Can reduce the diuretic, natriuretic, and antihypertensive effects of diuretics.

PRODUCT DETAILS OF EDARBI™ (AZILSARTAN MEDOXOMIL)[ii]

INDICATIONS:
Edarbi™ is an angiotensin II receptor blocker indicated for the treatment of hypertension, to lower blood pressure. Lowering blood pressure reduces the risk of fatal and nonfatal cardiovascular events, primarily strokes and myocardial infarctions. Edarbi™ may be used, either alone or in combination with other antihypertensive agents.

WARNING: AVOID USE IN PREGNANCY
When pregnancy is detected, discontinue Edarbi as soon as possible. Drugs that act directly on the renin-angiotensin system can cause injury and death to the developing fetus *[see Warnings and Precautions]*.

DOSAGE FORMS: 40 mg and 80 mg tablets

ADMINISTRATION:
The recommended dose in adults is 80 mg taken once daily. Consider a starting dose of 40 mg for patients who are treated with high doses of diuretics. Edarbi™ may be administered with or without food. Edarbi™ may be administered with other antihypertensive agents.

CONTRAINDICATIONS: None listed.

SPECIAL POPULATIONS:
- **Pregnancy Category C (first trimester) and D (second and third trimesters):** The use of drugs that act directly on the renin-angiotensin-aldosterone system during the second and third trimesters of pregnancy can cause fetal and neonatal morbidity and death.
- **Nursing Mothers:** Discontinue drug or nursing.
- **Pediatric:** Safety and effectiveness of Edarbi™ in pediatric patients have not been established.
- **Geriatric:** Abnormally high serum creatinine values were more likely to be reported for patients age 75 or older. No overall difference in efficacy versus younger patients, but greater sensitivity of some older individuals cannot be ruled out. In patients with an activated renin-angiotensin system, as by volume- or salt-depletion, renin-angiotensin-aldosterone system (RAAS) blockers such as azilsartan medoxomil can cause excessive hypotension. In susceptible patients, e.g., with renal artery stenosis, RAAS blockers can cause renal failure.

WARNINGS & PRECAUTIONS:
- Avoid fetal and neonatal exposure.
- Correct volume or salt depletion prior to administration of Edarbi.
- Monitor for worsening renal function in patients with renal impairment.

ADVERSE REACTIONS (reported in ≥ 2% of patients treated): diarrhea

DRUG INTERACTIONS: Non-Steroidal Anti-inflammatory Agents including Selective Cyclooxygenase-2 Inhibitors (COX-2 Inhibitors: Monitor renal function periodically in patients receiving azilsartan and NSAID therapy

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[i] . **Amturnide® Label Information. Novartis Pharmaceuticals Corporation**. Available online at: hhttp://www.amturnide.com/info/full_prescribing_info.jsp. Last revised April 2011

[ii] . **Edarbi™ Label Information. Takeda Pharmaceuticals Company**. Available online at: http://edarbi.com/ Last revised April 2011.

Appendix I

Fiscal Year 2011 Annual Review of Antidepressants PBPA Category and 30 Day Notice to Prior Authorize Viibryd® (vilazodone)

Oklahoma Health Care Authority
October 2011

Prior Authorization of Antidepressants

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.

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

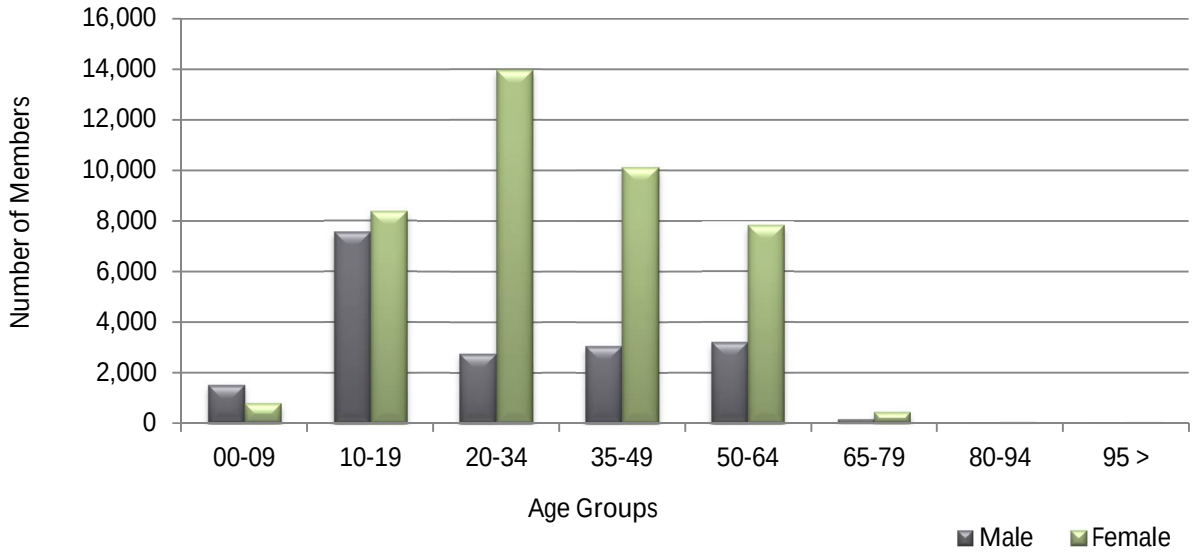
Mandatory generic plan applies
Tiers based on FY2011 Supplemental Rebate participation

Utilization of Antidepressant Medications

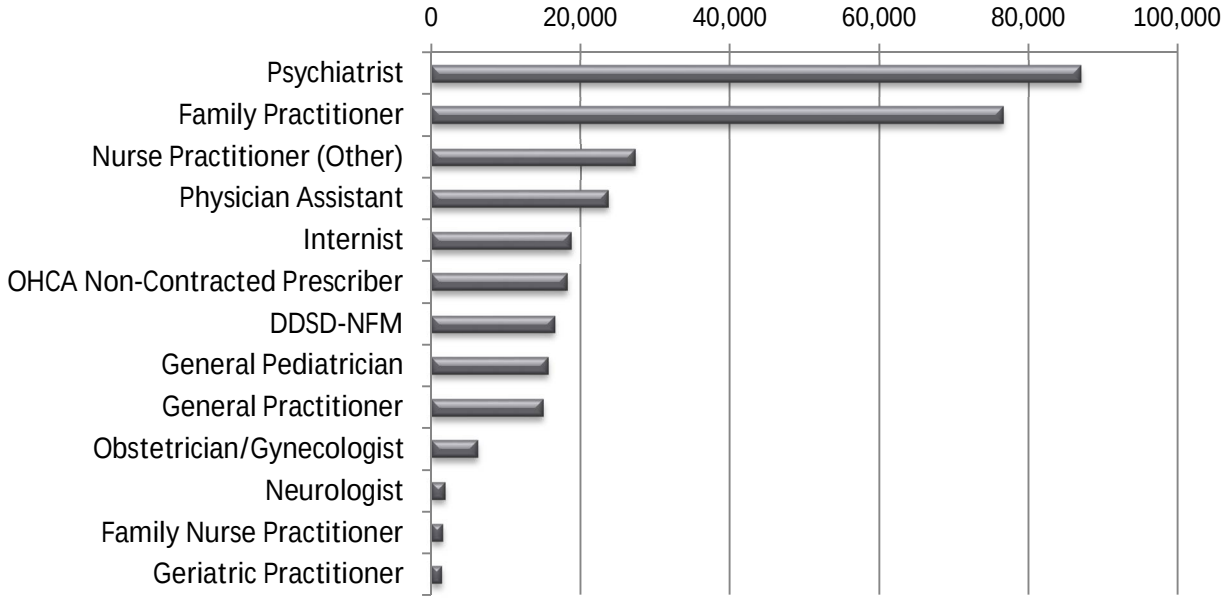
Fiscal Year Comparison

Fiscal Year	Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2010	54,018	271,660	$8,168,152.71	$30.07	$0.91	10,735,147	8,935,035
2011	59,811	316,365	$8,250,089.89	$26.08	$0.80	12,467,706	10,335,913
% Change	10.70%	16.50%	1.00%	-13.30%	-12.10%	16.10%	15.70%
Change	5,793	44,705	$81,937.18	-$3.99	-$0.11	1,732,559	1,400,878

Demographics of Members: FY 2011



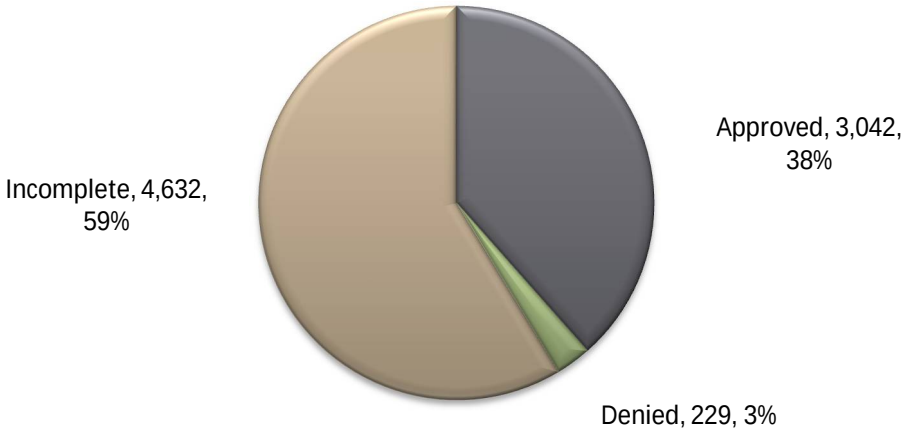
Top Prescriber Specialties: FY 2011



Prior Authorization of Antidepressant Medications

There were a total of 7,903 petitions submitted for this category during fiscal year 2011. Computer edits are in place to detect tier-1 medications in member's recent claims history and generate automated prior authorization where possible. The following chart shows the status of the submitted petitions.

Status of Petitions for Antidepressant Medications: FY 2011



Market News and Update

Anticipated Patent Expirations:

- Lexapro® – 2012
- Cymbalta® – 2013

Vilazodone is a novel dual-acting treatment for major depressive disorder that combines serotonin reuptake inhibition with a partial 5-hydroxytryptamine1A receptor agonist. It was marketed by Forrest Labs, Inc. towards the end of 2nd quarter of 2011 under the trade name Viibryd®. The recommended dose for Viibryd® is 40mg once daily. Initiation requires titration up to the recommended dose, and discontinuation requires gradual dose reduction. Viibryd® has similar black box warning regarding suicidality risks associated with all antidepressants. The efficacy of Viibryd® was established in two 8-week, placebo-controlled trials in adult patients with MDD. Although Viibryd® has a novel dual mechanism of action, its advantage has yet to be demonstrated by head to head trials with existing agents used in the treatment of depression.

Recommendation

The College of Pharmacy recommends the addition of Viibryd® (vilazodone) to Tier 3 of the antidepressants Product Based Prior Authorization Category. The existing criteria will apply.

Utilization Details of Antidepressant Medications

MEDICATION	CLAIMS	MEMBERS	COST	UNITS/ DAY	CLAIMS/ MEMBER	PERDIEM	% COST
CITALOPRAM TAB 10MG	7,387	2,742	$46,045.53	1.02	2.69	$0.20	0.56%
CITALOPRAM TAB 20MG	33,459	12,221	$213,621.99	1.09	2.74	$0.19	2.59%
CELEXA TAB 20MG	1	1	$3.37	1.00	1.00	$0.11	0.00%
CITALOPRAM TAB 40MG	23,032	6,542	$150,782.71	1.08	3.52	$0.19	1.83%
CITALOPRAM SOL 10MG/5ML	89	25	$4,524.20	8.22	3.56	$1.82	0.05%
Subtotals	63,968		$414,977.80	1.09	2.70	$0.20	5.03%
SERTRALINE TAB 25MG	6,839	2,306	$52,040.01	1.04	2.97	$0.25	0.63%
SERTRALINE TAB 50MG	22,202	7,942	$176,743.78	1.06	2.80	$0.24	2.14%
SERTRALINE TAB 100MG	25,187	6,197	$225,659.62	1.29	4.06	$0.27	2.74%
ZOLOFT TAB 100MG	25	3	$4,095.35	1.44	8.33	$5.46	0.05%
SERTRALINE CON 20MG/ML	244	61	$11,420.05	3.00	4.00	$1.61	0.14%
Subtotals	54,497		$469,958.81	1.17	4.43	$0.26	5.70%
TRAZODONE TAB 50MG	22,872	7,271	$149,153.39	1.25	3.15	$0.21	1.81%
TRAZODONE TAB 100MG	18,806	5,548	$139,158.04	1.36	3.39	$0.23	1.69%
TRAZODONE TAB 150MG	10,942	3,206	$99,992.68	1.29	3.41	$0.28	1.21%
TRAZODONE TAB 300MG	524	155	$59,630.40	0.98	3.38	$3.15	0.72%
Subtotals	53,144		$447,934.51	1.30	3.33	$0.27	5.43%
FLUOXETINE CAP 10MG	7,706	2,573	$54,602.67	1.18	2.99	$0.23	0.66%
FLUOXETINE CAP 20MG	27,835	8,327	$230,144.54	1.41	3.34	$0.25	2.79%
PROZAC CAP 20MG	30	4	$14,210.61	2.21	7.50	$13.93	0.17%
FLUOXETINE CAP 40MG	7,601	2,298	$120,234.84	1.02	3.31	$0.45	1.46%
FLUOXETINE TAB 10MG	1,629	653	$12,053.71	1.03	2.49	$0.24	0.15%
FLUOXETINE TAB 20MG	460	206	$10,181.56	1.14	2.23	$0.68	0.12%
FLUOXETINE SOL 20MG/5ML	884	177	$11,427.94	3.66	4.99	$0.44	0.14%
FLUOXETINE CAP 90MG DR	53	7	$5,044.11	0.14	7.57	$3.30	0.06%
PROZAC WEEKL CAP 90MG	24	6	$3,108.63	0.14	4.00	$4.60	0.04%
Subtotals	46,222		$461,008.61	1.32	4.27	$0.31	5.59%
BUPROPION TAB 75MG	1,196	396	$17,881.93	1.63	3.02	$0.48	0.22%
BUPROPION TAB 100MG	1,531	563	$26,204.75	1.91	2.72	$0.55	0.32%
BUPROPION TAB 100MG SR	1,347	518	$38,163.18	1.45	2.60	$0.92	0.46%
BUDEPRION TAB 100MG SR	85	35	$2,665.33	1.60	2.43	$1.03	0.03%
BUPROPION TAB 100MG ER	10	6	$307.18	1.60	1.67	$1.02	0.00%
BUPROPION TAB 150MG SR	7,739	2,596	$234,930.05	1.69	2.98	$0.97	2.85%
BUDEPRION TAB 150MG SR	240	94	$7,333.78	1.71	2.55	$0.99	0.09%
WELLBUTRIN TAB 150MG SR	3	1	$632.58	2.00	3.00	$7.03	0.01%
BUPROPION TAB 200MG SR	671	173	$29,655.27	1.63	3.88	$1.37	0.36%
WELLBUTRIN TAB 200MG SR	2	1	$396.66	1.00	2.00	$6.61	0.00%
BUPROPION TAB 200MG ER	2	2	$102.94	2.00	1.00	$1.72	0.00%
BUPROPN HCL TAB 150MG XL	4,291	1,730	$142,711.02	1.02	2.48	$1.02	1.73%
BUDEPRION XL TAB 150MG	701	275	$22,115.98	1.03	2.55	$0.96	0.27%
WELLBUTRIN TAB XL 150MG	5	1	$2,959.70	3.00	5.00	$19.73	0.04%
BUPROPN HCL TAB 300MG XL	4,656	1,195	$163,856.20	1.00	3.90	$1.03	1.99%
BUDEPRION XL TAB 300MG	909	217	$32,565.93	1.00	4.19	$1.05	0.39%
WELLBUTRIN TAB XL 300MG	15	4	$5,038.64	1.05	3.75	$8.66	0.06%
APLENZIN TAB 348MG	2	1	$389.44	1.00	2.00	$6.49	0.00%
APLENZIN TAB 522MG	3	1	$1,307.88	1.00	3.00	$14.53	0.02%
Subtotals	23,408		$729,218.44	1.37	2.88	$0.96	8.84%
PAROXETINE TAB 10MG	2,146	826	$20,427.47	0.99	2.60	$0.29	0.25%
PAXIL TAB 10MG	2	1	$218.62	1.00	2.00	$3.64	0.00%
PAROXETINE TAB 20MG	7,736	2,975	$65,986.36	1.00	2.60	$0.25	0.80%
PAXIL TAB 20MG	7	2	$1,335.54	1.58	3.50	$5.94	0.02%
PAROXETINE TAB 30MG	1,795	427	$23,046.33	1.19	4.20	$0.39	0.28%
PAXIL TAB 30MG	14	2	$3,245.64	2.00	7.00	$7.73	0.04%
PAROXETINE TAB 40MG	5,005	1,327	$59,743.47	1.05	3.77	$0.34	0.72%
PAXIL TAB 40MG	4	2	$1,251.28	1.00	2.00	$4.04	0.02%

PAXIL SUS 10MG/5ML	6	2	$1,150.32	8.33	3.00	$6.39	0.01%
PAROXETINE SUS 10MG/5ML	1	1	$87.48	5.00	1.00	$2.92	0.00%
PAROXETIN ER TAB 12.5MG	261	93	$26,863.09	1.00	2.81	$3.06	0.33%
PAXIL CR TAB 12.5MG	24	9	$3,554.10	1.00	2.67	$3.70	0.04%
PAROXETINE TAB 25MG ER	814	170	$98,007.44	1.09	4.79	$3.50	1.19%
PAXIL CR TAB 25MG	10	3	$1,162.82	1.00	3.33	$3.88	0.01%
PAROXETIN ER TAB 37.5MG	368	90	$44,000.30	1.02	4.09	$3.44	0.53%
PAXIL CR TAB 37.5MG	21	7	$2,468.03	1.00	3.00	$3.99	0.03%
PEXEVA TAB 10MG	3	1	$445.70	1.00	3.00	$4.95	0.01%
PEXEVA TAB 20MG	32	10	$6,461.00	1.00	3.20	$5.39	0.08%
PEXEVA TAB 40MG	19	5	$3,224.14	1.00	3.80	$5.66	0.04%
Subtotals	18,268		$362,679.13	1.04	3.28	$0.58	4.40%
MIRTAZAPINE TAB 7.5MG	66	29	$534.38	1.00	2.28	$0.27	0.01%
MIRTAZAPINE TAB 15MG	7,027	2,273	$69,737.53	0.93	3.09	$0.31	0.85%
MIRTAZAPINE TAB 30MG	5,585	1,596	$64,323.76	1.00	3.50	$0.35	0.78%
MIRTAZAPINE TAB 45MG	1,908	471	$27,032.76	1.02	4.05	$0.42	0.33%
MIRTAZAPINE TAB 15MG ODT	187	70	$5,787.64	0.96	2.67	$0.95	0.07%
MIRTAZAPINE TAB 30MG ODT	184	57	$6,602.67	1.04	3.23	$1.00	0.08%
MIRTAZAPINE TAB 45MG ODT	40	17	$2,027.89	1.00	2.35	$1.12	0.02%
Subtotals	14,997		$176,046.63	0.99	3.02	$0.36	2.14%
VENLAFAXINE TAB 25MG	133	68	$3,970.12	1.93	1.96	$1.00	0.05%
VENLAFAXINE TAB 37.5MG	1,639	746	$40,862.91	1.78	2.20	$0.83	0.50%
VENLAFAXINE TAB 50MG	328	131	$8,513.77	1.77	2.50	$0.84	0.10%
VENLAFAXINE TAB 75MG	4,448	1,423	$205,974.35	1.88	3.13	$1.49	2.50%
VENLAFAXINE TAB 100MG	737	238	$32,921.16	2.13	3.10	$1.48	0.40%
VENLAFAXINE CAP 37.5MG	153	77	$14,138.77	1.04	1.99	$3.13	0.17%
EFFEXOR XR CAP 37.5MG	44	16	$6,772.25	1.00	2.75	$4.23	0.08%
VENLAFAXINE CAP 75MG ER	1,277	383	$162,056.95	1.03	3.33	$3.63	1.96%
EFFEXOR XR CAP 75MG	179	87	$34,253.20	1.03	2.06	$4.73	0.42%
VENLAFAXINE CAP 150MG ER	3,136	702	$555,465.65	1.28	4.47	$5.18	6.73%
EFFEXOR XR CAP 150MG	526	233	$121,168.19	1.26	2.26	$6.28	1.47%
VENLAFAXINE TAB 37.5 ER	125	54	$10,858.97	0.96	2.31	$3.09	0.13%
VENLAFAXINE TAB 75MG ER	496	174	$59,969.56	1.00	2.85	$3.61	0.73%
VENLAFAXINE TAB 150MG ER	1,030	281	$164,912.05	1.21	3.67	$4.76	2.00%
VENLAFAXINE TAB 225MG ER	549	122	$146,898.76	1.02	4.50	$7.54	1.78%
Subtotals	14,800		$1,568,736.66	1.50	2.87	$3.25	19.02%
LEXAPRO TAB 5MG	161	37	$16,591.99	1.05	4.35	$3.31	0.20%
LEXAPRO TAB 10MG	5,216	1,329	$567,867.99	1.02	3.92	$3.32	6.88%
LEXAPRO TAB 20MG	8,182	1,670	$992,126.43	1.04	4.90	$3.55	12.03%
LEXAPRO 20MG TAB	1	1	$106.57	1.00	1.00	$3.55	0.00%
LEXAPRO SOL 5MG/5ML	32	4	$2,394.10	7.19	8.00	$4.48	0.03%
Subtotals	13,592		$1,579,087.08	1.04	4.43	$3.46	19.14%
CYMBALTA CAP 20MG	356	116	$59,298.16	1.34	3.07	$5.61	0.72%
CYMBALTA CAP 30MG	2,094	723	$423,499.06	1.28	2.90	$6.17	5.13%
CYMBALTA CAP 60MG	7,200	1,634	$1,328,697.88	1.10	4.41	$5.26	16.11%
Subtotals	9,650		$1,811,495.10	1.14	3.46	$5.46	21.96%
FLUVOXAMINE TAB 25MG	191	56	$2,874.37	1.00	3.41	$0.47	0.03%
FLUVOXAMINE TAB 50MG	837	197	$14,579.23	1.25	4.25	$0.58	0.18%
FLUVOXAMINE TAB 100MG	1,561	237	$34,957.98	1.97	6.59	$0.73	0.42%
LUVOX CR CAP 100MG	71	20	$17,405.17	1.52	3.55	$7.58	0.21%
LUVOX CR CAP 150MG	82	19	$21,293.49	1.56	4.32	$8.31	0.26%
Subtotals	2,742		$91,110.24	1.66	4.42	$1.08	1.10%
PRISTIQ TAB 50MG	592	159	$79,812.73	1.00	3.72	$4.10	0.97%
PRISTIQ TAB 100MG	404	106	$55,033.60	1.01	3.81	$4.06	0.67%
Subtotals	996		$134,846.33	1.01	3.77	$4.08	1.64%
NEFAZODONE TAB 50MG	12	1	$507.78	3.00	12.00	$1.41	0.01%
NEFAZODONE TAB 100MG	4	1	$110.56	2.00	4.00	$0.92	0.00%
NEFAZODONE TAB 150MG	21	3	$861.46	2.32	7.00	$1.15	0.01%
NEFAZODONE TAB 200MG	43	6	$1,385.09	1.90	7.17	$0.97	0.02%

Subtotals	80		$2,864.89	2.17	1.11	$1.08	0.04%
VIIBRYD TAB 40MG	1	1	$125.66	1.00	1.00	$4.19	0.00%
Subtotals	1	1	$125.66	1.00	1.00	$4.19	0.00%
TOTAL	316,365	59,811	$8,250,089.89	1.21	5.29	$0.80	100%

*Total number of unduplicated members.

Product Details of Viibryd® (vilazodone hcl) Tablets

FDA-APPROVED 2011

INDICATIONS: Viibryd® is indicated for the treatment of major depressive disorder (MDD).

DOSAGE FORMS: Viibryd® is available as 10 mg, 20 mg and 40 mg tablets.

ADMINISTRATION:

- The recommended dose for Viibryd® is 40 mg once daily.
- Viibryd® should be titrated to the 40 mg dose, starting with an initial dose of 10 mg once daily for 7 days, followed by 20 mg once daily for an additional 7 days, and then increased to 40 mg once daily.
- Viibryd® should be taken with food. Administration without food can result in inadequate drug concentrations and may diminish effectiveness.
- When discontinuing treatment, reduce the dose gradually.

CONTRAINDICATIONS:

Monoamine Oxidase Inhibitors: Do not use Viibryd® concomitantly with an MAOI or within 14 days of stopping or starting an MAOI.

SPECIAL POPULATIONS:

- Pregnancy: There are no controlled human data regarding Viibryd® use during pregnancy. Use only if the potential benefits outweigh the potential risks.
- Nursing Mothers: There are no human data regarding Viibryd® concentrations in breast milk. Women should breast feed only if the potential benefits outweigh the potential risks.
- Pediatric Use: The safety and efficacy of Viibryd® in pediatric patients have not been studied.
- Geriatric Use: No dose adjustment is recommended on the basis of age.
- Hepatic Impairment: No dose adjustment is recommended in patients with mild or moderate hepatic impairment. Viibryd® has not been studied in patients with severe hepatic impairment.
- Renal Impairment: No dose adjustment is recommended in patients with mild, moderate, or severe renal impairment.

WARNINGS & PRECAUTIONS:

- Clinical Worsening/Suicide Risk: Monitor patients for clinical worsening and suicidal thinking or behavior.
- Serotonin Syndrome or Neuroleptic Malignant (NMS) - like Syndrome: Can occur with treatment. Discontinue and initiate supportive treatment.
- Seizures: Can occur with treatment. Use with caution in patients with a seizure disorder.
- Abnormal Bleeding: Treatment can increase the risk of bleeding. Use with caution in association with nonsteroidal anti-inflammatory drugs (NSAIDs), aspirin, or other drugs that affect coagulation.
- Activation of Mania/Hypomania: Can occur with treatment. Screen patients for bipolar disorder.
- Discontinuation of Treatment with Viibryd®: A gradual reduction in dose is recommended rather than an abrupt cessation.
- Hyponatremia: Can occur in association with the syndrome of inappropriate antidiuretic hormone secretion (SIADH).

ADVERSE REACTIONS: (incidence ≥5% and at least twice the rate of placebo):

- diarrhea
- nausea
- vomiting
- insomnia

DRUG INTERACTIONS:

- MAOIs: Do not use Viibryd® concomitantly with an MAOI or within 14 days of stopping or starting an MAOI.

- CYP3A4 inhibitors: The Viibryd® dose should be reduced to 20 mg when co-administered with CYP3A4 strong inhibitors.
- CYP3A4 inducers: Concomitant use of Viibryd® with inducers of CYP3A4 can result in inadequate drug concentrations and may diminish effectiveness. The effect of CYP3A4 inducers on systemic exposure of vilazodone has not been evaluated.

REFERENCES

1. Viibryd® Label Information. Forest Laboratories, Inc. Available online at: http://www.frx.com/pi/Viibryd_pi.pdf. Last revised 2011.

Appendix J

U.S. Department of Health & Human Services

FDA U.S. Food and Drug Administration

Drugs

FDA Drug Safety Communication: Safety review update on the possible increased risk of blood clots with birth control pills containing drospirenone

This update is in follow-up to the FDA Drug Safety Communication: Safety Review of possible increased risk of blood clots with birth control pills containing drospirenone[1] on 5/31/2011.

Safety Announcement

[09-26-2011] The U.S. Food and Drug Administration (FDA) is informing the public that it has not yet reached a conclusion, but remains concerned, about the potential increased risk of blood clots with the use of drospirenone-containing birth control pills. FDA has completed its review of the two 2011 studies that evaluated the risk of blood clots for women who use drospirenone-containing birth control pills, previously mentioned in FDA's Drug Safety Communication issued on May 31, 2011[2]. FDA is continuing its review of a separate FDA-funded study that evaluated the risk of blood clots in users of several different hormonal birth control products (contraceptives). Preliminary results of the FDA-funded study suggest an approximately 1.5-fold increase in the risk of blood clots for women who use drospirenone-containing birth control pills compared to users of other hormonal contraceptives.

Given the conflicting nature of the findings from six published studies evaluating this risk, as well as the preliminary data from the FDA-funded study (See Data Summary), FDA has scheduled a joint meeting of the Reproductive Health Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee on December 8, 2011[3] to discuss the risks and benefits and specifically the risk of blood clots of drospirenone-containing birth control pills.

A list of drospirenone-containing birth control pills is available here.

Patients should talk to their healthcare professional about their risk for blood clots before deciding which birth control pill to use. Known risk factors that increase the risk of a blood clot include smoking, being overweight (obesity), and family history of blood clots, in addition to other factors that contraindicate use of birth control pills.

Women currently taking a drospirenone-containing birth control pill should be informed of the potential risk for blood clots. FDA previously communicated preliminary information about these concerns to the public on May 31, 2011[4].

FDA has prepared a list of questions and answers[5] to provide an overview of this potential safety issue. FDA will continue to communicate any new information to the public as it becomes available.

Additional Information for Patients

- If your birth control pill contains drospirenone, do not stop taking it without first talking to your healthcare professional.
- Discuss any questions or concerns about your birth control pill with your healthcare professional.
- Know the symptoms of blood clots, including persistent leg pain, severe chest pain, or sudden shortness of breath. Contact your healthcare professional immediately if you develop any of these symptoms.
- Side effects from the use of birth control pills should be reported to the FDA MedWatch program, using the information in the "Contact Us" box at the bottom of the page.

Additional Information for Healthcare Professionals

- Consider the risks and benefits of drospirenone-containing combination oral contraceptives for a specific patient in light of her risk for developing blood clots (venous thromboembolism, VTE) before prescribing a drospirenone-containing oral contraceptive.
- Counsel patients about the current information regarding the risk of VTE with drospirenone-containing oral contraceptives compared to levonorgestrel-containing oral contraceptives.
- Factors for increased risk of VTE in users of birth control pills include smoking, obesity, and family history of VTE, in addition to other factors that contraindicate use of combination oral contraceptives.
- The studies assessing the risk of blood clots have evaluated only the specific drospirenone-containing product that combines 3 mg of drospirenone with 0.03 mg of ethinyl estradiol (an estrogen). It is not known whether these study results apply to other drospirenone-containing products with a lower dose of estrogen (e.g., 0.02 mg ethinyl estradiol).
- Adverse events involving oral contraceptives should be reported to the FDA MedWatch program using the information in the "Contact Us" box at the bottom of this page.

Data Summary

FDA has reviewed six published epidemiologic studies that evaluated the risk of blood clots (venous thromboembolism, VTE) in women using birth control pills containing drospirenone. These studies have conflicting findings. Two were postmarketing studies required by the FDA or European regulatory agencies.[1,2] These studies did not report any difference in VTE risk between drospirenone-containing products and products containing levonorgestrel or other progestins. Two publications from 2009, however, reported a 1.5- to 2-fold higher VTE risk in women who use drospirenone-containing contraceptives as compared to the risk in women who use levonorgestrel-containing contraceptives.[3,4] More recently, two articles published in 2011 in the British Medical Journal reported a 2- to 3-fold greater risk of blood clots in women using oral contraceptives containing drospirenone rather than levonorgestrel.[5,6] As with all epidemiologic studies, there are methodological issues that make interpretation of these conflicting results complex. FDA has not reached a conclusion on the risk for blood clots in women using drospirenone-containing birth control pills, but remains concerned about the potential increased risk.

Initial data from an FDA-funded epidemiologic study exploring the association of blood clots with several different hormonal contraceptive products, including

levonorgestrel-containing contraceptives, appear consistent with results from the 2009 and 2011 published studies. Although FDA's review is ongoing, the preliminary data from the FDA-funded study are consistent with an approximately 1.5-fold increase in the risk of blood clots for users of drospirenone-containing contraceptives compared to users of other hormonal contraceptives. To put this risk into perspective, if the risk of developing a blood clot among women using other hormonal contraceptives is about 6 women in 10 thousand, then the risk of developing a blood clot among women using drospirenone-containing oral contraceptives would be about 10 women in 10 thousand. For additional information on the FDA-funded study, please see information on study design [6]. The full study report of this study, along with the completed FDA review of the results of the study, will be presented and discussed at the joint meeting of the Reproductive Health Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee in December 2011.

FDA notes that the available studies have only examined the risk of VTE in users of contraceptive pills that contain drospirenone and 0.03 mg of ethinyl estradiol (an estrogen) and not other pills that contain drospirenone combined with a lower dose of estrogen (e.g., 0.02 mg ethinyl estradiol). It is unknown at this time whether the reported VTE risk applies to all drospirenone-containing products.

References

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Table 1. Approved Oral Contraceptives containing Drospirenone

Brand name	Generic name
Drospirenone and ethinyl estradiol	Drospirenone 3 mg and ethinyl estradiol 0.03 mg
Ocella	Drospirenone 3 mg and ethinyl estradiol 0.03 mg
Safyral	Drospirenone 3 mg, ethinyl estradiol 0.03 mg, and levomefolate calcium 0.451 mg
Syeda	Drospirenone 3 mg and ethinyl estradiol 0.03 mg
Yasmin	Drospirenone 3 mg and ethinyl estradiol 0.03 mg
Zarah	Drospirenone 3 mg and ethinyl estradiol 0.03 mg
Beyaz	Drospirenone 3 mg, ethinyl estradiol 0.02 mg and levomefolate calcium 0.451 mg
Drospirenone and ethinyl estradiol	Drospirenone 3 mg and ethinyl estradiol 0.02 mg
Gianvi	Drospirenone 3 mg and ethinyl estradiol 0.02 mg
Loryna	Drospirenone 3 mg and ethinyl estradiol 0.02 mg
Yaz	Drospirenone 3 mg and ethinyl estradiol 0.02 mg

Related Information

- FDA Drug Safety Podcast for Healthcare Professionals: Safety review update on the possible increased risk of blood clots with birth control pills containing drospirenone [7]
  9/26/2011
- Questions and Answers - Safety review update on the possible increased risk of blood clots with birth control pills containing drospirenone [8]
  9/26/2011
- Joint Meeting of the Advisory Committee for Reproductive Health Drugs and the Drug Safety and Risk Management Advisory Committee, December 8, 2011 [9]
  9/23/2011
- FDA Drug Safety Communication: Safety Review of possible increased risk of blood clots with birth control pills containing drospirenone [10]
  5/31/2011
- Information about Drospirenone [11]

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Links on this page:

1. /Drugs/DrugSafety/ucm257164.htm

U.S. Department of Health & Human Services

FDA U.S. Food and Drug Administration

Drugs

Phase-Out of Epinephrine CFC Metered-Dose Inhalers

Primatene Mist With Chlorofluorocarbons No Longer Available After Dec. 31, 2011

Epinephrine metered dose inhalers (MDIs) that contain chlorofluorocarbons (CFC) are being phased out and cannot be sold in the United States after December 31, 2011. Patients who use epinephrine CFC inhalers need to talk to their health care professionals and switch to another medicine before that date.

FDA: Over-the-counter asthma inhalers containing chloroflouorocarbons (CFCs) will no longer be made or sold after Dec. 31, 2011[1] (Press Release, Sept. 22, 2011)

- Advice to Consumers Who Use Primatene Mist[2]
- Why are over-the-counter epinephrine CFC inhalers being phased out? [3]
- When will epinephrine CFC inhalers be gone?[4]
- What other inhalers can I use for my asthma?[5]
- What should I do if I use an epinephrine CFC inhaler?[6]
- The albuterol HFA inhalers cost more than the epinephrine CFC inhalers. What can I do if it's hard for me to pay for an HFA inhaler?[7]

Information for Consumers

- Primatene Mist With Chlorofluorocarbons No Longer Available After Dec. 31, 2011[8]
- Epinephrine CFC Metered-dose Inhalers - Questions and Answers[9]

Information for Health Professionals

- Inhaler Phaseout Approaching[10][11]
- Drug Treatments for Asthma and Chronic Obstructive Pulmonary Disease that Do Not Use Chlorofluorocarbons[12]

Information for Industry

- Final Rule for Removal of Essential-Use Designation for Epinephrine14 [13]
- Final Rule - Use of Ozone-Depleting Substances: Removal of Essential-Use Designations15 [14]
- Letter Regarding Phase-out of Epinephrine CFC MDIs[15]
- Educating the Public About Removal of Essential-Use Designation for Epinephrine[16]
- Public Meeting on Essential Uses of Ozone Depleting Substances, December 5, 2007[17]

General Information

- Phase-Out of CFC Metered-Dose Inhalers[18]
- Phase-Out of Albuterol CFC Metered-Dose Inhalers[19]
- Phase-Out of CFC Metered-Dose Inhalers Containing flunisolide, triamcinolone, metaproterenol, pirbuterol, albuterol and ipratropium in combination, cromolyn, and nedocromil[20]

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7. http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm080427.htm#q7
8. /ForConsumers/ConsumerUpdates/ucm247196.htm
9. /Drugs/DrugSafety/InformationbyDrugClass/ucm080427.htm
10. http://apha.imirus.com/Mpowered/book/vpt17/i5/p38

U.S. Food and Drug Administration

Drugs

FDA Drug Safety Communication: Abnormal heart rhythms may be associated with use of Zofran (ondansetron)

Safety Announcement

[09-15-2011] The U.S. Food and Drug Administration (FDA) is informing the public of an ongoing safety review of the anti-nausea drug Zofran (ondansetron, ondansetron hydrochloride and their generics). Ondansetron may increase the risk of developing abnormal changes in the electrical activity of the heart, which can result in a potentially fatal abnormal heart rhythm.

Changes in the electrical activity of the heart (prolongation of the QT interval of the electrocardiogram [ECG]) — see Data Summary below — can lead to an abnormal and potentially fatal heart rhythm (including Torsade de Pointes). Patients at particular risk for developing Torsade include those with underlying heart conditions, such as congenital long QT syndrome, those who are predisposed to low levels of potassium and magnesium in the blood, and those taking other medications that lead to QT prolongation.

Facts about Zofran (ondansetron and ondansetron hydrochloride)

- Used to prevent nausea and vomiting caused by cancer chemotherapy, radiation therapy and surgery.
- Is in a class of medications called 5-HT3 receptor antagonists. Works by blocking the action of serotonin, a natural substance that may cause nausea and vomiting.[1]
- Available as 4 mg and 8 mg tablets, 4 mg and 8 mg orally disintegrating tablets, and oral solution (4 mg/5 mL). Also available as an injection for intravenous use (2 mg/mL).

FDA has reviewed all available information and is making interim changes to the drug labels. The manufacturer of Zofran (GlaxoSmithKline) is being required to conduct a thorough QT study to assess the potential for the drug to prolong the QT interval. The results from this study are expected to be available in th summer of 2012. Additional label changes may result after the additional information has been reviewed.

The Zofran (ondansetron) drug labels already contain information about the potential for QT prolongation. The labels are being revised to include a warning to avoid use in patients with congenital long QT syndrome because these patients are at particular ris for Torsade. Additionally, recommendations for ECG monitoring in patients with electrolyte abnormalities (e.g., hypokalemia or hypomagnesemia), congestive heart failure, bradyarrhythmias, or in patients taking other medications that can lead to QT prolongation, are being included in the labels.

Additional Information for Patients

- Do not stop taking Zofran (ondansetron) without talking to your healthcare professional.
- Discuss any questions or concerns about Zofran (ondansetron) with your healthcare professional.
- While taking Zofran (ondansetron), your healthcare professional may occasionally order an electrocardiogram (ECG, EKG) to monitor your heart rate and rhythm.
- Seek immediate care if you experience an irregular heartbeat, shortness of breath, dizziness, or fainting while taking Zofran (ondansetron).
- Report any side effects you experience to the FDA MedWatch program using the information in the "Contact Us" box at the bottom of the page.

Additional Information for Healthcare Professionals

- ECG changes including QT interval prolongation have been seen in patients receiving Zofran (ondansetron). In addition, Torsade de Pointes, an abnormal heart rhythm, has been reported in some patients receiving ondansetron.
- The use of Zofran (ondansetron) should be avoided in patients with congenital long QT syndrome.
- ECG monitoring is recommended in patients with electrolyte abnormalities (e.g., hypokalemia or hypomagnesemia), congestive heart failure, bradyarrhythmias, or patients taking concomitant medications that prolong the QT interval.

- Advise patients to contact a healthcare professional immediately if they experience signs and symptoms of an abnormal heart rate or rhythm while taking Zofran (ondansetron).
- Report adverse events involving Zofran (ondansetron) to the FDA MedWatch program, using the information in the "Contact Us" box at the bottom of the page.

Data Summary

The FDA previously noted cardiovascular safety concerns that suggested Zofran (ondansetron) could cause QT prolongation, which can lead to a serious and sometimes fatal heart rhythm called Torsade de Pointes. Additionally, there are articles published in the medical literature that describe QT interval prolongation with ondansetron or droperidol.[2-4]

FDA is now adding a new warning to avoid the use of ondansetron in patients with congenital long QT syndrome because these patients are at particular risk for developing Torsade. Previous versions of the ondansetron labels included a warning on ECG interval changes (QT interval prolongation). Additional recommendations for ECG monitoring in patients with electrolyte abnormalities (e.g., hypokalemia or hypomagnesemia), congestive heart failure, bradyarrhythmias, or in patients taking other medications that can lead to QT prolongation, are being added to the ondansetron drug labels.

To further characterize this risk, FDA is requiring GlaxoSmithKline to conduct a thorough QT study to determine the degree to which Zofran (ondansetron) may cause QT interval prolongation. The FDA will continue to assess all available data supporting the safety and effectiveness of ondansetron and will update the public when more information becomes available.

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4. Nathan et al. Implicationa of Anesthesia in Children with Long QT syndrome. Anesthesia and Analgesia 2011; 112(5): 1163-1168.

Related Information

- Ondansetron (marketed as Zofran) Information[2]
- MedlinePlus: Ondansetron[3]
- FDA Drug Safety Podcast for Healthcare Professionals: Abnormal heart rhythms may be associated with use of Zofran (ondansetron)[4]
  9/16/2011

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2. /Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm271924.htm
3. http://www.nlm.nih.gov/medlineplus/druginfo/meds/a601209.html
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