Drug Utilization Review Board

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

Wednesday
June 8, 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 – June 8, 2011

DATE: June 2, 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 June meeting. Material is arranged in order of the Agenda.

Call to Order

Public Comment Forum

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

Update on DUR / MCAU Program – See Appendix B.

Action Item –Vote to Prior Authorize Topical Corticosteroid Products – See Appendix C.

Action Item – Vote to Prior Authorize Miscellaneous Products – See Appendix D.

Utilization Review and 60 Day Notice to Prior Authorize Diabetes Medications – See Appendix E.

Action Item – Annual Review of Anxiolytic Prior Authorization Category – See Appendix F.

Action Item – Annual Review of Anti-Emetics and 30 Day Notice to Prior Authorize Zuplenz™ – See Appendix G.

Action Item – Annual Review of Otic Antibiotics – See Appendix H.

FDA and DEA Updates – See Appendix I.

Future Business

Adjournment

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Oklahoma Health Care Authority
Drug Utilization Review Board
(DUR Board)
Meeting – June 8, 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. May 11, 2011 DUR Minutes – Vote
- B. May 12, 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 Response for February 2011
- B. Medication Coverage Activity Audit for May 2011
- C. Pharmacy Help Desk Activity Audit for May 2011

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

5. Action Item – Vote to Prior Authorize Topical Corticosteroid Products – See Appendix C.
- A. COP Recommendations

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

6. Action Item – Votes to Prior Authorize Miscellaneous Products – See Appendix D.
- A. Vote to Prior Authorize Practitioner Administered Drugs, Including Benlysta®
- B. Vote to Prior Authorize Adcirca®
- C. Vote to Prior Authorize Colcrys® and Uloric®
- D. Vote to Prior Authorize Miscellaneous Bladder Agents
- E. Vote to Prior Authorize Neudexta™
- F. Vote to Prior Authorize Testosterone Replacement Products

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

7. Utilization Review and 60 Day Notice to Prior Authorize Diabetes Medications – See Appendix E.

A. Utilization Overview
B. Current Clinical Guidelines
C. Market Update
D. COP Recommendations
E. Economic Impact

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

8. Action Item – Annual Review of Anxiolytic Prior Authorization Category – See Appendix F.

A. Current Authorization Criteria
B. Utilization Review
C. Analysis of New Prior Authorization Criteria
D. COP Recommendations

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

9. Action Item – Annual Review of Anti-Emetics and 30 Day Notice to Prior Authorize Zuplenz™ – See Appendix G.

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

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

10. Action Item – Annual Review of Otic Antibiotics – See Appendix H.

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

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

11. FDA and DEA Updates – See Appendix I.

12. Future Business

A. Annual Review of Antipsychotics
B. Utilization of Select Biological Agents
C. Utilization Review of Multiple Sclerosis Agents
D. New Product Reviews

13. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES of MEETING of MAY 11, 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): JoNel Speegle	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:		
Jody Legg, Avanir	David Mershon, Bristol-Myers Squibb	Jeff Himmelberg, GlaxoSmithKline
Russ Wilson, OMJPI	Dwayne Dossett, Alkermes	Mike Ketcher, Novo Nordisk
Anore Johnson, Avanir	Ron Schnare, Shire	Anthony Deleon, Shire
Warren Tayes, Merck	David Williams, Forest	Jim Chapman, Abbott
Ben Liniger, Alcon	Don Kempin, Novo Nordisk	Charlene Kaiser, Amgen
James Osbourne, GSK	Brian Maves, Pfizer	

PRESENT FOR PUBLIC COMMENT:	
Agenda Item No. 9	Anthony Deleon, Shire
Agenda Item No. 11	Jody Legg, Avanir

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. 9 Anthony Deleon, Shire

Agenda Item No. 11 Jody Legg, Avanir

ACTION: NONE REQUIRED

AGENDA ITEM NO. 3: APPROVAL OF DUR BOARD MINUTES

3A: April 13, 2011 DUR Minutes

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

ACTION: MOTION CARRIED

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

4A: Retrospective Drug Utilization Review: March 2011

4B: Retrospective Drug Utilization Review Response: December 2010

4C: Medication Coverage Activity Audit: April 2011

4D: Pharmacy Help Desk Activity Audit: April 2011

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: VOTE TO PRIOR AUTHORIZE PRADAXA®

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

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: VOTE TO PRIOR AUTHORIZE DULERA® AND UPDATE CRITERIA

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

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: VOTE TO PRIOR AUTHORIZE SUMAVEL® AND UPDATE ANTI-MIGRAINE PBPA CRITERIA

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

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: ANNUAL REVIEW OF ANTI-ULCER MEDICATIONS AND VOTE TO UPDATE PRIOR AUTHORIZATION CRITERIA

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

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: VOTE TO UPDATE ADHD/NARCOLEPSY PRIOR AUTHORIZATION CRITERIA

For Public Comment; Dr. Anthony Deleon: My name's Dr. Anthony Deleon, senior medical science liaison with medical affairs, Shire Pharmaceuticals. I just wanted to provide you some clarification points with regards to the statements that are made in the DUR document. First and foremost, Shire has not made any claims with regards to Intuniv being superior compared to immediate release. There really hasn't been any

comparisons or any head-to-head studies comparing Intuniv to immediate release. Probably the biggest reason with that is the fact that there really hasn't been a standard of care with regards to utilization of immediate release. I think clinically we see immediate release guanfacine being utilized anywhere from one to two to three to four times a day in really tight variable doses. I know the DUR document states that there's actually been studies that have demonstrated the safety and effectiveness of immediate release in ADHD, but I'm not sure you would really agree that being the case. Other studies that are being cited, the larger study was only 40 patients. They were all open labeled except for one which was placebo controlled, many of which actually weren't even assessing ADHD as the primary disease state. Also I think one of them was actually in adults and probably most importantly, there was a lot of variability with regards to how immediate release guanfacine was administered, tapered, titrated, duration which the patients were treated, etc., etc.. So there's a lot of variability in regards to how immediate release is utilized. That was really first and foremost the goal with regards to development of Intuniv was to have medication that we can dose once a day to minimize the PK fluctuations. We know it's an anti-hypertensive. If we're going to be using it in 6-year olds, we want to have the least amount of fluctuations with regards to their pharmacokinetics and so forth. Looking at your half-life compared to immediate release and extended release isn't going to tell you anything. Elimination half-life of a drug is going to be the elimination half-life of the drug regardless of whether it's in an extended release product or not. So as far as that's concerned Shire would just like to really express their concern, just a sincere concern with regards to mandating the use of immediate release especially without any formal recommendation or guidance provided to physicians with regards to how to utilize it. Just a matter of safety, especially for those physicians that may not be familiar with utilizing immediate release guanfacine. With that I'll close and I'll be available for any questions. If I can also ask as well if there's any clarification that can be made with regards to prior authorization recommendations for Kapvay versus Intuniv. I believe Kapvay is requiring recent use of immediate release clonidine only, whereas Intuniv is requiring a recent trial of both immediate release clonidine and immediate release guanfacine. So with that I'll close.
Materials included in agenda packet; presented by Dr. Le.
Board members asked to change:
Criteria 3 and 4: specify "14 day trial".
Criteria 4: change from " …… clonidine and guanfacine …… " to " …… clonidine or guanfacine …… ".
Criteria 5: DELETE last sentence "Concomitant use of stimulants and Intuniv or Kapvay will not be covered, due to the availability of the immediate release products without prior authorization."
Dr. Bell moved to approve as revised above; seconded by Dr. Preslar.
ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: 30-DAY NOTICE TO PRIOR AUTHORIZE TOPICAL CORTICOSTEROIDS
Materials included in agenda packet; presented by Dr. Sipols.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 11: QUESTIONS REGARDING POSTED 30-DAY NOTICES
No presentation; questions only.
For Public Comment; Jody Legg: Hello. My name is Jody Legg. I'm with Avanir Pharmaceuticals. One of the medications under review, Nuedexta, is the first and only FDA approved treatment for pseudobulbar affect, also called PBA. My goal today is to help explain why Medicaid beneficiaries in Oklahoma should have unrestricted access to this FDA approved treatment. So what is PBA? PBA is secondary to a variety of otherwise unrelated neurologic conditions and is characterized by involuntary sudden and frequent episodes of laughing and/or crying. The episodes typically occur out of proportion or incongruent to the patient's underlying emotional state. PBA is believed to be caused by lesions in the brain brought about by an underlying disease or injury that disrupts voluntary control of emotional expression. Who suffers from PBA? It's estimated one to two million Americans suffer from pseudobulbar affect. PBA occurs in approximately 10-20% of patients with underlying neurologic diseases or injuries such as MS, stroke, traumatic brain injury, Lou Gehrig's disease, heart disease, dementia and certain others. This patient population is well defined and managed by a physician specialist. So why treat PBA? PBA can disrupt lives, causing significant functional impairment, including a reduced ability to work, socialize and even participate in their rehabilitative therapy. The symptoms of PBA can further complicate the lives of patients already suffering from their underlying condition. Treating PBA, reducing episodes, may diminish the functional and social impact of this condition. Thank you for your time and your consideration today. I request that this committee provide unrestricted access to the first and only FDA approved treatment for pseudobulbar affect to the benefit of patients suffering from this debilitating condition, and if appropriate, I have a letter from a psychiatrist that we just received in support. You want me to read that? I'll be fast. It's from Dr. Robert Morton, a psychiatrist here in Oklahoma.
"To whom it may concern: I have been actively involved in caring for a large number of Medicaid patients since becoming a Psychiatrist in 2000. Prior to that time I participated in the Medicaid program as an Internist for many years. I currently provide care to a great many intellectually disabled adults both as inpatients and outpatients, many of which suffer from traumatic brain injuries (TBI) and glutamatergic neurotransmitter dysfunctions. Nuedexta has recently been approved for the treatment of Psuedobulbar Affect (PBA), a neurological disorder with debilitating expressions of affect. It is the only medication with FDA approval for effective treatment of this disorder. The FDA did not limit their approval to just ALS or MS, the original study populations, but included other neurological disorders that were impacted by PBA such as dementia, CVA, Parkinson's Disease and TBI. Through sampling from the manufacturer, I have been able to see impressive results with this medication in inpatients with TBI through the stabilization and resolution of these extreme disabilities that had severely impaired their quality of life. I am hopeful that the Health Care Authority will not place impediments to the use of this very unique medication that will benefit our neediest and at times our most difficult to treat patients." Thank you. I'll be available to answer any questions.
Dr. Kuhls: Can you get these two medicines prescribed by themselves generically?
Ms. Legg: You're asking me but quinidine only comes in 200 mg tablet and this only includes 10 mg and so as far as trying to break that down, I don't believe it would be …… .
Dr. Winegardener: What's the dose of dextromethorphan? Is it 20 mg?

Ms. Legg: Yeah, 20 mg of dextromethorphan.
Dr. Muchmore: Is there any indication that this drug would be used inappropriately or pretty much prescribed by people that know what they're doing?
Dr. Le: Are you asking the College? Not yet because it was just released into market so it's brand new.
Dr. Muchmore: Well it might be perfectly reasonable just to say approved diagnosis of pseudobulbar affect, period; rather than saying what it's due to.
Dr. Le: We considered that, except in their package labeling, their wording is very specific and I brought the labeling with me. It says "Studies to support the effectiveness of NUEDEXTA were performed in patients with amyotrophic lateral sclerosis (ALS) and multiple sclerosis (MS). NUEDEXTA has not been shown to be safe and effective in other types of emotional lability that can commonly occur, for example, in Alzheimer's disease and other dementias." Because of that, we just stuck to what it has been shown to be effective in and the effectiveness was demonstrated in ALS and MS.
Ms. Legg: The label has been confusing but the confusion is that the other types of emotional lability that can occur like in Alzheimer's are the anger and aggression, but it's not the crying and the laughing.
Dr. Muchmore: Well certainly there are pseudobulbar affects, stokes, traumatic brain injuries and things like that and my logic says that this is not something that's going to be prescribed willy-nilly but is going to be prescribed for problems and I'm not sure it's in our best interests to restrict it. You know, people aren't going to be tripping out on this. I can tell you dextromethorphan is dysphoric; people aren't going to want to take it unless they've got a good reason.
Dr. Le: Does the Board recommend any changes so that when we bring it back next time we'll change it?
Dr. Kuhls: Well, here's a general comment I have about this. I really think the way you're doing these approvals for every 90 days, you're just abusing doctors, okay? It's the same thing with Intuniv. I got in an argument over the phone this month because basically you guys want to every six months, expect a doctor to go through all the paperwork for no reason other than to meet doctor abuse. If the doctor has this medication for thirty days, that doctor can decide and should be assessing whether they want it or not, and just to make them go through paperwork every three months to get this drug, to me is just abuse.
Dr. Muchmore: Well especially since you have a drug that isn't likely to be used for non-appropriate … .
Dr. Kuhls: It's just to make doctors go through paperwork for no reason.
Dr. Le: Shellie's working on automatic edits for that. The purpose for the six months is to check for component stimulants because there are two non-stimulants that the member can get without PA and when Strattera was the only non-stimulant there were like … …
Dr. Kuhls: Alright we've been through this. But right now, the Intuniv, I have a patient who's sleepy on 2 mg so I drop it to 1 mg and I have to go through a PA process to get a 1 mg tablet after I've been on 2 mg tablets.
Dr. Le: Yeah, she's working on automatic … … ..
Dr. Kuhls: Well I've heard that for a year now, and it's the same kind of thing with this kind of every 90-day interval to me. Why is that?
Dr. Le: Because in the package labeling it says it should be assessed periodically to make sure that the member still needs this medication. Most of these are … … … .
Dr. Kuhls: That's my whole point. You're not the physician. That's what the physician is for.
Dr. Le: OK, basically most of these recommendations are based on the package labeling, but if the Board feels to change it in any way, we just take what's on the label, we put it in the criteria. If the Board wants to change it that's fine. That's why I'm asking which changes would you like for us to bring it back that way next time.
Dr. Muchmore: Do we have a motion to limit that sentence to pseudobulbar affect and approval be for a year?
Dr. Le: You don't need a motion. This is not a voting item, just tell us what you want.
Dr. Kuhls: A year's fine. But Intuniv every three months, writing papers and going through all the hassle is not a good thing.
Dr. Muchmore: You'll need one more hassle. OK, we also, these are 30-day notices for tadalafil by another name that smells as sweet and then we have belimumab which is going to be an important drug in transplant, and we also have a 30-day notice on Colcrys, colchicine and febuxostat for uric acid control. Does anybody have any questions on the approval criteria? We're going to get presented these as action items next month, so we need to clarify anything now that we want to have different.
Board members discussed criteria for drugs named above by Dr. Muchmore.
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 Diabetes Products
B: Annual Review of Anxiolytics
C: Annual Review of Antiemetics
D: Annual Review of Otic Antibiotics
E: New Product Reviews
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: ADJOURNMENT

The meeting was adjourned at 7:30 p.m.

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

Memorandum

Date: May 12, 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 May 11, 2011

Recommendation 1: Vote to Prior Authorize Pradaxa® (dabigatran etexilate mesylate)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends prior authorization of Pradaxa® (dabigatran etexilate mesylate) requiring an FDA approved indication (special consideration will be given for a diagnosis of DVT when warfarin is not a viable option).

Recommendation 2: Vote to Prior Authorize Dulera® (mometasone/formoterol) and Update the Criteria for Inhaled Corticosteroid Combination Products

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends prior authorization of Dulera® (mometasone/formoterol) with the following update to the inhaled corticosteroid combination product criteria:

1. Diagnosis of COPD: Approve for one year
2. Diagnosis of Asthma:
    a. Member must be at or above the minimum age indicated, AND
    b. Have used inhaled corticosteroid for at least one month immediately prior, AND
    c. Considered uncontrolled by provider (required rescue medication > 2 days a week (not for prevention of exercise induced bronchospasms) and/or needed oral systemic corticosteroids), OR
    d. Clinical situation warranting initiation with combination therapy due to severity of asthma.
3. A quantity limit of one inhaler per 30 days will apply.

The College also recommends prior authorization of all LABA single products with the following criteria:

1. Diagnosis of COPD: Approve for one year
2. Diagnosis of Asthma:
    a. Member must be 12 years of age or older, AND
    b. Must have used an inhaled corticosteroid for at least one month immediately prior with inadequate results and plan to continue using ICS concomitantly with the LABA.
    c. Reason why member cannot use and ICS/LABA combination product.
    d. Approval will be for only 3 months to ensure use for the shortest duration of time required to achieve control of asthma symptoms.

Recommendation 3: Vote to Prior Authorize Sumavel DosePro® (sumatriptan) and Update Anti-Migraine Product Based Prior Authorization Criteria

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following changes to the existing tier structure:

1. Placement of Naratripan (Amerge®) into Tier 2.
2. Placement of Sumatriptan (Sumavel DosePro®) into Tier 3.
    a. Must also provide clinical reason why member cannot use all other available formulations of sumatriptan.
3. Existing criteria will apply.

Tier 1	Tier 2	Tier 3
Sumatriptan (Imitrex®)	Naratriptan (Amerge®)	Almotriptan (Axert®) Eletriptan (Relpax®) Frovatriptan (Frova®) Rizatriptan (Maxalt®; Maxalt MLT®) Sumatriptan (Sumavel DosePro®) Sumatriptan/Naproxen (Treximet®) Zolmitriptan (Zomig®; Zomig-ZMT®)

Recommendation 4: Annual Review of Anti-Ulcer Products and Vote Update Product Based Prior Authorization Criteria

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following change to the current criteria:

Criteria for Approval of a Tier-2 medication:

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

Recommendation 5: Vote to Update ADHD/Narcolepsy Product Based Prior Authorization Criteria

MOTION CARRIED by majority approval.

The College of Pharmacy recommends the following changes to the current criteria:

Approval of Tier 2 Products:

1. FDA approved diagnosis.
2. Trials of long acting medications from both the amphetamine and methylphenidate category, or a non-stimulant medication if a Tier 2 non-stimulant medication is requested, that did not yield adequate response.
   a. Trials should have been within the last 30-60 days.
   b. Dosed up to maximum recommended dose or provide information regarding side effects at higher dose.
   c. If trials are not in member's claim history, the pharmacy profile should be submitted or detailed information regarding dates and doses should be included along with the signature from the physician.
3. Use of Kapvay® also requires recent 14 day trial with immediate release clonidine and clinically significant reason why member cannot use immediate release products.
4. Use of Intuniv® also requires recent 14 day trial with ~~both~~ immediate release clonidine ~~and~~ or guanfacine and clinically significant reason why member cannot use immediate release products.
5. ~~5.~~ Concomitant use of stimulants and Strattera® is approved only for members with severe disease who have tried multiple stimulant medications alone, titrated to maximum recommended dose, AND the non-stimulant medication alone, titrated to maximum recommended dose, that did not yield adequate response. ~~Concomitant use of stimulants and Intuniv® or Kapvay® will not be covered, due to the availability of the immediate release products without prior authorization.~~

Appendix B

Retrospective Drug Utilization Review Report

Claims Reviewed for February 2011

Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
Limits which were applied	Established, Major, Males and Females, Age 19-35	Androgens / Anabolic Steroids, Age 0-150	Contraindicated, Myocardial Infarction, Males and Females, Age 56-150	Low Dose, Zyprexa, Clozapine, Loxapine, Seroquel, & Saphris Males and Females, Age 19-150

Response Summary (Prescriber)
Letters Sent: 38
Response Forms Returned: 16

The response forms returned yielded the following results:

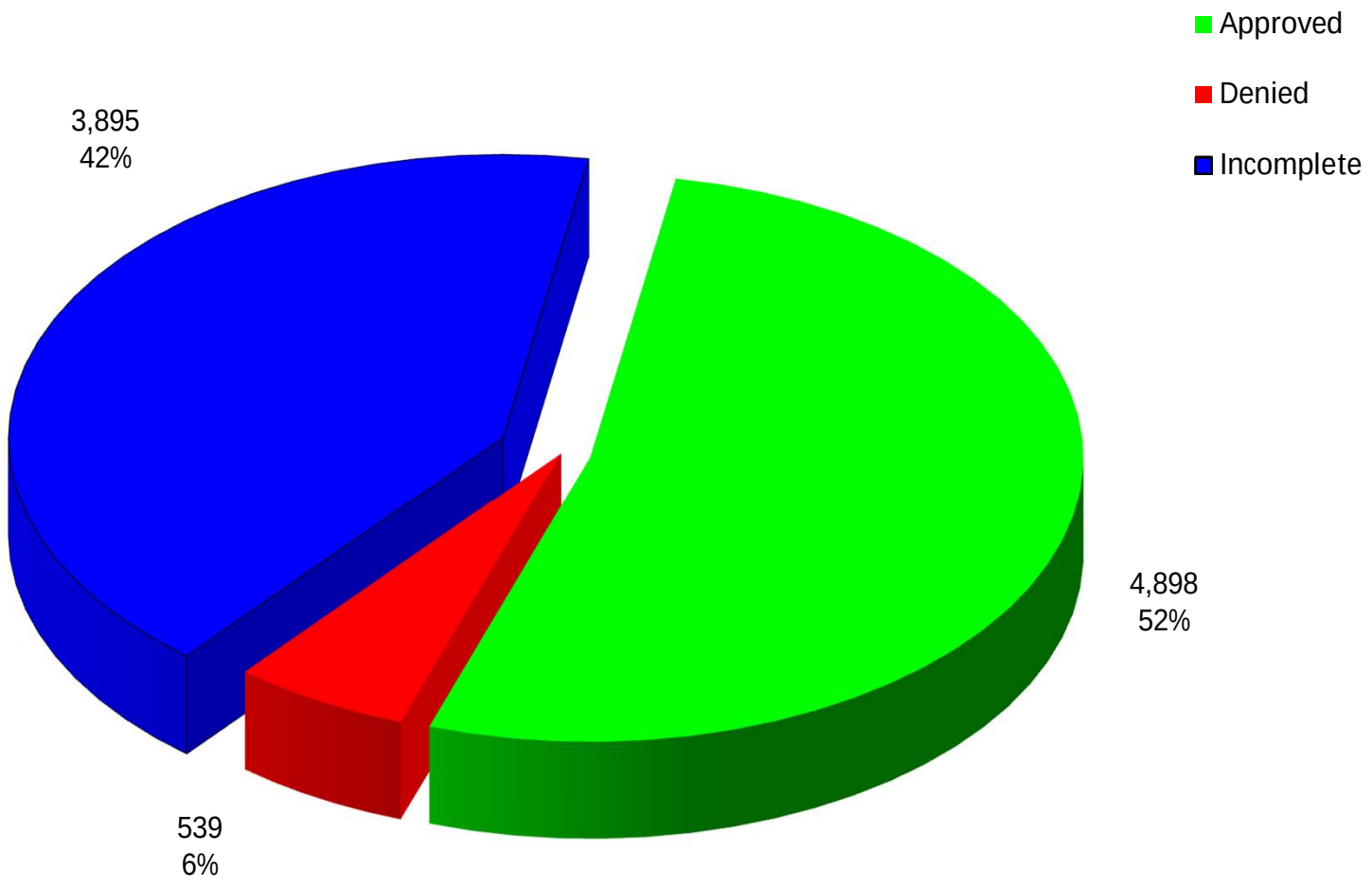
1 (6%)	*Record Error—Not my patient.*
3 (19%)	*No longer my patient.*
1 (6%)	*Medication has been changed prior to date of review letter.*
0 (0%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
9 (56%)	*I am aware of this situation and will plan to continue monitoring therapy.*
2 (13%)	*Other*

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

The response forms returned yielded the following results:

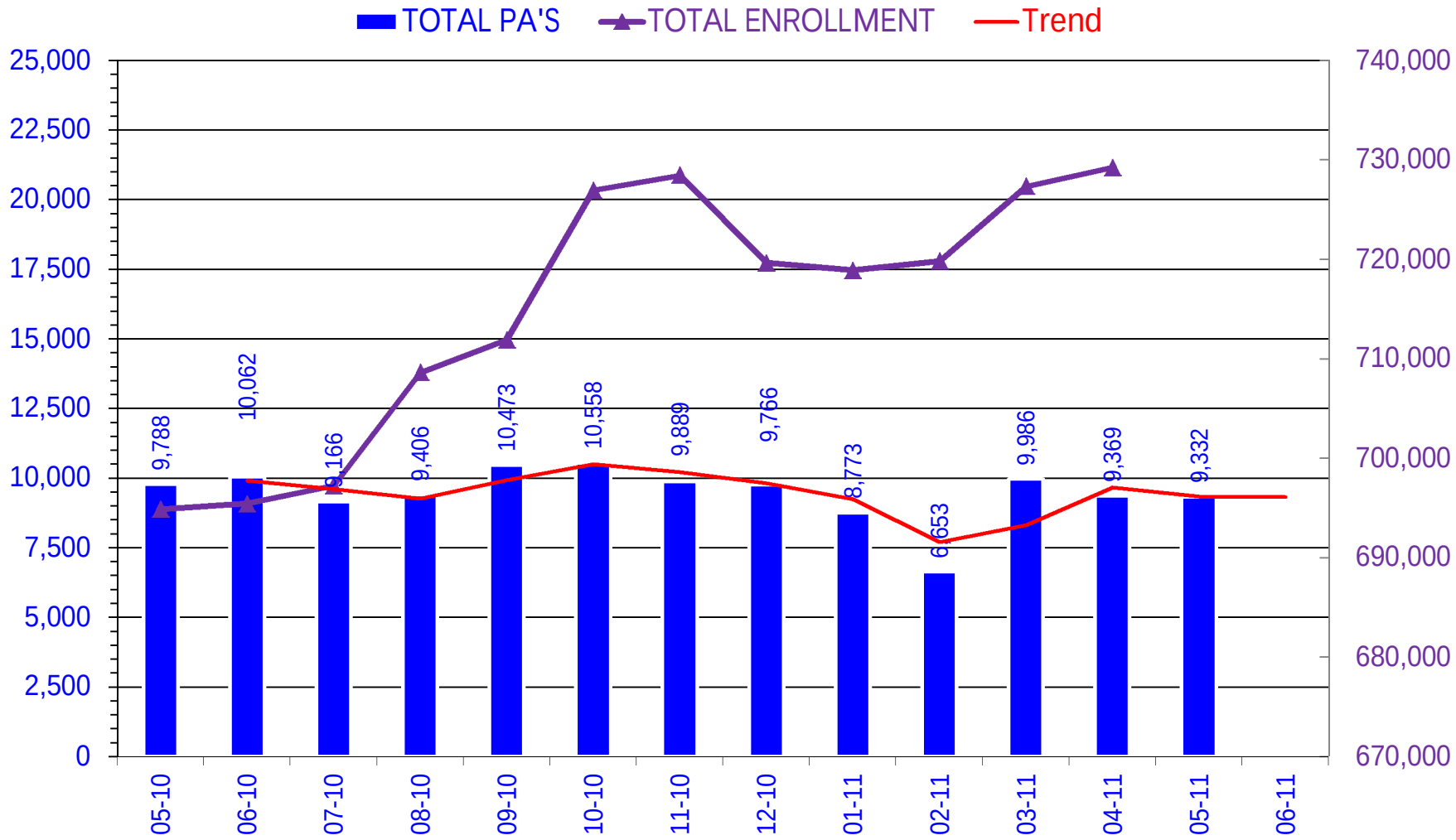
0 (0%)	*Record Error—Not my patient.*
0 (0%)	*No longer my patient.*
0 (0%)	*Medication has been changed prior to date of review letter.*
2 (50%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
1 (25%)	*I am aware of this situation and will plan to continue monitoring therapy.*
1 (25%)	*Other*

PRIOR AUTHORIZATION ACTIVITY REPORT: May 2011



PA totals include overrides

PRIOR AUTHORIZATION REPORT: May 2010 – May 2011



PA totals include overrides

Prior Authorization Activity

May 2011

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort	333	140	10	183	358
Amitiza	14	6	0	8	248
Anti-Ulcer	406	82	65	259	107
Antidepressant	344	129	9	206	354
Antihistamine	340	186	14	140	344
Antihypertensives	91	23	7	61	323
Antimigraine	66	31	4	31	316
Atypical Antipsychotics	669	337	24	308	353
Benzodiazepines	91	45	2	44	213
Bladder Control	39	6	1	32	318
Brovana (Arformoterol)	2	2	0	0	361
Byetta	7	3	0	4	364
Elidel/Protopic	62	27	4	31	93
ESA	110	81	3	26	81
Fibric Acid Derivatives	5	0	1	4	0
Fibromyalgia	132	40	16	76	358
Fortamet/Glumetza	2	0	0	2	0
Forteo	4	1	1	2	361
Glaucoma	26	13	0	13	363
Growth Hormones	58	50	4	4	156
HFA Rescue Inhalers	77	38	2	37	291
Insomnia	110	31	7	72	166
Misc Analgesics	53	3	36	14	272
Muscle Relaxant	147	53	51	43	57
Nasal Allergy	289	92	26	171	100
NSAIDS	137	36	12	89	325
Ocular Allergy	120	30	4	86	90
Ocular Antibiotics	43	14	3	26	13
Opioid Analgesic	316	184	18	114	235
Other	777	311	84	382	249
Otic Antibiotic	88	56	1	31	14
Pediculicides	88	44	3	41	14
Plavix	222	165	2	55	310
Qualaquin (Quinine)	1	0	1	0	0
Singulair	901	507	24	370	237
Smoking Cessation	53	24	1	28	51
Statins	108	39	7	62	355
Stimulant	990	596	24	370	290
Suboxone/Subutex	438	255	18	165	97
Symlin	2	1	0	1	365
Synagis	3	0	3	0	0
Topical Antibiotics	22	3	1	18	72
Topical Antifungals	21	5	2	14	34
Ultram ER and ODT	3	1	0	2	361
Xolair	6	4	0	2	261
Xopenex Nebs	36	15	2	19	321
Zetia (Ezetimibe)	19	8	3	8	328
Emergency PAs	6	6	0	0	
Total	**7,877**	**3,723**	**500**	**3,654**	

** Changes to existing PAs: Backdates, changing units, end dates, etc.*

6/1/2011 2:17:16 PM

Overrides					
Brand	52	34	4	14	181
Dosage Change	509	487	4	18	11
High Dose	6	5	0	1	158
Ingredient Duplication	11	10	0	1	7
Lost/Broken Rx	118	116	1	1	13
NDC vs Age	10	10	0	0	195
Nursing Home Issue	61	57	0	4	6
Other	31	27	0	4	27
Quantity vs. Days Supply	652	424	30	198	264
Quantity vs. Days SupplyQ	3	0	2	1	0
Stolen	3	3	0	0	5
Third Brand Request	1	1	0	0	2
Wrong D.S. on Previous Rx	1	1	0	0	365
Overrides Total	**1,455**	**1,175**	**39**	**241**	
Total Regular PAs + Overrides	**9,332**	**4,898**	**539**	**3,895**	

Denial Reasons

Unable to verify required trials.	2,730
Lack required information to process request.	1,167
Does not meet established criteria.	488

Duplicate Requests: 691

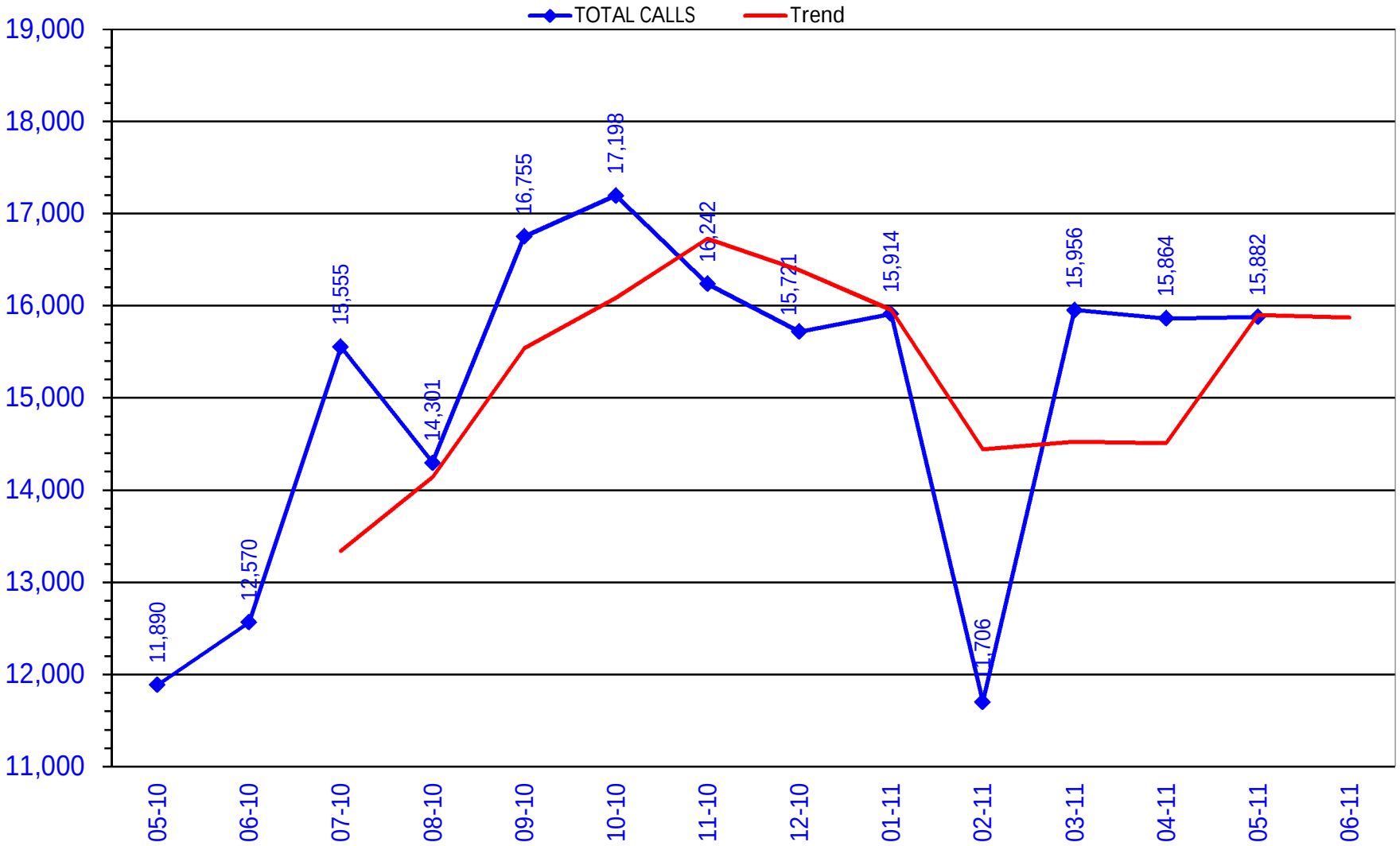
Letters: 1,509

No Process: 317

Changes to existing PAs: 431

** Changes to existing PAs: Backdates, changing units, end dates, etc.*

CALL VOLUME MONTHLY REPORT:
May 2010 – May 2011



Appendix C

Vote to Prior Authorize Topical Corticosteroid Products

Oklahoma Health Care Authority, June 2011

This category was introduced for possible inclusion in the Product Based Prior Authorization program in March 2011. See the March and April DUR packets 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.

Recommendations

The College of Pharmacy recommends the addition of the Topical Corticosteroid class of medications to the Product Based Prior Authorization program. The following Tier 1 drug list has been reviewed and determined to be an acceptable combination for use as initial therapy for the majority of members. The College of Pharmacy recommends this list to the Drug Utilization Review Board based on cost and clinical effectiveness for approval before referral to the Oklahoma Healthcare Authority. The following is the proposed Tier list and approval criteria. When Tier 2 products receive a State Maximum Allowable Cost designation and approach the cost of Tier 1 products, they will be moved to Tier 1.

Tier 2 Approval Criteria:

1. Documented trials of ALL Tier 1 topical corticosteroids of similar potency in the past 30 days that did not yield adequate relief.
    a. If Tier 1 trials are completed and do not yield adequate relief, the member must also provide a clinical reason for requesting a Tier 2 in the same potency instead of trying a higher potency.
2. When the same medication is available in Tier 1, a clinical reason must be provided for using a special dosage form of that medication in Tier 2 (foams, shampoos, sprays, kits, etc.).

Topical Corticosteroids	
Tier 1	Tier 2
Ultra high to high potency	
Augmented betamethasone dipropionate (Diprolene AF® G,C)	Amcinonide (O)
Betamethasone dipropionate (Diprosone® O)	Augmented betamethasone dipropionate (Diprolene® O, L)
Clobetasol propionate (Temovate® C,G,O,So)	Clobetasol propionate (Clobex® L,Sh,Spr; Olux® F)
Diflorasone diacetate (Apexicon® O, Apexicon E® C)	Desoximetasone 0.25% (Topicort® C,O,) 0.05% (G)
Fluocinonide 0.025% (Lidex® G,C,O)	Fluocinonide 0.01% (Vanos® C)
Halobetasol propionate (Ultravate® C,O)	Flurandrenolide tape (Cordran®)
	Halcinonide (Halog® C,O)
Med/high to medium potency	
Betamethasone dipropionate (Betanate® C,L)	Amcinonide (Cyclocort® C,L)
Betamethasone valerate (Beta-Val® C,O,L)	Betamethasone dipropionate/calcipotriene (Taclonex® O, Sus, Spr)
Fluocinolone acetonide (Synalar® C,O)	Betamethasone valerate (Luxiq® F)
Fluocinonide emollient (Lidex E® C)	Desoximetasone 0.05% (Topicort LP ® C)
Fluticasone propionate (Cutivate® C,O)	Fluticasone propionate (Cutivate® L)
Hydrocortisone valerate 0.2% C	Hydrocortisone butyrate (Locoid® O,C, L; Locoid Lipo C)
Mometasone furoate (Elocon® O,C,L)	Hydrocortisone probutate (Pandel® C)
Triamcinolone acetonide (Kenalog® C,O,L)	Hydrocortisone valerate (Westcort® C,O)
	Prednicarbate (Dermatop® O,C)
	Triamcinolone acetonide (Kenalog® Spr)
Low potency	
Alclometasone dipropionate (Aclovate® C,O)	Coclortolone pivalate (Cloderm® C)
Desonide (LoKara® C,O,L)	Desonide (Desonate® G, Verdeso® F)
Fluocinolone acetonide (So, C; Derma-Smooth®; Derma-Smooth FS® oil)	Desonide/emollient (Desowyn® kit C,O)
Hydrocortisone acetate 2.5% (C,O,L)	Fluocinolone acetonide (Capex® Sh)
Hydrocortisone/urea (U-Cort® C)	Hydrocortisone acetate 2%/aloe (Nucort®, L)
	Hydrocortisone/lidocaine (LidaMantle HC® C)

Appendix D

Vote to Prior Authorize Practitioner Administered Drugs, Including Benlysta® (belimumab)

Oklahoma Health Care Authority
June 2011

Manufacturer	Human Genome Sciences, Inc.
Classification	Monoclonal antibody
Status	Prescription Only

Summary

Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder which may affect the skin, joints, kidney, and other organs. The specific mechanism of this disorder is not known. According to a recent report from the National Arthritis Data Working Group, approximately 250,000 Americans have SLE. The prevalence of SLE is highest among women aged 14-64 years. The presentation and course are highly variable, ranging from mild to potentially fatal. Joint pain is one of the most common reasons for the initial clinical presentation in patients with SLE, and may involve the hands, wrists, and knees. Cutaneous manifestations are common and include the "butterfly rash", an erythematous rash over the cheeks and nasal bridge; photosensitivity; discoid rash; and alopecia. The kidney is the most commonly involved visceral organ in SLE, although any organ system may be affected.

Treatment of systemic lupus erythematosus (SLE) depends on disease severity. Milder symptoms such as fever, rash, musculoskeletal manifestations, and serositis generally respond to treatment with hydroxychloroquine, NSAIDS, and low-to-moderate–dose corticosteroids, as necessary, for acute flares. Medications such as methotrexate may be useful in chronic lupus arthritis, and azathioprine and mycophenolate have been widely used in moderate severity lupus. CNS involvement and renal disease constitute more serious disease and often require high-dose steroids and other immunosuppressive agents such as cyclophosphamide, azathioprine, or mycophenolate. Class IV diffuse proliferative lupus nephritis has also been treated with aggressive cyclophosphamide induction therapy. Recent observational evidence suggests that hydroxychloroquine may have protective benefits in patients with SLE, including improved survival.

Belimumab is indicated for the treatment of adult patients with active, autoantibody-positive, systemic lupus erythematosus (SLE) who are receiving standard therapy. Belimumab inhibits a B-lymphocyte stimulator (BLyS) protein, which leads to a decrease in the amount of abnormal B cells in the body. It is available as an intravenous infusion only, and is supplied as a 120 mg and 400 mg vial. The recommended dosage regimen is 10 mg/kg at 2 week intervals for the first 3 doses, and then it may be given every 4 weeks. The infusion is given over an hour but may be slowed if an infusion reaction occurs, and must be discontinued immediately if hypersensitivity develops. To prevent infusion and hypersensitivity reactions, it is advised that patients be premedicated with antihistamines.

Common adverse effects reported with belimumab include nausea, diarrhea, fever, infusion-site reactions, nasopharyngitis, bronchitis, insomnia, extremity pain, depression, migraine, and pharyngitis. A greater number of deaths and serious infections were reported in patients treated with belimumab than in those treated with placebo. It should be used with caution in patients with chronic infections, because serious and sometimes fatal infections have been reported in patients receiving belimumab or other immunosuppressive agents. Live vaccines should not be given during treatment with belimumab. Depression and suicidality have been reported

in clinical trials of belimumab, so patients should be monitored for new or worsening depression, suicidal thoughts, or other mood changes.

The safety and effectiveness of belimumab was demonstrated in 2 clinical trials that randomized a total of 1684 patients to receive either belimumab or placebo in combination with standard therapy. Treatment with belimumab plus standard therapy reduced disease activity and possibly decreased the number of severe flares and steroid use.

The current pricing for a 120 mg vial is $468, and for a 400 mg vial is $1,560. For a 70 kg patient, it is estimated the cost for a year of therapy with belimumab would be approximately $43,680. For the same 70 kg patient, estimated annual cost of therapy for cyclophosphamide is $2,538; azathioprine is $2,747; mycophenolate is $10,051; and hydroxychloroquine is $98.

Recommendations

1. The College of Pharmacy recommends prior authorization of Benlysta® (belimumab) for medical claims with the following approval criteria:
    a. FDA approved indication of adults with active, autoantibody-positive, systemic lupus erythematosus already receiving standard therapy.
    b. Documented inadequate response to at least two of the following medications:
        i. High-dose oral corticosteroids
        ii. Azathioprine
        iii. Mycophenolate
        iv. Cyclophosphamide
    c. Member must not have severe active lupus nephritis or severe active central nervous system lupus.
    d. No combination use with biologic therapies or intravenous cyclophosphamide.

2. In order to apply a consistent prior authorization policy to drug products supplied by either a pharmacy or practitioner's office, the College of Pharmacy recommends prior authorization of physician administered medications until these products can be formally reviewed by the DUR Board. The package labeling approved by the Food & Drug Administration (FDA) will be used as the interim criteria. Over the course of the next few months, several of these products will be presented and reviewed.

30 Day Notice to Prior Authorize **Adcirca® (Tadalafil)**

Oklahoma Health Care Authority
May 2011

Manufacturer:	Eli Lilly & Co., Marketed by Lung Rx, LLC
Medical Classification:	Phosphodiesterase Type 5 (PDE-5) Inhibitor
FDA Status:	Prescription Only

Summary

Adcirca® (tadalafil) is indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise ability. Adcirca® reduces arterial hypertension by inhibition of phosphodiesterase type 5 (PDE5) which increases the concentrations of cGMP, resulting in relaxation of pulmonary vascular smooth muscle cells and vasodilation of the pulmonary vascular bed. Tadalafil is also marketed under the brand name Cialis®, which is indicated for the treatment of erectile dysfunction.

Adcirca® (tadalafil) is available as 20mg non-scored tablets indicated to be dosed once daily as one single dose of two 20mg tablets with or without food. Adcirca® is only available as 20mg tablets. Adcirca® is contraindicated in patients also using organic nitrates. Adcirca® interacts with medications metabolized via the cytochrome P450 system such as theophylline, warfarin, midazolam, lovastatin, etc. Patients taking potent inhibitors or inducers of CYP3A such as ritonavir, rifampin, ketoconazole, and itraconazole, should avoid using Adcirca®. Common and rare serious adverse effects along with warning and precautions are included in the product information.

The estimated acquisition cost (EAC) of Adcirca® is $20.50 per tablet ($41.00 per day), which is comparable to Revatio® (sildenafil) which has an EAC of $15.85 ($47.55 per day.)

Recommendations

The College of Pharmacy recommends prior authorization of Adcirca® with similar approval criteria to the Revatio®:

1. FDA approved diagnosis of pulmonary arterial hypertension.
2. Medical supervision by a pulmonary specialist and/or cardiologist.
3. Quantity limit of #60 tablets per 30 days will apply.

REFERENCES

Adcirca® Label Information. Eli Lilly and Company. Available online at: www.adcirca.com/pdf/Learn-about-Adcirca.pdf. Last revised February 8, 2011.

ecommendations

The College of Pharmacy recommends prior authori ation of Colcrys® (Colchicine) and Uloric® (febuxostat) with the following criteria

C rr **C** will have a free floating 2 days supply of 6 tablets per 365 days. Long term use of Colchicine will require a petition and member must have

1. Failure of allopurinol defined by persistent gouty attacks with serum urate levels below 6.5mg/dL.
2. Clinical reason why colchicine/probenecid would not be a viable option for the member.
3. uantity limit of 60 per 30 days will apply for gout.
4. Members with the diagnosis of Familial Mediterranean Fever verified by genetic testing will be approved for up to 2.4mg per day.

U r approval criteria

1. Failure of allopurinol defined by persistent gouty attacks with serum urate levels below 6.5mg/dL.
2. Clinical reason why allopurinol is not a viable option for the member.
3. uantity limit of 30 per 30 days will apply.

[1] **C r L r** URL Pharma, Inc Available online at http//www.colcrys.com/healthcare-professional/about-colcrys.htm. Last revised September 6, 2010.

[2] FDA News Release **DA rd r r d** http//www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm227796.htm

[3] **U r L r** Takeda Pharmaceuticals North America, Inc. Available at http//www.uloricrx.com/

Vote to Prior Authorize Colcrys® (Colchicine) and Uloric® (Febuxostat)

Oklahoma Health Care Authority
June 2011

Manufacturers: URL Pharma, Inc. and Takeda Pharmaceuticals North America, Inc.
Medical Classification: Antimitotic (colchicine) and Xanthine Oxidase Inhibitor (febuxostat)
FDA Status: Prescription Only

Colcrys® (Colchicine) Summary[1]

Colcrys® (colchicine) is indicated for prophylaxis and treatment of gout flares in adults, and Familial Mediterranean Fever (FMF) in adults and children 4 years or older. Colchicine is an old drug that has been on the market before the establishment of the Food and Drug Administration (FDA). On October 1, 2010, the FDA ordered all unapproved cholchicine products be removed from the market.[2] Colcrys® is a new extended release formulation of colchicine and is currently the only single-ingredient colchicine product on the market that is FDA approved. The combination products containing colchicine/probenecid manufactured by Watson Laboratories and Ivax Pharmaceuticals are still available on the market. The therapeutic ratio of benefits to adverse effects is usually poorer for colchicine than for other available oral treatments.

Colcrys® (colchicine) is available as 0.6mg tablets. For acute treatment, Colcrys® is taken as 1.2mg (2 tablets) at the first sign of a gout flare followed by 0.6 mg (1 tablet) one hour later. For prophylaxis, the dose is 0.6mg once or twice daily in adults and adolescents older than 16 years of age up to a maximum dose of 1.2 mg per day.

Uloric® (febuxostat) Summary[3]

Uloric® (febuxostat) is a new xanthine oxidase inhibitor indicated for the chronic management of hyperuricemia in patients with gout. Allopurinol is currently the only other xanthine oxidase inhibitor on the market. Unlike allopurinol, Uloric® (febuxostat) is eliminated via both hepatic and renal pathways and does not require dosage reduction in patients with mild to moderate renal impairment.

Uloric® (febuxostat) is recommended at 40mg or 80mg once daily with or without food. The recommended starting dose of Uloric® is 40 mg once daily. For patients who do not achieve a serum uric acid less than 6mg/dL after 2 weeks with 40 mg, Uloric® 80mg is recommended. In comparative trials listed in the Uloric® label, Uloric® 80mg, but not the 40mg, was shown to be superior to allopurinol in lowering serum uric acid less than 6mg/dL. However, the allopurinol doses used in the trials ranged from 100mg to 300mg per day, which is listed as the minimal to average effective dose in allopurinol's medication label. The maximum recommended dose for allopurinol may be up to 800mg to 900mg per day.

Cost Comparison (January – March 2011)

CHEMICAL NAME	BRAND NAME	CLAIMS	UNITS	DAYS	MEMBERS	COST	UNITS/ DAY	COST/ DAY
Allopurinol	ALLOPURINOL TAB 100MG	407	20,829	14,747	233	$2,723.22	1.41	$0.18
Allopurinol	ALLOPURINOL TAB 300MG	485	22,679	21,327	309	$3,297.38	1.06	$0.15
Colchicine	COLCRYS TAB 0.6MG	59	2,408	1,432	40	$12,310.30	1.68	$8.60
Febuxostat	ULORIC TAB 40MG	40	1,186	1,186	19	$6,136.92	1	$5.17
Febuxostat	ULORIC TAB 80MG	19	555	570	11	$2,861.19	0.97	$5.02
Probenecid	PROBENECID TAB 500MG	19	1,260	543	8	$530.93	2.32	$0.98
Colchicine/Probenecid	PROBEN/COL TAB 500-0.5	2	120	120	2	$75.51	1	$0.63

Recommendations

The College of Pharmacy recommends prior authorization of Colcrys® (Colchicine) and Uloric® (febuxostat) with the following criteria:

Colcrys® (Colchicine) will have a free floating 2 days supply of 6 tablets per 365 days. Long term use of Colchicine will require a petition and member must have:

1. Failure of allopurinol defined by persistent gouty attacks with serum urate levels below 6.5mg/dL.
2. Clinical reason why colchicine/probenecid would not be a viable option for the member.
3. Quantity limit of #60 per 30 days will apply for gout.
4. Members with the diagnosis of Familial Mediterranean Fever verified by genetic testing will be approved for up to 2.4mg per day.

Uloric® (febuxostat) approval criteria:

1. Failure of allopurinol defined by persistent gouty attacks with serum urate levels below 6.5mg/dL.
2. Clinical reason why allopurinol is not a viable option for the member.
3. Quantity limit of #30 per 30 days will apply.

[1] **Colcrys® Label Information.** URL Pharma, Inc**.** Available online at: http://www.colcrys.com/healthcare-professional/about-colcrys.htm. Last revised September 6, 2010.
[2] FDA News Release: **FDA orders halt to marketing of unapproved single-ingredient oral colchicine.** http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm227796.htm
[3] **Uloric® Label Information.** Takeda Pharmaceuticals North America, Inc. Available at: http://www.uloricrx.com/

Vote to Prior Authorize Miscellaneous Bladder Agents

Oklahoma Health Care Authority
June 2011

Summary

Painful urination can be due to a number of causes, including but not limited to kidney stones or kidney infections, sexually transmitted diseases, prostatitis, urethritis, yeast infections, diagnostic procedures, or causes as simple as dehydration. There are a group of combination products indicated for the relief of local symptoms of irritative voiding. The chart below outlines the products that are currently covered by SoonerCare, their mechanisms of action, and comparative cost:

Name	Methenamine	Methylene Blue	Hyoscyamine	Sodium Phosphate	Salicylate	Benzoic Acid	Cost/ Tablet
Urelle®	X	X	X	X	X		$3.21
Prosed-DS®	X	X	X		X	X	$2.36
Darpaz®	X	X	X	X	X		$1.75
Urogesic Blue®	X	X	X	X			$0.62
Uroqid Acid #2®	X			X			$0.38
Utira-C®	X	X	X	X	X		$0.37
Utrona-C®	X	X	X	X	X		$0.37
Darcalma®	X	X	X	X	X		$0.37

Methenamine and methylene blue are antiseptics.
Salicylate is a pain reliever.
Sodium phosphate acidifies the urine, aiding in the antiseptic effects.
Hyoscyamine is an antispasmodic.
Benzoic Acid is a topical antiseptic.

The dosing is usually one tablet orally 4 times per day followed by liberal fluid intake. Common adverse reactions include tachycardia, flushing, dizziness, nausea, acute urinary retention or difficult micturition, discoloration of urine (blue), blurred vision, and shortness of breath.

Recommendations

The College of Pharmacy recommends prior authorization of Urelle®, Prosed DS®, and Darpaz® with the following approval criteria:

1. Recent 14 day trials within the past 30-60 days of:
    a. Urogesic Blue®, and
    b. Utira-C®, Utrona-C®, or Darcalma®

REFERENCES
Prosed® DS Label Information. Ferring Pharmaceuticals, Inc. Available online at: http://www.prosed.com//. Accessed April 20, 2011.
Urelle® Label Information. Azur Pharma, Inc. Available online at: http://www.empr.com/urinary-tract-disorders/urelle/drug/6920/.
Darpaz® Label Information. River's Edge Pharmaceuticals, Inc. Available online at: http://www.drugs.com/pro/darpaz.html

Vote to Prior Authorize Nuedexta™ (dextromethorphan/quinidine)

Oklahoma Health Care Authority
June 2011

Manufacturer:	Avanir Pharmaceuticals, Inc.
Medical Classification:	Not Current Classification
FDA Status:	Prescription Only

Summary[1]

Nuedexta™ is indicated for the treatment of pseudobulbar affect (PBA), also called pathological laughing and crying, affective lability, emotional dyscontrol, emotional incontinence, and involuntary emotional expression disorder. Studies to support the effectiveness of Nuedexta™ were performed in patients with underlying amyotrophic lateral sclerosis (ALS) or multiple sclerosis (MS). Nuedexta™ has not been shown to be safe or effective in other types of emotional lability that can commonly occur, for example, in Alzheimer's disease and other dementias. Nuedexta™ is a combination of dextromethorphan 20mg and quinidine 10mg. Dextromethorphan is an uncompetitive N-methyl-D-aspartate (NMDA) receptor antagonist and a sigma-1 receptor agonist with an unknown mechanism of therapeutic effectiveness in pseudobulbar affect. Quinidine competitively inhibits the metabolism of dextromethorphan by CYP2D6, thereby increasing and prolonging plasma levels of dextromethorphan.

Nuedexta™ is indicated to be dosed once daily for 7 days, then twice daily therafter. Nuedexta™ can be taken with or without food. The patient should be assessed periodically to determine if continued use is necessary.

Nuedexta™ is contraindicated in patients with prolonged QT interval, congenital long QT syndrome, history suggestive of torsades de pointes, heart failure, or patients taking monoamine oxidase inhibitors (MAOIs), patients who are allergice to quinidine, mefloquine, or dextromethorphan. Diarrhea, flatulence, and dizziness are the most commonly reported adverse effects. Other serious adverse effects, mostly related to the use of quinidine, are listed in the product information.

The estimated acquisition cost (EAC) of Nuedexta™ is $8.61 per tablet ($17.22 per day), which makes Nuedexta™ therapy $516 per month and $6,192.00 per year.

Recommendations

The College of Pharmacy recommends prior authorization of Nuedexta™ with the following approval criteria:

1. FDA approved diagnosis of pseudobulbar affect.
2. Member must be 18 years of age or older.
3. Quantity limit of #60 tablets per 30 days will apply.
4. Approvals will be for the duration of a year.

[1] **Nuedexta™ Label Information.** Avanir™ Pharmaceuticals, Inc,. Available online at: www.**nuedexta**.com/**NUEDEXTA** Full Prescribing Information-1.pdf. Last revised October 2010.

Vote to Prior Authorize Testosterone Replacement Products

Oklahoma Health Care Authority
June 2011

Recommendations

The College of Pharmacy recommends prior authorization of all testosterone products to ensure safe and appropriate use. The following is the recommended approval criteria:

1. Approved diagnosis:
    a. Testicular failure due to cryptorchidism, bilateral torsions, orchitis, vanishing testis syndrome; or orchidectomy.
    b. Idiopathic gonadotropin or luteinizing-hormone-releasing hormone (LHRH) deficiency, or pituitary hypothalamic injury from tumors, trauma, or radiation.
    c. Delayed puberty.
    d. Advanced inoperable metastatic mammary cancer in females 1 to 5 years postmenopausal, or premenopausal women with breast cancer benefitting from oophorectomy and have been determined to have a hormone-responsive tumor.
2. Must include two labs showing pre-medication testosterone level below 300ng/dL and other labs necessary to demonstrate diagnosis.
3. Oral agents are only approved in cases where member cannot use all other available formulations of testosterone.

Appendix E

Utilization Review and 60 Day Notice to Prior Authorize Diabetes Medications

Oklahoma Health Care Authority
June 2011

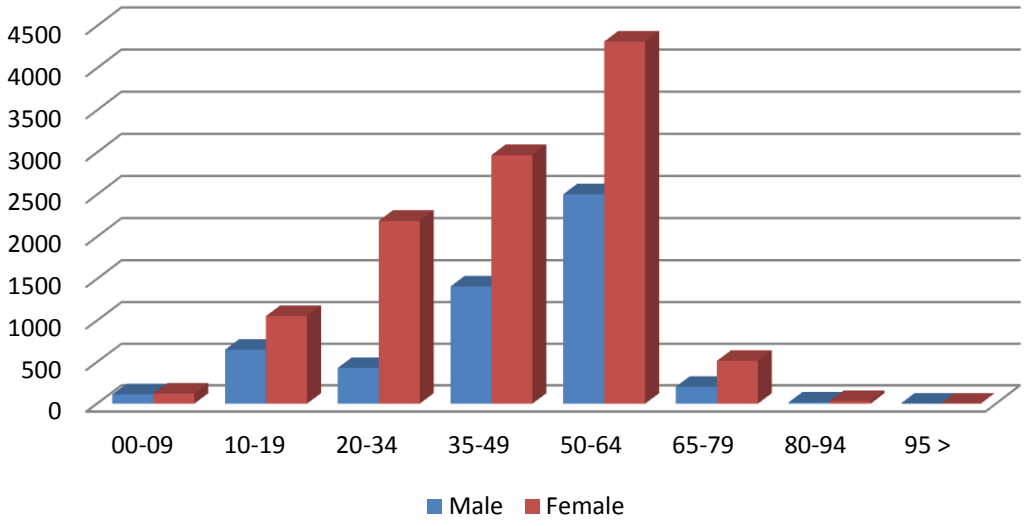
This notice and statement of potential economic impact are presented to meet the statutory requirements of 63 O.S. Sec. 5030.5.

Utilization Review of Diabetes Medications – Calendar Year 2010

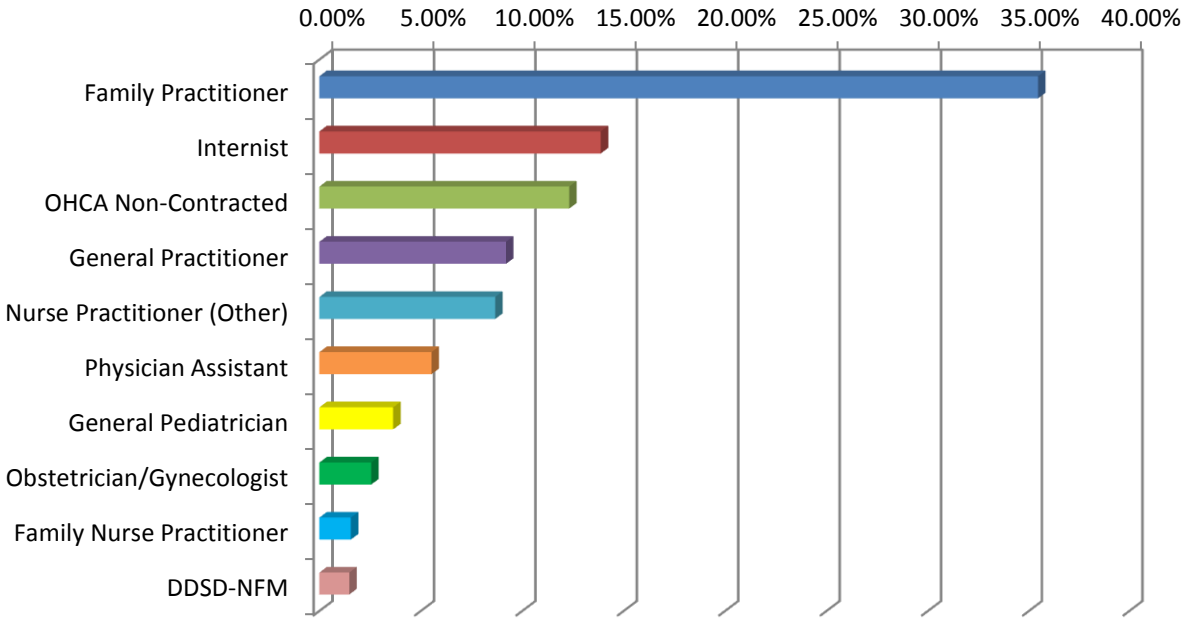
Comparison of CY09 versus CY10

	Total Members	Total Claims	Total Cost	Cost per Claim	Per-Diem Cost	Total Units	Total Days
2009	14,413	119,482	$13,180,436.61	$110.31	$3.44	5,281,352	3,829,756
2010	16,528	135,704	$15,666,202.39	$115.44	$3.56	6,100,617	4,406,494
Percent Change	**14.7%**	**13.6%**	**18.9%**	**4.7%**	**3.5%**	**15.5%**	**15.1%**
Amount Change	**2,115**	**16,222**	**$2,485,765.78**	**$5.13**	**$0.12**	**819,265**	**576,738**

Number of Member by Age and Gender



Top 10 Prescriber Specialties by Percent of Diabetic Medications Claims



Utilization Details by Sub-Therapeutic Group

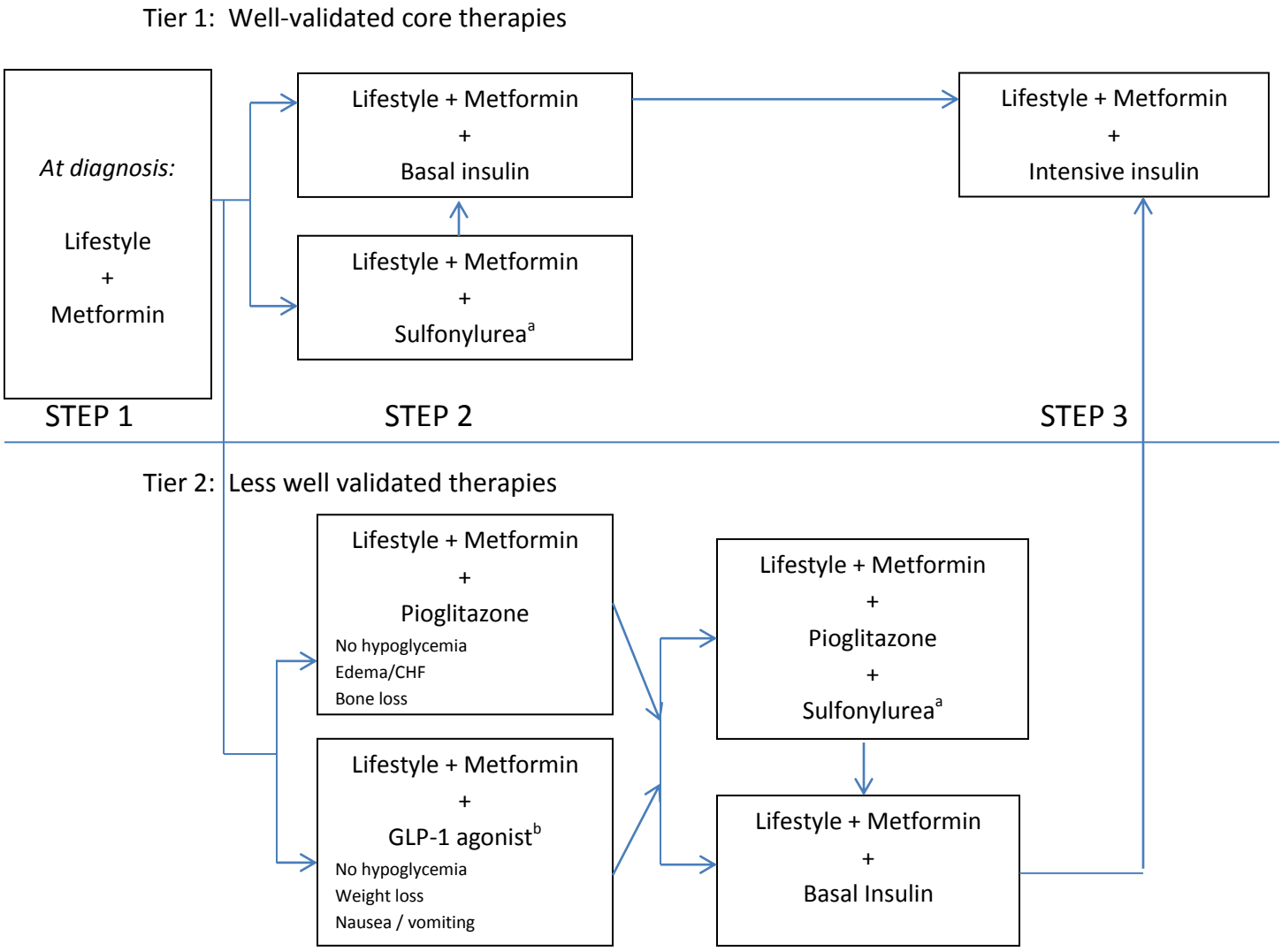
GENERIC NAME	CLAIMS	UNITS	DAYS	MEMBERS	COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ DAY	PERCENT COST
Insulin	52,797	1,022,176	1,606,345	7,075	$9,990,774.23	0.64	7.46	$6.22	63.77%
Biguanides	39,690	2,719,499	1,286,687	9,133	$352,832.72	2.11	4.35	$0.27	2.25%
Sulfonylureas	20,819	1,287,207	723,949	4,839	$246,900.41	1.78	4.30	$0.34	1.58%
Insulin Sensitizing Agents	9,437	387,860	371,094	1,997	$2,541,233.07	1.05	4.73	$6.85	16.22%
Combinations	6,372	475,024	206,098	1,178	$921,764.46	2.3	5.41	$4.47	5.88%
DPP-4 Inhibitors	3,364	139,613	135,035	838	$885,411.85	1.03	4.01	$6.56	5.65%
Miscellaneous	1,605	12,642	22,785	795	$323,187.63	0.55	2.02	$14.18	2.06%
Incretin Mimetic Agents	1,023	4,024	35,442	274	$320,872.66	0.11	3.73	$9.05	2.05%
Meglitinide Analogues	308	27,166	9,770	67	$45,047.89	2.78	4.60	$4.61	0.29%
α-Glucosidase Inhibitors	255	24,980	8,278	54	$17,415.70	3.02	4.72	$2.10	0.11%
Amylin Analogs	34	427	1,011	8	$20,761.77	0.42	4.25	$20.54	0.13%
Total	**135,704**	**6,100,618**	**4,406,494**	***16,528**	**$15,666,202.39**	**1.38**	**8.21**	**$3.56**	

*Unduplicated members

Current Clinical Guidelines

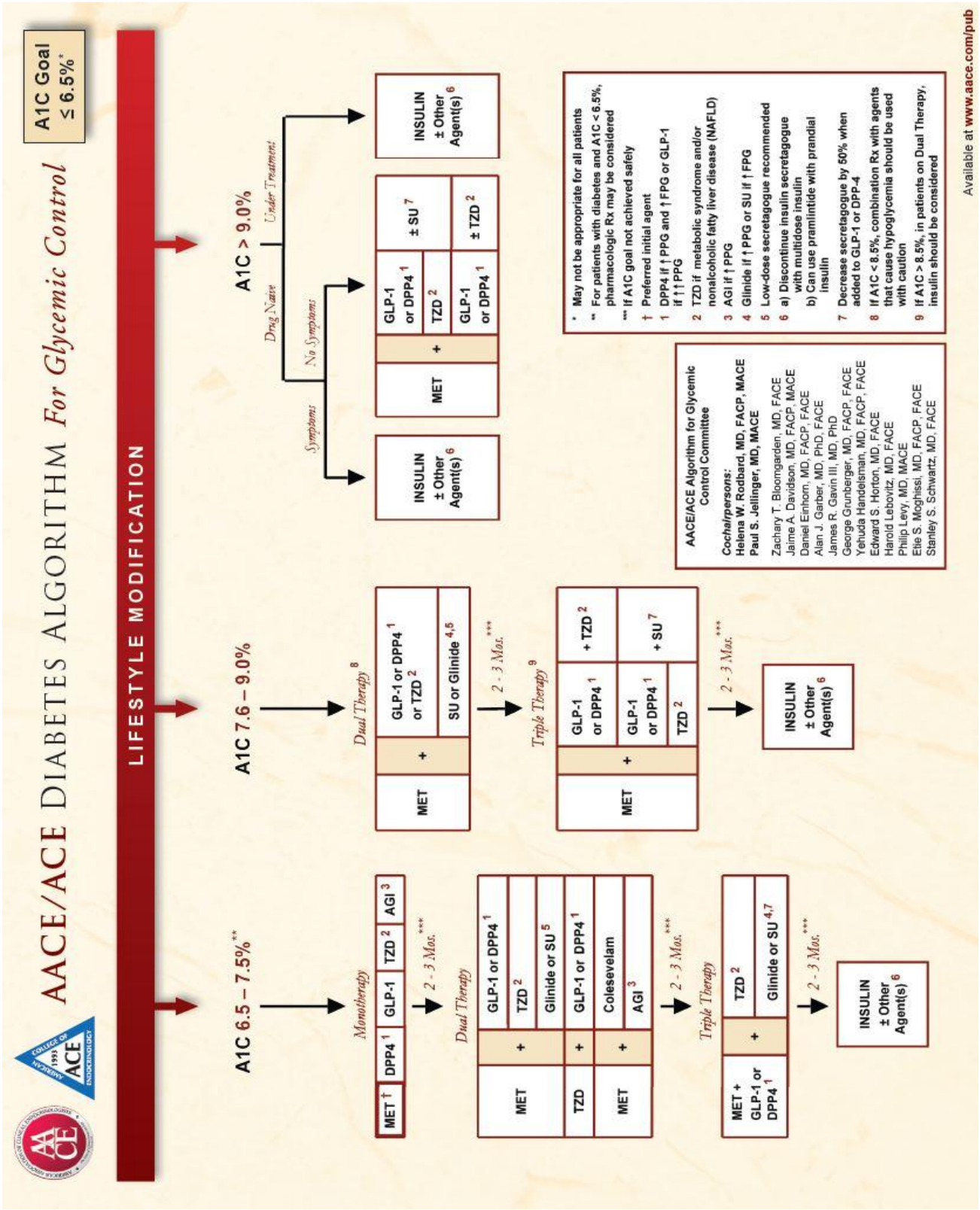
The goal of therapy is to reduce the A1C level below 7% according to the American Diabetes Association[1] (ADA) and below 6.5% according to the American Association of Clinical Endocrinologist (AACE)[2]. Both the AACE and ADA state the first therapy to be used is lifestyle modification which includes diet and exercise.

Algorithm for the Metabolic Management of Type 2 Diabetes[1]



Reinforce lifestyle interventions at every visit and check A1C every 3 months until A1C is <7% and then at least every 6 months. The interventions should be changed if A1C is >/= 7%. [a]Sulfonylureas other than glybenclamide (glyburide) or chlorpropamide. [b]Insufficient clinical use to be confident regarding safety.[1]

AACE/ACE Diabetes Algorithm for Glycemic Control[2]



Reprinted with written permission from the AACE.

Market Update

The following are the anticipated patent expirations:

- Pioglitazone (Actos®) generic should be available in 2012
- Rosiglitazone (Avandia®) generic should be available in 2012/13

The following new products are expected on the market:

- Linagliptin (Tradjenta™) a new DDP-4 Inhibitor was recently approved in 2011.

FDA modified the REMS program for rosiglitazone products in May 2011. Rosiglitazone may only be used for patients who are being successfully treated currently and for patients who cannot control their blood sugar with other medications. Both healthcare providers and patients must be enrolled in the Avandia-Rosiglitazone Medicines Access Program and after November 18, 2011 the products will only be available through certified mail order pharmacies.

Recommendations

The College of Pharmacy recommends the addition of the Diabetes Medications to the Product Based Prior Authorization program. The following tiered drug list has been reviewed and determined to be an acceptable combination for use as initial therapy for the majority of members. The College of Pharmacy recommends this list to the Drug Utilization Review Board based on clinical effectiveness and cost for approval before referral to the Oklahoma Healthcare Authority. The following are the recommendations for this category:

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.

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.	**DDP-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.
†One Tier 2 for each category will be determined based on supplemental rebate or best federal rebate.
‡Special criteria currently apply.

Economic Impact

Potential Secondary Costs

Overall efficacy is considered to be similar across the class levels of this therapeutic category, 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

Based on potential use of the final Tier 2 products of 75%, it is estimated that approximately 4,000 petitions annually might be required if the step therapy was not initially followed by all members. The proposed tier changes would affect approximately 2.4% of the total population for this PBPA category.

Previously, it has been theorized that 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 $30,520 and $59,280 annually. Anticipated actual administrative cost to the program is projected to be less than $30,000.

Potential Program Savings

Potential net ingredient savings to the program after rebates based on the recommended tiers and a potential use of 75% of Tier 2 products versus Tier 3 products is estimated to be approximately $1.2 million.

REFERENCES

1. Nathan DM, Buse JB, Davidson MB, Ferrannini E, Holman RR, Sherwin R, Zinman B. Medical Managemnt of Hyperglycemia in Type 2 Diabetes: A Consensus Algorithm for the Initiation and Adjustment of Therapy. Diabetes Care. 2008;31:1-11.

2. Robdard HW, Jellinger PS, Davidson JA, Einhorn D, Garber AJ, Grunberger G, et al. American Association of Clinical Endocrinologist/American College of Endocrinology Consensus Panel on Type 2 Diabetes Mellitus: An Algorithm for Glycemic Control. Endocrine Practice. 2009;15:540-559.

Appendix F

ANNUAL REVIEW OF ANXIOLYTIC PRIOR AUTHORIZATION CATEGORY

OKLAHOMA HEALTHCARE AUTHORITY

JUNE 2011

CURRENT PRIOR AUTHORIZATION CRITERIA

Members 19 Years and Older:

1. No prior authorization needed, but Quantity Limits set at 3 units per day for most products.
2. No requests for dosing greater than 3 times daily will be approved unless a Chronic Physical Diagnosis exists; for these diagnoses the maximum allowed dosing would be 4 times daily.
3. A member may receive more than 3 units per day if the following criteria exist:
    a. The number of units per day is greater than 3, but less than the maximum daily dose for the product (or for a total daily dosing of TID).
    b. The member has a Chronic Diagnosis and a clinical reason for excessive units has been provided.

Members 0-18 Years of Age:

Members 13 through 18 years of age the criteria for approval would be as follows:

1. Chronic Behavioral Health Related Diagnosis:
    a. No concurrent stimulant ADHD medications, AND
    b. No Contraindicated Conditions, AND
    c. Maximum dosing of 3 times daily.
2. Chronic Physical Diagnosis:
    a. Up to TID dosing if a hypnotic is being used concurrently; up to QID otherwise.
3. Exceptions can be granted for administration prior to procedures.

Members 12 or younger will have the same criteria AND prescription originally written by a psychiatrist.

Approvals will generally be for the duration of one year.

UTILIZATION REVIEW

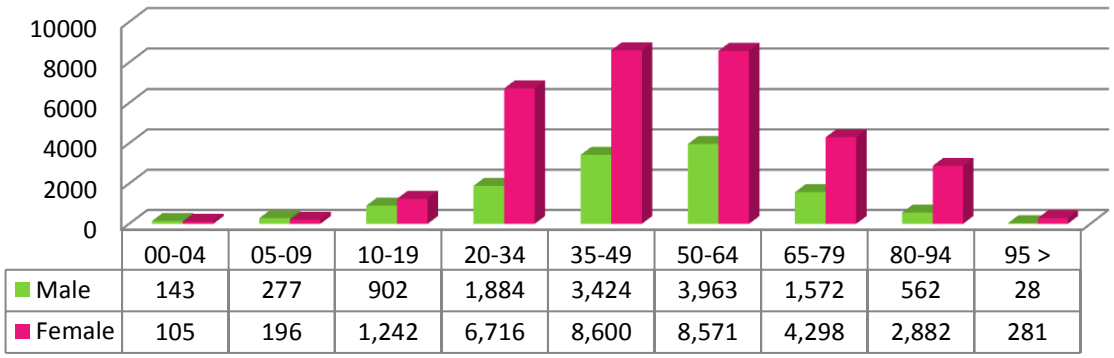
Fiscal Year	Total Members	Total Claims	Total Cost	Cost per Claim	Per-Diem Cost	Total Units	Total Days
2009	42,357	212,649	$2,056,099.16	$9.67	$0.36	14,266,093	5,663,225
2010	45,666	234,915	$2,098,719.86	$8.93	$0.33	15,566,648	6,331,577
% Change	**7.80%**	**10.50%**	**2.10%**	**-7.70%**	**-8.30%**	**9.10%**	**11.80%**
Actual Change	**3,309**	**22,266**	**$42,620.70**	**-$0.74**	**-$0.03**	**1,300,555**	**668,352**

FISCAL YEAR 2010

RANK CLAIMS	RANK COST	PRODUCT	CLAIMS	UNITS	DAYS	MEMBERS	AMOUNT PAID	UNITS / DAY	CLAIMS /MEMEBER
1	1	Alprazolam	95,890	6,790,923	2,611,842	20,243	$899,802.67	2.60	4.74
2	2	Clonazepam	63,078	4,209,227	1,818,787	11,695	$571,898.16	2.31	5.39
3	3	Lorazepam	38,119	2,108,292	919,960	10,058	$318,190.56	2.29	3.79
4	4	Diazepam	33,007	2,146,288	849,813	9,034	$233,193.03	2.53	3.65
5	5	Chlorazepate	2,661	174,165	76,796	534	$45,692.02	2.27	4.98
6	7	Chlordiazepoxide	1,647	104,452	39,476	553	$14,999.86	2.65	2.98
7	6	Oxazepam	513	33,301	14,903	98	$14,943.56	2.23	5.23
			234,915	**15,566,648**	**6,311,577**	**45,666***	**$2,098,719.86**	**2.46**	**5.14**

*Unduplicated Members

MEMBER DEMOGRAPHICS FY10



	00-04	05-09	10-19	20-34	35-49	50-64	65-79	80-94	95 >
Male	143	277	902	1,884	3,424	3,963	1,572	562	28
Female	105	196	1,242	6,716	8,600	8,571	4,298	2,882	281

20 Unknown

PRIOR AUTHORIZATIONS FY10

Variable	Total
Total Prior Authorizations	44,331
Total Approved	36,254 (81.8 %)
Total Denied	312
Total Unapproved	7,765

TOP 10 PRESCRIBERS BY NUMBER OF CLAIMS FY10

Prescribers	Percent of Claims
Family Practitioner	35.6
Psychiatrist	15.4
Internist	13.4
General Practitioner	9.6
DDSD-NFM	4.5
Nurse Practitioner	3.4
Physician Assistant	3.3
Non-OHCA Contracted	2.5
General Pediatrician	2.4
Neurologist	1.6

ANALYSIS OF NEW PRIOR AUTHORIZATION CRITERIA

MEANS AND TOTALS FOR SELECTED VARIABLES

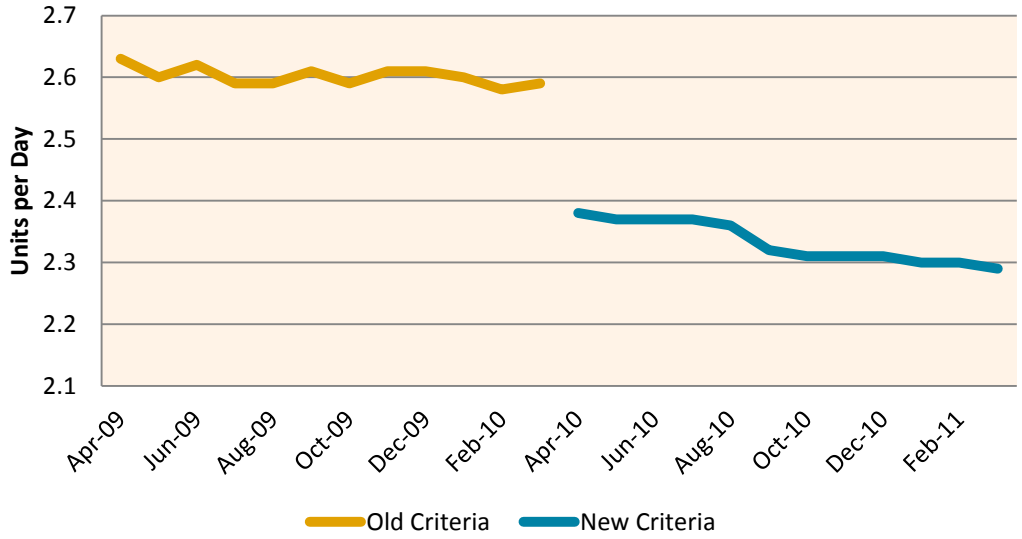
Variable	CY09	4/10 – 3/11
Total Members	43,382	47,339
Average Day Supply per Member	134	161
Average Units per Member	336	372
Number of Dual Eligibles	19,682 (45.4 %)	19,131 (40.4 %)
Number of Claims for Duals	112,032 (51.6 %)	125,446 (45.3 %)
Number of Members Under 21	3,601 (8.3 %)	1,943 (4.1 %)
Number of Claims for Members Under 21	12,038 (5.5 %)	8,900 (3.2 %)

MEMBERS ON CONCURRENT THERAPIES 4/10 THROUGH 3/11

Therapy	Number of Members
Hypnotics	7,759
Narcotics	21,617
Both	5,049

TRENDS IN UNITS PER DAY 4/10 THROUGH 3/11

There appears to be a statistically significant change (p-value <0.0001) between the number of units per day before and after the April 2010 criteria change.



RECOMMENDATIONS

The College of Pharmacy recommends continuation of the current criteria for this drug category with the following addition:

Add the anxiolytic products to the Ingredient Duplication ProDUR module which is currently set to require prior authorization when claims are attempted for the same ingredient when less than 90 % of the previously submitted day supply has been used. Claims from the same prescriber are exempt under this module.

Appendix G

Fiscal Year 2010Annual Review of Anti-Emetics and 30 Day Notice to Prior Authorize Zuplenz™ (ondansetron oral soluble film)

Oklahoma HealthCare Authority
June 2011

Current Prior Authorization Criteria

Approval Criteria for granisetron (Kytril® and Sancuso®), dolasetron (Anzemet®), and aprepitant (Emend®):

1. Approved Diagnosis
2. A recent (within the past 6 months) trial of ondansetron used for at least 3 days or one cycle that resulted in inadequate response.
3. Approval length based on duration of need.
4. Quantity limits apply.

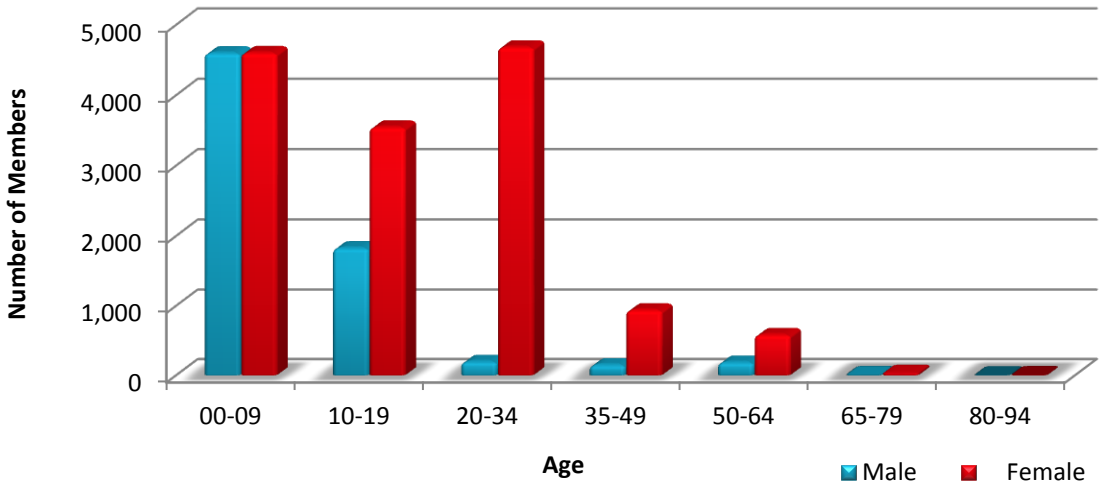
Approval Criteria for cannabinoids (Marinol® and Cesamet®):

1. For the diagnosis of HIV related loss of appetite: approve for 6 months
2. For chemotherapy induced nausea and vomiting: A recent (within the past 6 months) trial of ondansetron used for at least 3 days or one cycle that resulted in inadequate response.
3. Approval length based on duration of need.
4. A quantity limit of 60 per 30 days also applies.

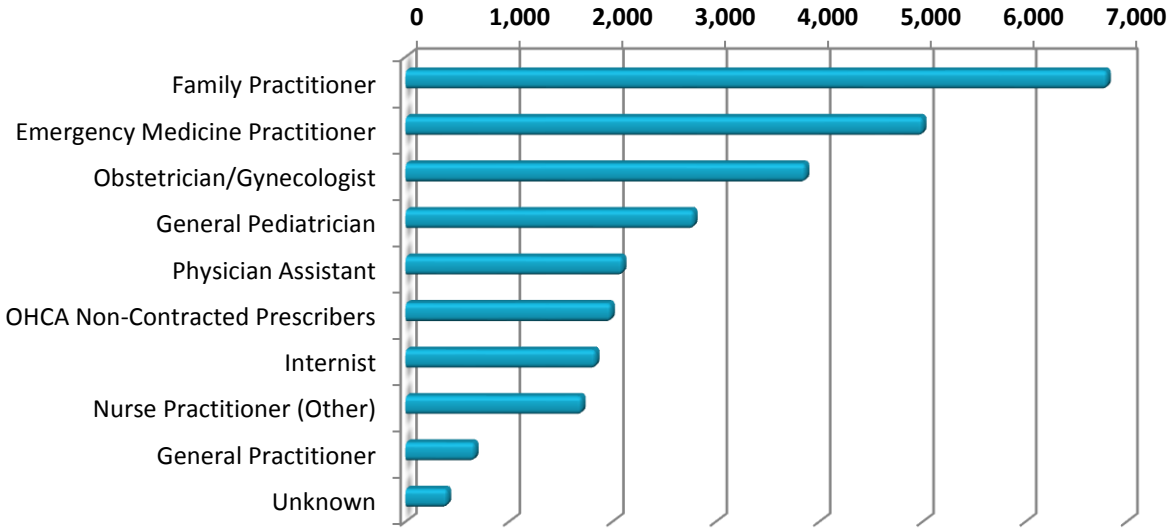
Utilization of 5HT Antagonists, Emend and Marinol

Fiscal Year	Members	Claims	Cost	Cost/Claim	Perdiem	Units	Days
2009	13,029	18,997	$720,023.67	$37.90	$2.06	268,114	349,056
2010	21,340	28,534	$637,167.62	$22.33	$0.93	330,163	687,555
% Change	**63.80%**	**50.20%**	**-11.50%**	**-41.10%**	**-54.90%**	**23.10%**	**97.00%**
Change	**8,311**	**9,537**	**-$82,856.05**	**-$15.57**	**-$1.13**	**62,049**	**338,499**

Members Demographics for Fiscal Year 2010



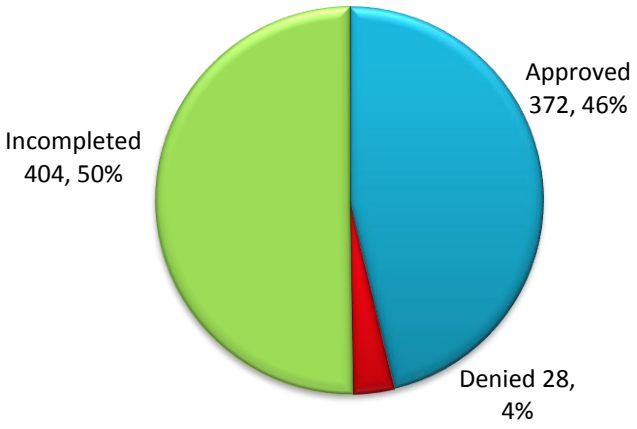
Top Prescribers of Anti-Emetic Products by Claims: FY 2010



Prior Authorization of Anti-Emetics

There were a total of 804 petitions submitted for PBPA category during fiscal year 2010. The following chart shows the status of the submitted petitions.

Status of Petitions for Anti-Emetic Medications: FY 2010



Market News and Update

Zuplenz™ (ondansetron oral soluble film) was approved July 2010 for the prevention of postoperative-induced, highly and moderately emetogenic cancer chemotherapy-induced, and radiotherapy-induced nausea and vomiting. It's available as 4mg and 8mg of ondansetron in an orally disintegrating film. The dosing is similar to ondansetron oral tablets.

Conclusion and Recommendations

The College of Pharmacy recommends prior authorization of Zuplenz™ (ondansetron) with the following criteria:

1. FDA-approved indication.
2. Must provide a clinically significant reason why the member cannot take all other available formulations of generic ondansetron.

Utilization Details of Anti-Emetics: Fiscal Year 2010

GENERIC NAME	BRAND NAME	CLAIMS	DAYS	MEMBERS	COST	CLAIMS/ MEMBER	COST/ DAY	% COST
Ondansetron	ONDANSETRON TAB 4MG ODT	14,681	331,500	12,879	$130,061.72	1.14	$0.39	20.41%
Ondansetron	ONDANSETRON TAB 4MG	5,116	134,733	3,999	$43,311.32	1.28	$0.32	6.80%
Ondansetron	ONDANSETRON TAB 8MG ODT	3,869	101,877	2,604	$40,175.24	1.49	$0.39	6.31%
Ondansetron	ONDANSETRON TAB 8MG	2,613	72,939	1,737	$24,294.32	1.5	$0.33	3.81%
Ondansetron	ONDANSETRON SOL 4MG/5ML	1,401	28,977	1,265	$95,183.21	1.11	$3.28	14.94%
Aprepitant	EMEND PAK 80 & 125	229	4,435	93	$92,911.63	2.46	$20.95	14.58%
Dronabinol	DRONABINOL CAP 5MG	194	5,267	57	$91,054.30	3.4	$17.29	14.29%
Dronabinol	DRONABINOL CAP 2.5MG	145	3,806	67	$34,991.60	2.16	$9.19	5.49%
Granisetron	GRANISETRON TAB 1MG	108	1,117	35	$17,727.21	3.09	$15.87	2.78%
Dronabinol	DRONABINOL CAP 10MG	61	1,728	11	$52,987.73	5.55	$30.66	8.32%
Ondansetron	ONDANSETRON INJ 4MG/2ML	47	334	24	$606.00	1.96	$1.81	0.10%
Aprepitant	EMEND CAP 80MG	30	204	16	$7,235.72	1.88	$35.47	1.14%
Ondansetron	ONDANSETRON INJ 40/20ML	19	383	9	$1,156.16	2.11	$3.02	0.18%
Granisetron	SANCUSO DIS 3.1MG	8	168	1	$2,633.82	8	$15.68	0.41%
Dolasetron	ANZEMET TAB 100MG	6	29	4	$2,045.65	1.5	$70.54	0.32%
Granisetron	GRANISETRON INJ 1MG/ML	3	10	3	$299.95	1	$29.99	0.05%
Aprepitant	EMEND CAP 40MG	2	3	2	$151.34	1	$50.45	0.02%
Ondansetron	ONDANSETRON TAB 8MG	1	15	1	$7.66	1	$0.51	0.00%
Granisetron	GRANISOL SOL 2MG/10ML	1	30	1	$333.04	1	$11.10	0.05%
TOTAL		**28,534**	**687,555**	**21,340***	**$637,167.62**	**1.34**	**$0.93**	**100%**

***Total number of unduplicated members**

PRODUCT DETAILS OF ZUPLENZ™ (ONDANSETRON) ORAL SOLUBLE FILM

INDICATIONS: Zuplenz™ is indicated for the prevention of postoperative-induced, highly and moderately emetogenic cancer chemotherapy-induced, and radiotherapy-induced nausea and vomiting.

DOSAGE FORMS:

- Zuplenz™ is an oral soluble film that is available in 4mg and 8mg strengths.

ADMINISTRATION:

- Place the film on top of the tongue where it dissolves in 4 to 20 seconds, then swallow.
- **Prevention of nausea and vomiting associated with highly emetogenic cancer chemotherapy:**
  - The adult oral dosage is 24 mg given successively as three 8 mg films 30 minutes before the start of chemotherapy.
- **Prevention of nausea and vomiting associated with moderately emetogenic cancer therapy:**
  - Adults and pediatric patients 12 years of age and older: One 8 mg film 30 minutes before chemotherapy followed by an 8 mg dose 8 hours later. Administer one 8 mg film twice a day (every 12 hours) for 1 to 2 days after completion of chemotherapy.
  - Pediatric patients 4 through 11 years of age: One 4 mg film three times a day. Administer the first dose 30 minutes before chemotherapy, with subsequent doses 4 and 8 hours later. Administer one 4 mg film three times a day (every 8 hours) for 1 to 2 days after completion of chemotherapy.
- **Prevention of nausea and vomiting associated with radiotherapy:**
  - Adult only: 8mg three times a day.
- **Prevention of postoperative nausea and/or vomiting:**
  - Adult only: 16mg dose (two 8mg films given successively) 1 hr before induction of anesthesia.

CONTRAINDICATIONS:

- Concomitant use with **apomorphine:** reports of hypotension and loss of consciousness.
- **Hypersensitivity**: Patients with a history of hypersensitivity to ondansetron: anaphylactic reactions have been reported.

SPECIAL POPULATIONS:

- **Pregnancy Category B.**
- **Nursing Mothers:** It is not known whether Zuplenz™ is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Zuplenz™ is administered to a nursing woman.
- **Renal Impairment**: Dosage recommendation is the same as for the general population.
- **Hepatic Impairment:** In severe hepatic impairment (Child-Pugh score of 10 or greater), a total daily dose of 8 mg should not be exceeded.

WARNINGS & PRECAUTIONS:

- **Hypersensitivity reactions**, including anaphylaxis and bronchospasm, have been reported in patients who have exhibited hypersensitivity to other selective 5-HT3 receptor antagonists.
- **Masking of Progressive Ileus and/or Gastric Distention:** in abdominal surgery or with chemotherapy-induced nausea and vomiting patients may mask a progressive ileus and/or gastric distension.

- **Effect on Peristalsis:** Zuplenz™ is not a drug that stimulates gastric or intestinal peristalsis. It should not be used instead of nasogastric suction.

ADVERSE REACTIONS:

- **Gastrointestinal:** headache, malaise/fatigue, constipation, diarrhea, hypoxia, dizziness (depending upon dosing regimens for different indications)
- **Central nervous system:** There have been rare reports consistent with, but not diagnostic of, extrapyramidal reactions in patients receiving ondansetron.
- **Hepatic:** In 723 patients receiving cyclophosphamide-based chemotherapy in US clinical trials, AST and/or ALT values have been reported to exceed twice the upper limit of normal in approximately 1% to 2% of patients receiving ondansetron HCl tablets.
- **Rash** has occurred in approximately 1% of patients receiving ondansetron.
- **Other:** Rare cases of anaphylaxis, bronchospasm, tachycardia, angina (chest pain), hypokalemia, electrocardiographic alterations, vascular occlusive events, and grand mal seizures have been reported. Except for bronchospasm and anaphylaxis, the relationship to ondansetron was unclear.

DRUG INTERACTIONS:

- **Apomorphine:** Profound hypotension and loss of consciousness.
- **Phenytoin, Carbamazepine, Rifampin:** The clearance of ondansetron was significantly increased and ondansetron blood concentration was decreased when treated with potent inducers of CYP3A4.
- **Tramadol:** Data from two small studies indicate that concomitant use of ondansetron may result in reduced activity of tramadol.

PATIENT INFORMATION:

- Patients should be advised to read the “Patient Information” and “Instructions for Use”.
- Advise patients that Zuplenz™ may cause headache, malaise/fatigue, constipation, and diarrhea.
- Advise patients to inform their healthcare provider immediately if they use apomorphine and ondansetron concomitantly or tramadol and ondansetron concomitantly.
- Inform patients that Zuplenz™ may cause hypersensitivity reactions such as anaphylaxis and bronchospasm.
- Instruct patients on how to use Zuplenz™ film.

REFERENCES

Zuplenz™ Label Information. Strativa Pharmaceuticals, Inc,. Available online at: http://www.zuplenz.com/pdf/Zuplenz_PI_July-2010.pdf Last revised July 2010.

Appendix H

Annual Review of Otic Antibiotics - Fiscal Year 2010

Oklahoma HealthCare Authority

June 2011

Current Prior Authorization Criteria

Otic Antibiotics		
Tier 1	**Tier 2**	**Special PA***
Ofloxacin **(Floxin Otic®)**	Ciprofloxacin, Dex or HC **(Ciprodex®, Cipro HC®, Cetraxal® Drop.**)	Acetic Acid, Antipyrine, Benzocaine, Glycerin **(Auralgan®)**
Acetic acid **(Vosol®, Acetasol®)**	Neomycin,Polymixin B, HC, thonzonium **(Cortisporin TC®)**	Acetic Acid, HC **(Acetasol HC®, Vosol HC®)**
Neomycin, Polymixin B, HC **(Cortisporin®, Cortomycin®, Pediotic®)**	Neomycin,Colistin, HC **(Coly-Mycin®, and Coly Mycin-ES®)**	Acetic Acid, aluminum **(Borofair®)**
Chloroxylenol/Pramoxine **(Pramotic®)**	Chloroxylenol/Pramoxine/Zinc **(Zinotic®, Zinotic ES®, Chlorpram Z®)**	Acetic Acid/antpy/bcain/polico/al acet 5.4%-1.4% drops **(AABP®, PR Otic®, Otic Edge®)**
	Chloroxylenol, benzocaine, and HC **(Trioxin®)**	Antipyrine, benzocaine, glycerin, zinc 5.4-1-2-1% **(Neotic®)**

Prior Authorization Criteria

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

Criteria for Auralgan®:
Failed trials of an available generic product containing benzocaine/antipyrine /glycerin, and two (2) trials of oral pain relievers for a duration of 360 days.

Criteria for Acetasol HC®, Vosol HC®, Borofair®, AABP®, PR Otic®, Otic Edge® and Neotic®:

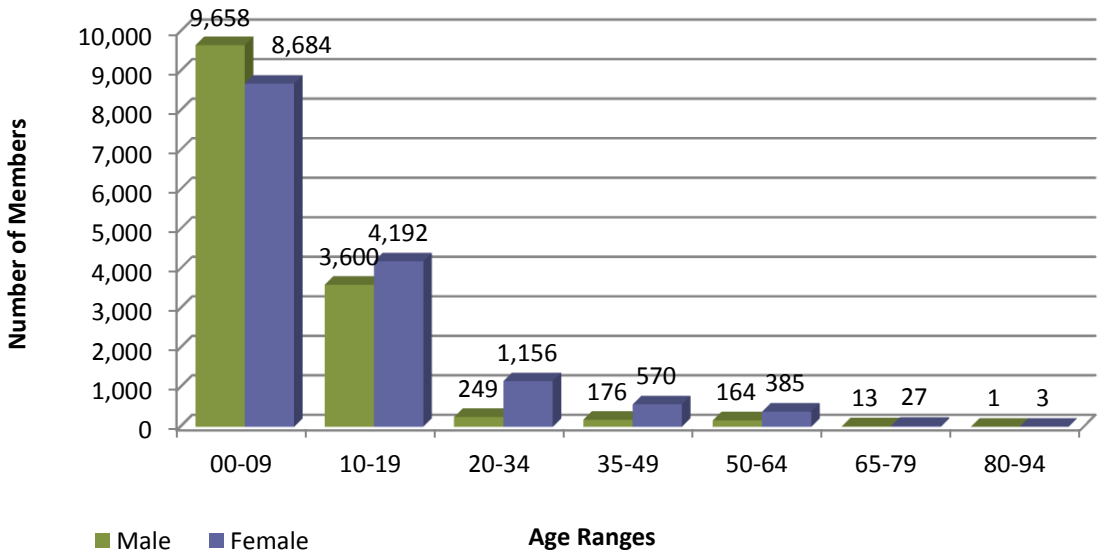
1. Diagnosis of acute otitis externa.
2. Recent (within 6 months) trials with all other commonly used topical otic anti-infectives that have failed to resolve infection, or
3. Allergy to all available products and failure of acetic acid alone.

Utilization of Otic Antibiotics

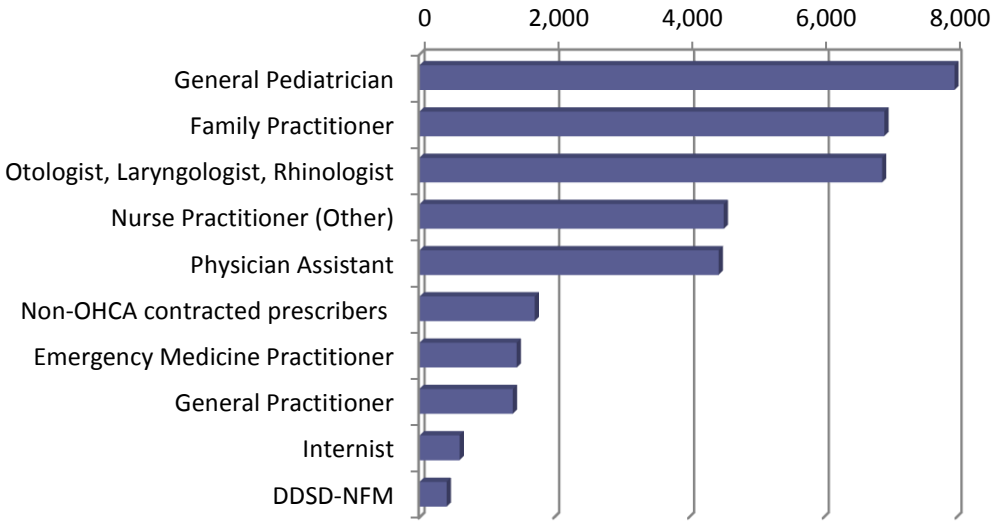
Comparison of Fiscal Years

Fiscal Year	Members	Claims	Cost	Cost/ Claim	Per-Diem	Units	Days
2009	26,404	35,055	$2,189,869.65	$62.47	$6.20	302,124	353,122
2010	28,878	37,202	$1,611,830.50	$43.33	$4.38	329,461	368,095
Percent Change	**9.40%**	**6.10%**	**(26.40%)**	**(30.60%)**	**(29.40%)**	**9.00%**	**4.20%**
Change	**2,474**	**2,147**	**($578,039.15)**	**($19.14)**	**($1.82)**	**27,337**	**14,973**

Demographics of Members Utilizing Otic Antibiotics: FY 2010

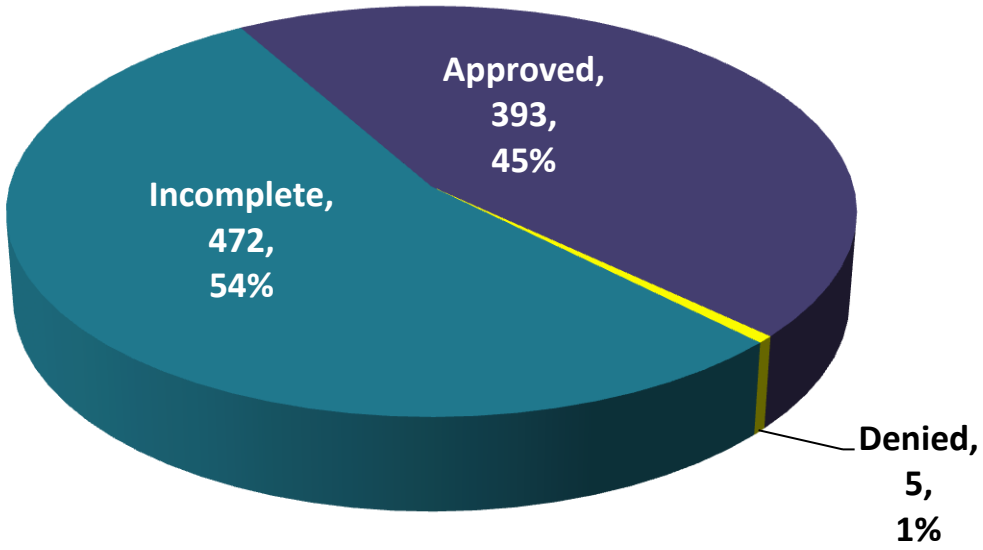


Top Ten Prescribers of Otic Antibiotics by Number of Claims: FY 2010



Prior authorization of Otic Antibiotics

There were a total of 870 petitions submitted for this PBPA category during fiscal year 2010. 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.



Market News and Update

- Ciprodex® (ciprofloxacin/dexamethasone) – patent anticipated to expire in 2020.
- Auralgan®
    - Warning letter was issued to Deston Therapeutics on 2/5/10 regarding the manufacture of new drugs that lack approved applications. Follow-up letters were also sent in April, June, and September 2010. The company continued to distribute.
    - U.S. Marshals, acting on behalf of the FDA, seized all lots of Auralgan® Otic Solution on 2/16/11, citing that the product did not have FDA approval and its labeling did not include adequate directions for use.

Recommendations

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

Utilization Details of Otic Antibiotics: Fiscal Year 2010

DRUG NAME	CLAIMS	MEMBERS	DAYS	COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
OFLOXACIN DROPS 0.3% Ofloxacin Otic	13,546	11,202	121,491	$201,152.21	$14.85	1.21	12.48%
CIPRODEX® SUSP 0.3-0.1% Ciprofloxacin/Dexamethasone	8,730	7,332	88,066	$941,274.02	$107.82	1.19	58.40%
NEO/POLY/HC SUSP 1% Neomycin-polymyxin/HC	7,939	7,448	80,326	$133,319.02	$16.79	1.07	8.27%
NEO/POLY/HC SOLN 1% Neomycin-polymyxin/HC	3,666	3,511	39,255	$58,788.92	$16.04	1.04	3.65%
CIPRO HC® SUSP 0.2-1% Ciprofloxacin/hydrocortisone	923	868	10,785	$99,648.25	$107.96	1.06	6.18%
NEOTIC® DROPS Antipyrine-benzocaine-glycerine-zinc 5.4-1-2-1%	859	789	10,206	$43,756.78	$50.94	1.09	2.71%
OTIC EDGE® SOLN antipyrine-benzocaine-polycosanol 5.4-1.4-0.0097%	629	618	5,739	$90,391.12	$143.71	1.02	5.61%
ACETIC ACID SOLN 2%	221	205	4,482	$7,484.90	$33.87	1.08	0.46%
CHLORPHENYL® DROPS Benzocaine-phenylephrine-Antipyrine 0.25-5-5%	185	178	2,084	$4,483.93	$24.24	1.04	0.28%
ZINOTIC® DROPS Chloroxylenol-glycerin-pramoxine-zinc 0.1-1-0.5-0.1%	177	164	2,012	$13,269.93	$74.97	1.08	0.82%
ZINOTIC ES® DROPS Chloroxylenol-glycerin-pramoxine-zinc 0.1-1-1-1%	103	100	823	$7,461.61	$72.44	1.03	0.46%
CORTISPORIN SUSP-TC® Neomycin-colistin-HC-thonzonium 3.3-3-10-0.5 MG/ML	54	51	690	$4,092.80	$75.79	1.06	0.25%
EAR-GESIC® DROPS Benzocaine-phenylephrine-antipyrine 0.25-5-5%	50	50	770	$736.30	$14.73	1	0.05%
ACETIC ACID/ALUMINUM SOLN 2%	35	24	423	$1,396.73	$39.91	1.46	0.09%
FLOXIN® DROPS (Singles)** Ofloxacin 0.3%	33	31	408	$2,239.68	$67.87	1.06	0.14%
COLY-MYCIN S® SUSP MG/ML Neomycin-colistin-HC-thonzonium 3.3-3-10-0.5	13	13	126	$746.90	$57.45	1	0.05%
CORTOMYCIN® SUSP 1% Neomycin-polymyxin-HC 3.5 MG/ML-10000 Unit/ML-1%	12	11	122	$188.72	$15.73	1.09	0.01%
CORTOMYCIN® SOLN 1% Neomycin-polymyxin-HC 1%	9	9	95	$106.17	$11.80	1	0.01%
PRAMOXINE/CHLORXYL Pramoxine-chloroxylenol 1-0.1%	6	6	66	$78.34	$13.06	1	0.00%
ACETIC ACID/ANTIPYRINE SOLN/ BNZ/PLY Acetic Acid-antipyrine-benzocaine-polycosanol Soln	5	5	50	$553.67	$110.73	1	0.03%
PR OTIC® SOLN Acetic Acid-antipyrine-benzocaine-polycosanol soln	4	4	49	$530.17	$132.54	1	0.03%
CHLORPRAM Z® DROPS Chloroxylenol/pramoxine/zinc 0.1%-0.5%	2	2	22	$110.16	$55.08	1	0.01%
HYDRO® EAR DROPS Hydrocortisone/pramoxine/chloroxylenol/benzalkonium 10-10-1/ML	1	1	5	$20.17	$20.17	1	0.00%
TOTALS	37,202	28,878	368,095	$1,611,830.50	$43.33	1.29	100%

***Total number of unduplicated members**

**** No longer on the market**

Appendix I

U.S. Food and Drug Administration

News & Events

FDA NEWS RELEASE

For Immediate Release: May 23, 2011
Media Inquiries: Erica Jefferson, 301-796-4988, erica.jefferson@fda.hhs.gov
Consumer Inquiries: 888-INFO-FDA

FDA approves Incivek for hepatitis C

The U.S. Food and Drug Administration today approved Incivek (telaprevir) to treat certain adults with chronic hepatitis C infection. Incivek is used for patients who have either not received interferon-based drug therapy for their infection or who have not responded adequately to prior therapies. Incivek is approved for use with interferon therapy made up of peginterferon alfa and ribavirin.

The current standard of care for patients with chronic hepatitis C infection is peginterferon alfa and ribavirin taken for 48 weeks. Less than 50 percent of patients respond to this therapy.

The safety and effectiveness of Incivek was evaluated in three phase 3 clinical trials with about 2,250 adult patients who were previously untreated, or who had received prior therapy. In all studies patients also received the drug with standard of care. In previously untreated patients, 79 percent of those receiving Incivek experienced a sustained virologic response (i.e. the infection was no longer detected in the blood 24 weeks after stopping treatment) compared to standard treatment alone.

The sustained virologic response for patients treated with Incivek across all studies, and across all patient groups, was between 20 and 45 percent higher than current standard of care.

The studies indicate that treatment with Incivek can be shortened from 48 weeks to 24 weeks in most patients. Sixty percent of previously untreated patients achieved an early response and received only 24 weeks of treatment (compared to the standard of care of 48 weeks). The sustained virologic response for these patients was 90 percent.

When a person achieves a sustained virologic response after completing treatment, this suggests that the hepatitis C infection has been cured.

Sustained virologic response can result in decreased cirrhosis and complications of liver disease, decreased rates of liver cancer (hepatocellular carcinoma), and decreased mortality.

"With the approval of Incivek, there are now two important new treatment options for hepatitis C that offer a greater chance at a cure for some patients with this serious condition," said Edward Cox, M.D., M.P.H, director, Office of Antimicrobial Products in FDA's Center for Drug Evaluation and Research. "The availability of new therapies that significantly increase responses while potentially decreasing the overall duration of treatment is a major step forward in the battle against chronic hepatitis C infection."

According to the U.S. Centers for Disease Control and Prevention, about 3.2 million people in the United States have chronic hepatitis C infection, a viral disease that causes inflammation of the liver that can lead to diminished liver function or liver failure.
Most people with hepatitis have no symptoms of the disease until liver damage occurs, which may take several years.

Most liver transplants performed in the United States are due to progressive liver disease caused by hepatitis C virus infection. After the initial infectio with hepatitis C (HCV), most people develop chronic hepatitis C. Some will develop cirrhosis of the liver over many years. Cirrhosis can lead to liver damage with complications such as bleeding, jaundice (yellowish eyes or skin), fluid accumulation in abdomen, infections, or liver cancer.

People can get HCV in a number of ways, including: exposure to blood that is infected with the virus; being born to a mother with HCV; sharing a needle; having sex with an infected person; sharing personal items such as a razor or toothbrush with someone who is infected with the virus, or from unsterilized tattoo or piercing tools.

Incivek is a pill taken three times a day with food. Incivek should be taken for the first 12 weeks in combination with peginterferon alfa and ribavirin. Most people with a good early response to the Incivek combination regimen can be treated for 24 weeks rather than the recommended 48 weeks of treatment with the standard of care. Incivek is part of a class of drugs referred to as protease inhibitors, which work by binding to the virus and preventing it from multiplying.

The most commonly reported side effects in patients receiving Incivek in combination with peginterferon alfa and ribavirin include rash, low red blood cell count (anemia), nausea, fatigue, headache, diarrhea, itching (pruritus), and anal or rectal irritation and pain. Rash can be serious and can require stopping Incivek or all three drugs in the treatment regimen.

On May 13, FDA approved Victrelis (boceprevir), another new treatment for chronic hepatitis C, marketed by Merck of Whitehouse Station, N.J.

Incivek is marketed by Cambridge, Mass.-based Vertex Pharmaceuticals.

For more information:

FDA: Incivek Approval Letter [1]

FDA: Incivek Prescribing Information [2]

FDA: Approved Drugs: Questions and Answers [3]

FDA: What's New at FDA in Hepatitis [4]

FDA: Hepatitis C Tests [5]

CDC: Hepatitis C Information for the Public [6]

The FDA, an agency within the U.S. Department of Health and Human Services, protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products.

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9. http://www.fda.gov/AboutFDA/ContactFDA/StayInformed/RSSFeeds/ucm144575.htm

U.S. Food and Drug Administration

News & Events

FDA NEWS RELEASE

For Immediate Release: May 20, 2011
Media Inquiries: Erica Jefferson, 301-796-4988, erica.jefferson@fda.hhs.gov
Consumer Inquiries: 888-INFO-FDA

FDA approves new HIV treatment

The U.S. Food and Drug Administration today approved Edurant (rilpivirine) in combination with other antiretroviral drugs for the treatment of HIV-1 infection in adults who have never taken HIV therapy (treatment-naïve).

Edurant belongs to a class of HIV drugs called non-nucleoside reverse transcriptase inhibitor (NNRTI). The drug works by blocking HIV viral replication Edurant is to be used as part of a highly active antiretroviral therapy (HAART) regimen that is designed to suppress the amount of HIV (viral load) in the blood. Edurant is a pill taken once a day with food.

"Patients may respond differently to various HIV drugs or experience varied side effects. FDA's approval of Edurant provides an additional treatment option for patients who are starting HIV therapy, "said Edward Cox, M.D., M.P.H, director, Office of Antimicrobial Products in the FDA's Center for Drug Evaluation and Research.

The safety and effectiveness of Edurant is based on 48-week data from two Phase 3 clinical trials with 1,368 adult subjects with HIV infection, and fror a 96-week (with extension to 192 weeks) trial. Patients had not received prior HIV therapy and were selected to receive treatment with Edurant or efavirenz (another FDA-approved NNRTI for the treatment of HIV infection). Both drugs were given in combination with other antiretroviral drugs.

Edurant was as effective as efavirenz in lowering viral load. In the Edurant and efavirenz groups, 83 percent and 80 percent of subjects, respectively, had undetectable amounts of HIV in their blood after 48 weeks of treatment. Patients receiving Edurant who had a higher viral load at the start of therapy were more likely not to respond to the drug than were patients with a lower viral load at the start of therapy. In addition, persons who failed therapy with Edurant developed more drug resistance than patients who failed efavirenz.

The most commonly reported side effects in patients taking Edurant included depression, difficulty sleeping (insomnia), headache and rash. Fewer patients stopped taking the drug due to side effects as compared to patients taking efavirenz.

Edurant does not cure HIV infection. Patients must stay on continuous HIV therapy to control HIV infection and decrease HIV-related illnesses.

Edurant is manufactured by Raritan, N.J-based Tibotec Therapeutics, a division of Centocor Ortho Biotech Inc.

For more information:

FDA: HIV and AIDS Activities [1]

FDA: Antiretroviral drugs used in the treatment of HIV infection [2]

CDC: HIV/AIDS [3]

HHS: AIDS News and Resources [4]

NIH: AIDS Information [5]

The FDA, an agency within the U.S. Department of Health and Human Services, protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products.

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3. http://www.cdc.gov/hiv/default.htm
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U.S. Food and Drug Administration

News & Events

FDA NEWS RELEASE

For Immediate Release: May 20, 2011
Media Inquiries: Erica Jefferson, 301-796-4988, erica.jefferson@fda.hhs.gov
Consumer Inquiries: 888-INFO-FDA

FDA approves Sutent for rare type of pancreatic cancer

The U.S. Food and Drug Administration today approved Sutent (sunitinib) to treat patients with progressive neuroendocrine cancerous tumors located in the pancreas that cannot be removed by surgery or that have spread to other parts of the body (metastatic).

Neuroendocrine tumors found in the pancreas are slow-growing and rare. It is estimated that there are fewer than 1,000 new cases in the United States each year.

This is the second new approval by the FDA to treat patients with this disease; on May 5, the agency approved Afinitor (everolimus).

"FDA believes it is important to provide cancer patients with as many treatment options as possible," said Richard Pazdur, M.D., director of the Office of Oncology Drug Products in the FDA's Center for Drug Evaluation and Research. "The agency is committed to working with companies to bring innovative new therapies to the market and encourages companies to continue exploring additional uses for approved products."

The safety and effectiveness of Sutent was established in a single study of 171 patients with metastatic (late-stage) or locally advanced (disease that could not be removed with surgery) disease who received Sutent or a placebo (sugar pill). The study was designed to measure the length of time a patient lived before their disease spread or worsened (progression-free survival).

Results from the study demonstrate that Sutent provided benefit to patients by prolonging the median length of time they lived without the cancer spreading or worsening to 10.2 months compared to 5.4 months for patients who received placebo.

In patients treated with Sutent for neuroendocrine pancreatic tumors, the most commonly reported side effects included diarrhea, nausea, vomiting, fatigue, anorexia, high blood pressure, energy loss (asthenia), stomach (abdominal) pain, changes in hair color, inflammation of the mouth (stomatitis), and a decrease in infection-fighting white blood cells (neutropenia).

Sutent is also FDA-approved to treat patients with late-stage kidney cancer (metastatic renal cell carcinoma) and to treat patients with GIST (gastrointestinal stromal tumor), a rare cancer of the stomach, bowel, or esophagus.

Sutent is marketed by New York City-based Pfizer.

For more information:

FDA: Office of Oncology Drug Products [1]

FDA: Approved Drugs: Questions and Answers [2]

NCI: Pancreatic Cancer [3]

The FDA, an agency within the U.S. Department of Health and Human Services, protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products.

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6. http://www.fda.gov/AboutFDA/ContactFDA/StayInformed/RSSFeeds/ucm144575.htm

U.S. Food and Drug Administration

Safety

Avandia (rosiglitazone): REMS - Risk of Cardiovascular Events

includes Avandia, Avandamet, and Avandaryl

[UPDATED 05/18/2011] FDA notified healthcare professionals and the public of new restrictions to the prescribing and use of rosiglitazone-containing medicines. These medicines to treat type II diabetes are sold under the names Avandia, Avandamet, and Avandaryl. Healthcare providers and patients must enroll in a special program in order to prescribe and receive these drugs.

FDA has modified the REMS for Avandamet and Avandaryl because previously, the REMS consisted of only a Medication Guide. The REMS, which now includes a restricted access and distribution program, applies to all three rosiglitazone products.

[UPDATED 02/04/2011] FDA notified healthcare professionals and patients that information on the cardiovascular risks (including heart attack) of rosiglitazone has been added to the physician labeling and patient Medication Guide. This information was first announced by FDA on September 23, 2010 as part of new restrictions for prescribing and use of this drug.

Rosiglitazone is sold as a single-ingredient product under the brand name Avandia. Rosiglitazone is also sold as a combination product under the branc name Avandamet (contains rosiglitazone and metformin) and under the brand name Avandaryl (contains rosiglitazone and glimepiride).

In addition to describing the cardiovascular risks, the drug labels have been revised to state that rosiglitazone and rosiglitazone-containing medicines should only be used:

- In patients already being treated with these medicines
- In patients whose blood sugar cannot be controlled with other anti-diabetic medicines and who, after consulting with their healthcare professional, do not wish to use pioglitazone-containing medicines (Actos, Actoplus Met, Actoplus Met XR, or Duetact).

[Posted 09/23/2010]

AUDIENCE: Endocrinology, Cardiology

ISSUE: FDA notified healthcare professionals and patients that it will significantly restrict the use of the diabetes drug Avandia (rosiglitazone) to patients with Type 2 diabetes who cannot control their diabetes on other medications. These new restrictions are in response to data that suggest an elevated risk of cardiovascular events, such as heart attack and stroke, in patients treated with Avandia.

BACKGROUND: Avandia is in a class of drugs known as thiazolidinediones, or TZDs. It is intended to be used in conjunction with diet and exercise to improve glucose (blood sugar) control in patients with Type 2 diabetes mellitus. Rosiglitazone also is available in combination with other diabetes medications, metformin under the brand name Avandamet or glimepiride under the brand name Avandaryl.

RECOMMENDATION: FDA will require that GSK develop a restricted access program for Avandia under a risk evaluation and mitigation strategy, or REMS. Under the REMS, Avandia will be available to new patients only if they are unable to achieve glucose control on other medications and are unable to take Actos (pioglitazone), the only other drug in this class. Current users of Avandia who are benefiting from the drug will be able to continu using the medication if they choose to do so.

Doctors will have to attest to and document their patients' eligibility; patients will have to review statements describing the cardiovascular safety concerns associated with this drug and acknowledge they understand the risks. The agency anticipates that the REMS will limit use of Avandia significantly.

Healthcare professionals and patients are encouraged to report adverse events or side effects related to the use of these products to the FDA's MedWatch Safety Information and Adverse Event Reporting Program:

- Complete and submit the report Online: www.fda.gov/MedWatch/report.htm [1]
- Download form [2] or call 1-800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178

[05/18/2011 - Drug Safety Communication [3] - FDA]
[02/03/2011 - Drug Safety Communication [4] - FDA]
[02/03/2011 - Prescribing Information/Medication Guide [5] - GSK]
[09/23/2010 - News Release [6] - FDA]
[09/23/2010 - Q&As [7] - FDA]
[09/23/2010 - Avandia Related Information [8] - FDA]

Links on this page:

1. http://www.fda.gov/MedWatch/report.htm
2. /Safety/MedWatch/HowToReport/DownloadForms/default.htm
3. /Drugs/DrugSafety/ucm255005.htm
4. /Drugs/DrugSafety/ucm241411.htm
5. http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/021071s038lbl.pdf

6. /NewsEvents/Newsroom/PressAnnouncements/2010/ucm226975.htm
7. /Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm226976.htm
8. /Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm226956.htm

U.S. Food and Drug Administration

Inspections, Compliance, Enforcement, and Criminal Investigations

Shire Pharmaceuticals, Inc. 5/6/11

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Silver Spring, MD 20993

TRANSMITTED BY FACSIMILE

Angus Russell
Chief Executive Officer
Shire Pharmaceuticals, Inc.
725 Chesterbrook Blvd.
Wayne, PA 19087-5637

RE: NDA 021977
Vyvanse® (lisdexamfetamine dimesylate) Capsules, CII
MACMIS #19828

WARNING LETTER

Dear Mr. Russell:

The Division of Drug Marketing, Advertising, and Communications (DDMAC) of the U.S. Food and Drug Administration (FDA) has reviewed a magnet (LDX1617) for Vyvanse (lisdexamfetamine dimesylate) Capsules, CII (Vyvanse) of Shire Pharmaceuticals, Inc. (Shire). Photographs of this piece were taken at a pediatric medical office in 2011 and submitted as part of a complaint to the DDMAC Bad Ad Program. The magnet is violative because it makes representations regarding the use of Vyvanse, but omits the full indication and risks associated with the use of the drug. Thus, the magnet misbrands the drug in violation of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. 352(a) and 321(n). Cf. 21 CFR 202.1(e)(3)(i), (ii); (e (5) & (e)(6)(i). These violations are concerning from a public health perspective because they suggest that Vyvanse is safer and more effective than has been demonstrated.

Background

According to its FDA-approved product labeling (PI),[1] Vyvanse is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in children. The efficacy of Vyvanse in the treatment of ADHD was established in children aged 6-12 years. The INDICATIONS AND USAGE section of the PI also includes information regarding special diagnostic considerations, the need for comprehensive treatment, and long-term use.

Vyvanse is associated with a number of serious risks, some of which are fatal, including a Boxed Warning concerning the potential for abuse. Vyvanse has numerous Contraindications, including use in patients with advanced arteriosclerosis, symptomatic cardiovascular disease, moderate to severe hypertension, hyperthyroidism, known hypersensitivity or idiosyncratic reaction to sympathomimetic amines, glaucoma, agitated states, history of dru abuse; and use during or within 14 days following the administration of monoamine oxidase inhibitors. The PI includes Warnings related to serious cardiovascular events, psychiatric adverse events, long-term suppression of growth, seizures, and visual disturbances. The PI also contains a general Precaution regarding overdosage and use in patients who use other sympathomimetic drugs, as well as Precautions for patients with tics and Tourette ' syndrome. The most common adverse reactions associated with the use of Vyvanse include upper abdominal pain, decreased appetite, dizziness, dry mouth, irritability, insomnia, nausea, vomiting, and decreased weight.

Omission of Indication and Risk Information

Promotional materials are misleading if they fail to reveal facts that are material in light of the representations made by the materials or with respect to the consequences that may result from the use of the drug as recommended or suggested by the materials.

Photographs, submitted as part of this Bad Ad complaint, show a promotional magnet for Vyvanse. Scanning from top to bottom, the magnet includes the product trade and established names, certain claims described below, images of six different dosage strengths of Vyvanse capsules, and the statement, "Your Vyvanse sales representative is." Immediately below this statement there is a clear plastic sleeve, which, at the time the photograph were taken, included a Shire sales representative's business card. Behind the clear plastic sleeve, the magnet contains printed risk information. As explained further below, the design of this magnet resulted in the inserted business card covering the majority of risk information.

The presentation includes the following claims (emphasis in original):

- "Vyvanse™ CII . . .
The First Prodrug Stimulant" (magnet)

- "Vyvanse – Titrate to achieve maximum efficacy and tolerability" (magnet)

- "Shire US Inc.
your ADHD Support Company™ " (magnet)

- "[Sales representative name] . . .
ADHD sales " (business card)

The totality of this presentation makes representations about the use of Vyvanse in the treatment of ADHD. However, this promotional piece fails to adequately communicate the full indication for Vyvanse including important information regarding special diagnostic considerations, the need for comprehensive treatment, and long-term use.

The magnet also fails to adequately disclose risk information associated with the use of Vyvanse. As mentioned above, DDMAC notes that risk information is printed on the lower-half of the magnet below the statement, "Your Vyvanse sales representative is. " However, as a practical matter, this information is not communicated to the viewer. The magnet is designed for a Shire ADHD sales representative to place his or her business card in the sleeve, thus covering the majority of the important risk information. For example, a photograph that was submitted as part of this Bad Ad complaint shows a business card positioned in the sleeve of the magnet such that only the most common adverse reactions are visible. Presenting the risk information in this manner is not sufficient to ensure that the claims on the magnet are truthful and non-misleading. This omission of risk information is particularly concerning given that the PI for Vyvanse discusses numerous risks, including a Boxed Warning regarding the potential for abuse.

As a result, the totality of this presentation misleadingly suggests that Vyvanse is safer and more effective than has been demonstrated by substantial evidence or substantial clinical experience. We note that the statement, "Please see accompanying Full Prescribing Information, including Boxed Warning, " is included on the bottom of the magnet; however, this statement does not mitigate the omission of indication and risk information.

Conclusion and Requested Action

For the reasons discussed above, the magnet misbrands Vyvanse in violation of the Act, 21 U.S.C. 352(a) and 321(n). Cf. 21 CFR 202.1(e)(3)(i), (ii); (e)(5) & (e)(6)(i).

DDMAC requests that Shire immediately cease the dissemination of violative promotional materials for Vyvanse such as those described above. Please submit a written response to this letter on or before May 20, 2011, stating whether you intend to comply with this request, listing all promotional materials (with the 2253 submission date) for Vyvanse that contain violations such as those described above, and explaining your plan for discontinuing use of such violative materials. Because the violations described above are serious, we request, further, that your submission include a comprehensive plan of action to disseminate truthful, non-misleading, and complete corrective messages about the issues discussed in this letter to th audience(s) that received the violative promotional materials. Please direct your response to me at the Food and Drug Administration, Center for Drug Evaluation and Research, Division of Drug Marketing, Advertising, and Communications, 5901-B Ammendale Road, Beltsville, MD 20705-1266, or facsimile at 301-847-8444. In all future correspondence regarding this matter, please refer to MACMIS# 19828 in addition to the NDA number. We remind you that only written communications are considered official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for Vyvanse comply with each applicable requirement of the Act and FDA implementing regulations.

Failure to correct the violation discussed above may result in FDA regulatory action, including seizure or injunction, without further notice.

Sincerely,
{See appended electronic signature page}
Thomas W. Abrams, RPh, MBA
Director
Division of Drug Marketing,
Advertising, and Communications
Reference ID: 2943099

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

THOMAS W ABRAMS
05/06/2011
Reference ID: 2943099

[1] The magnet that is the subject of this letter is dated March 2008. Therefore, the PI referred to in this letter is the one approved in December 2007; however, the most recent version of the approved PI was approved in March 2011.

Links on this page: