Drug Utilization Review Board

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

Thursday
November 12, 2009
6:00 p.m.

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

MEMORANDUM

TO: Drug Utilization Review Board Members

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

SUBJECT: **Packet Contents for Board Meeting – November 12, 2009**

DATE: November 4, 2009

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

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

Enclosed are the following items related to the November 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.

OHCA Budget Report

Action Item – Vote to Prior Authorize Effient™ – See Appendix C.

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

Action Item – Vote to Prior Authorize Edluar™ and Intermezzo®– See Appendix E.

30 Day Notice to Prior Authorize Antiemetics – See Appendix F.

30 Day Notice to Prior Authorize Valturna™ – See Appendix G.

30 Day Notice to Prior Authorize Intuniv™ – See Appendix H.

FDA and DEA Updates – See Appendix I.

Future Business

Adjournment

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Drug Utilization Review Board

(DUR Board)

Meeting – November 12, 2009 @ 6:00 p.m.

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

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

1. Call To Order

A. Roll Call – Dr. Graham

Items to be presented by Dr. Muchmore, Chairman:

2. Public Comment Forum

A. Acknowledgment of Speakers and Agenda Items

Items to be presented by Dr. Muchmore, Chairman:

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

A. October 14, 2009 DUR Minutes – Vote
B. October 15, 2009 DUR Recommendation Memorandum

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

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

A. Retrospective Drug Utilization Review for August 2009
B. Retrospective Drug Utilization Review Response for July 2009
C. Medication Coverage Activity Audit for October 2009
D. Help Desk Activity Audit for October 2009

Items to be presented by Carrie Evans, OHCA Chief Financial Officer, Dr. Muchmore, Chairman:

5. OHCA Budget Report

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

6. Action Item - Vote to Prior Authorize Effient™ – See Appendix C.

A. COP Recommendations

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

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

A. COP Recommendations

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

8. Action Item – Vote to Prior Authorize Edluar™ and Intermezzo® – See Appendix E.

A. Product Summaries
B. COP Recommendations

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

9. 30 Day Notice to Prior Authorize Antiemetics – See Appendix F.

A. Product Summaries
B. Utilization Review
C. COP Recommendations

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

10. 30 Day Notice to Prior Authorize Valturna™ – See Appendix G.

A. Product Summary
B. COP Recommendations

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

11. 30 Day Notice to Prior Authorize Intuniv™ – See Appendix H.

A. Product Summary
B. COP Recommendations
C. Product Details

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

12. FDA and DEA Updates – See Appendix I.

13. Future Business

A. Anxiolytic Criteria Review
B. Antipsychotic Review
C. New Product Reviews
D. Annual Reviews

14. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES of MEETING of OCTOBER 14, 2009

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

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

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

OTHERS PRESENT:

Kirsten Mar, Lilly	Suzanne Baker, Lilly	Mark DeClerk, Lilly
Aaron Mays, Alcon	William Dozier, Gilead	Jeff Himmelberg GSK
John Seidenberger, B-I	Janie Huff, Takeda Pharma	Tracy Copeland, DSI
Ron Schnare, Shire	Linda Cantu, BMS	Carlos Palasciano, Hawthorn
Katheleen Pinto, BMS	Randy Ziss, BMS	Donna Erwin, BMS
David Cushing, Sciele Pharma Sales	Rob Thomas, Sciele	David Williams, Forest
Pat Trahan, Taro	Kelly Rogers, Taro	Steve Witten, Taro
Toby Thompson, Pfizer	Darryl Davis, Pfizer	Jim Graham, Ortho McNeil Janssen
M.P. Laster, Genentech	Richard Ponder, Johnson & Johnson	Charlene Kaiser, Amgen
David Barton	Schering Plough	Jim Fowler, Astra Zeneca
Brian Maves, Pfizer	Daniel Ting, Pfizer	Zann McMahan, M.D.
Chris Aiken, Pfizer		

PRESENT FOR PUBLIC COMMENT:

Agenda Item No. 5	Zann McMahan, M.D.
Agenda Item No. 8	Randy Ziss, Katheleen Pinto; Bristol-Myers Squibb
Agenda Item No. 9	Steve Whiten, Taro Pharmaceuticals

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

1A: Roll Call

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

ACTION: NONE REQUIRED

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

Dr. Muchmore recognized the speakers for public comment.

Agenda Item No. 5 Zann McMahan, M.D.

Agenda Item No. 8 Randy Ziss and Katheleen Pinto; Bristol-Myers Squibb

Agenda Item No. 9 Steve Whiten, Taro Pharmaceuticals

ACTION: NONE REQUIRED

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

3A: September 9, 2009 DUR Minutes

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

ACTION: MOTION CARRIED

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

4A: Retrospective Drug Utilization Review: July 2009

4B: Retrospective Drug Utilization Review Response: May 2009

4C: Medication Coverage Activity Audit: September 2009

4D: Help Desk Activity Audit: September 2009

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: **VOTE TO PRIOR AUTHORIZE FIBROMYALGIA MEDICATIONS**

For Public Comment, Zann McMahan, M.D.: Thanks everyone for the opportunity to speak real fast. I am a family practice doc. I, without knowing a lot of the background on the issue at hand as far as prescription habits and things like that, I would just like to say that I think it would be taking a huge piece of the armamentarium out of the battle that we face with fibromyalgia. If we were to remove this medicine, move it down the tier I guess, so to speak, but I think it's a, whether some in the medical community won't admit to how impactful fibro can be. I know doctors who, who are taking Medicaid patients, it's, sometimes you kind of got to do a lot of things on your own that typically you'd rather refer that out to, but I think that's a huge piece of the puzzle that we'd be taking away with things made harder to get to than it is now. I think that, like I said before, I don't know prescription habits of my colleagues, but I don't, I think that, it is a, I think it's a part that we would sorely miss in addition to other medications, I don't. Plus I don't know when you start adding combinations of medications such as Cymbalta and Lyrica, those types of medications, I don't know really how you would differentiate sometimes between fibro which, as we know, doesn't have a, you know, a great test we can do to say, okay, this patient has it, this patient doesn't, and you kind of treat the symptoms and we have a limited amount of drugs out there anyway to use for it and so I don't know that it makes a whole lot of sense to whittle that lot down much by hamstringing us with this proposal that, plus I think it's been beneficial to actually have one that's been FDA approved for fibro, so that's, that's, that speaks volumes I think for that medication, so anyway, that's all I had to say.

Dr. Muchmore: I have a question. Has the FDA ever reviewed amitriptyline, cyclobenzaprine, fluoxetine for use in fibromyalgia?

Dr. McMahan: Not that I'm aware of. Probably not much money in it.

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

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE OTIC ANTI-INFECTIVES**

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

Dr. Harrell moved to approve as amended (PA Criteria #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."*; seconded by Ms. Varalli-Claypool.

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: **VOTE TO PRIOR AUTHORIZE NEW NARCOTIC ANALGESIC MEDICATIONS**

Materials included in agenda packet; presented by Dr. Keast.
Dr. Feightner moved to approve as submitted; seconded by Dr. Kuhls.
ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: **ANNUAL REVIEW OF PLAVIX® AND 30-DAY NOTICE TO PRIOR AUTHORIZE EFFIENT™**

For Public Comment, Katheleen Pinto; Bristol-Myers Squibb: Hello, thank you all for having us to give this testimony. My name is Katheleen Pinto. I'm the medical science liaison for Bristol Myers cardiovascular. I want to talk to you a little bit about Plavix and just kind of give you some refreshers for your memory in terms of what we, what we do, with this compound. Remember that Plavix has had eight clinical trials in which the safety and efficacy data was born out of for over 100,000 patients and that safety profile was over a broad range of patients. That included patients with coronary artery disease, recent MI, established PAD, peripheral arterial disease, recent ischemic stroke. And then we also had safety in real world patients in over 70 million patients. Accordingly, our safety profile was not limited to patient type, i.e., whether or not in acute coronary syndromes, whether or not a patient's artery anatomy was known or not known, whether they were, their body habitus is small or large, age was not a limiting factor as well, nor was gender. But we talk about the CURE trial and looked at the ACS component of that and looked specifically in terms of safety at bleeding. We find that bleeding was very sensitive, is a sensitive marker in that trial, in which 1% of patients bled on the combination of dual antiplatelet therapy over aspirin alone. And this is much different, in opposed to the TRITON, I'm sorry, the TIMI definition which was a lot more robust in terms of defining that criteria for bleeding. Lastly we want you to know that Bristol Myers Squibb voluntarily changed our verbiage in our package insert according to the FDA, in accordance with the FDA. We included information on polymorphism and drug interactions, the latter of which we had two clinical, two current congresses that were just recently in which, it was recently presented where the drug interactions were actually cited to not be as big of a problem as we once thought. Those trials actually did not show endpoints as far as cardiovascular events. Bristol Myers Squibb is currently sponsoring clinical studies to analyze that data a little bit further so that we can come back and tell the community and the public that the drug interactions really do not exist in terms of causing cardiovascular events. With that, I'll ask if you have any questions.
Materials included in agenda packet; presented by Dr. Keast.
Dr. Kuhls moved to approve as submitted; seconded by Dr. Feightner.
ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: **ANNUAL REVIEW OF TOPICAL ANTIPARASITICS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ULESFIA™**

For Public Comment, Steve Whiten, Taro Pharmaceuticals: I'm Steve Whiten. I'm senior national director of integrated health care with Taro Pharma. What that means is I have the whole United States, all payer systems, private and public. Here to talk about a category nobody really likes to talk about, you know, it's head lice and nobody gets excited. Generally head lice and all antiparasitics are less than one-half of one percent of total drug expenditure in most drug programs and there's certainly no mortality and probably no real morbidity associated with it, so you may ask why I'm up here. Well it does have financial and social implications for the taxpayers and the children and their families and pediatric providers in Oklahoma and every state. Here on the front line of dealing with it in communities like Shawnee and like Muskogee, places where head lice is rampant. I'm just here to restate some of the reasons that was considered last year. According to the most recently well controlled clinical direct comparison of the older Permethrin 1% products and the Ovide, the two numbers I would ask you to remember are 98 and 45. 98% is the response rate for Ovide. It's well controlled, clinical met comparative trial and one patient was (unintelligible) one could not respond. 45% was the response rate to Permethrin 1% and this was with skilled head lice professions applying the medication more than one time if necessary, so it wasn't a matter of compliance. So I'm just here to say that for the pharmacoeconomic total decision for the State of Oklahoma, equal access, not Ovide preferred over any other agent, but equal first line access with no resistance reported in the US and over 30 years of systemic use with no systemic side effects worldwide from malathion. And that's essentially it. I'll be glad to take any questions, comments, or have a seat.
Materials included in agenda packet; presented by Dr. Patel.
Dr. Kuhls moved to approve only generics and OTC in Tier 1; must try one of Tier 1's to move to Tier 2 trial, then on to Tier 3 after trials; seconded by Dr. Feightner.
ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: **ANNUAL REVIEW OF HYPNOTIC MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE EULUAR™ AND INTERMEZZO®**

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

AGENDA ITEM NO. 11: **FDA & DEA UPDATES**

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 12: **FUTURE BUSINESS**

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

12A: The November meeting will be held on Thursday, November 12, 2009.

12B: Anxiolytic Criteria Review

12C: Antiemetic Utilization Review

12D: New Product Reviews

ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: **ADJOURNMENT**

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

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

Memorandum

Date: October 29, 2009

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

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

Subject: DUR Board Recommendations from Meeting of October 14, 2009

Recommendation 1: Vote to Prior Authorize Fibromyalgia Medications

MOTION CARRIED by unanimous approval.

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

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

*May be rebated to Tier 2 status only.

Approval Criteria:

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

Recommendation 2: Vote to Prior Authorize Otic Anti-Infectives

MOTION CARRIED by unanimous approval.

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

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

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

Prior Authorization Criteria

1. Member must have adequate 14-day trial of at least two Tier 1 medications, or
2. Approval may be granted if there is a unique FDA approved indication not covered by Tier 1 products or infection by organism not known to be covered by ~~all~~ 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.

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

Recommendation 3: Vote to Prior Authorize New Narcotic Analgesic Medications

MOTION CARRIED by unanimous approval.

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

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

Recommendation 4: Annual Review of Plavix

MOTION CARRIED by unanimous approval.

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

1. Plavix® therapy will be approved for members who:
    a. meet approved diagnostic criteria, ~~and~~
    b. ~~have failed aspirin therapy (due to either side effects or event recurrence), or have a documented aspirin allergy, or use Plavix® concomitantly with aspirin.~~

2. The approved diagnoses are as follows:
    a. Recent stroke
    b. Recent myocardial infarction
    c. Established peripheral artery disease

d. Acute coronary syndrome (unstable angina/non-Q-wave MI)
e. Percutaneous coronary intervention with stent placement ~~(aspirin trial not required)~~
f. Transient ischemic attacks

3. Length of approval: 1 year.

Recommendation 4: Annual Review of Anti-Parasitics

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommended no changes at this time.

The DUR Board recommended the following changes to the current criteria:

Approval of Tier 2 medication requires a recent trial of one Tier 1 medication with inadequate response or adverse effect.

Approval of Tier 3 medication requires recent trial(s) with all available Tier 2 medication(s) with inadequate response or adverse effect.

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

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

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

Crotamiton lotion (Eurax®)
- Member must be at least 18 years of age
- Quantity limit of 60 grams or milliliters for 30 day supply

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

Appendix B

Retrospective Drug Utilization Review Report

Claims Reviewed for August 2009

Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
Total # of messages returned by system when no limits were applied	43,843	56,783	990,328	30,844
Limits which were applied	Established, Major, Males and Females, Age 19-35	Males and Females, Narcotics, Age 28-29	Contraindicated, Epilepsy, Males and Females, Age 51-150	High Dose Only, Modified Cyclics (Trazodone), Males and Females, Age 0-150
Total # of messages after limits were applied	57	150	39	12
Total # of members reviewed after limits were applied	57	122	26	12

LETTERS			
Prescribers		**Pharmacies**	
Sent	**Responded**	**Sent**	**Responded**
146		25	

Retrospective Drug Utilization Review Report

Claims Reviewed for July 2009

Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
Limits which were applied	Established, Major, Males and Females, Age 0-18	Narcotics, Males and Females, Age 26-27	Contraindicated, Epilepsy, Males and Females, Age 19-50	High Dose and Duration, Tetracyclics, Males and Females, Age 0-150

Response Summary (Prescriber)
Letters Sent: 121
Response Forms Returned: 75

The response forms returned yielded the following results:

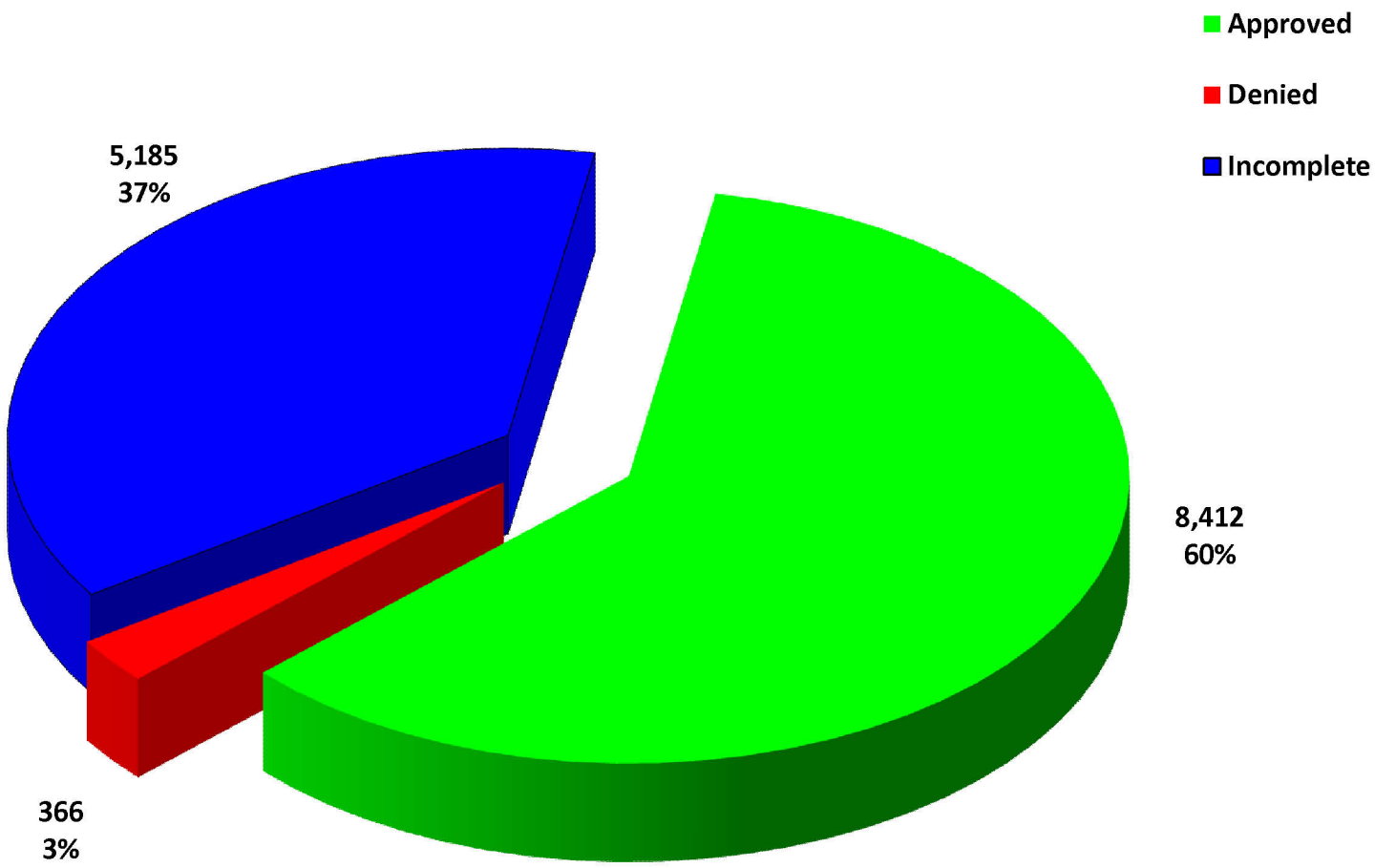
6 (8%)	*Record Error—Not my patient.*
14 (19%)	*No longer my patient.*
3 (4%)	*Medication has been changed prior to date of review letter.*
19 (25%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
23 (31%)	*I am aware of this situation and will plan to continue monitoring therapy.*
10 (13%)	*Other*

Response Summary (Pharmacy)
Letters Sent: 0
Response Forms Returned: 0

The response forms returned yielded the following results:

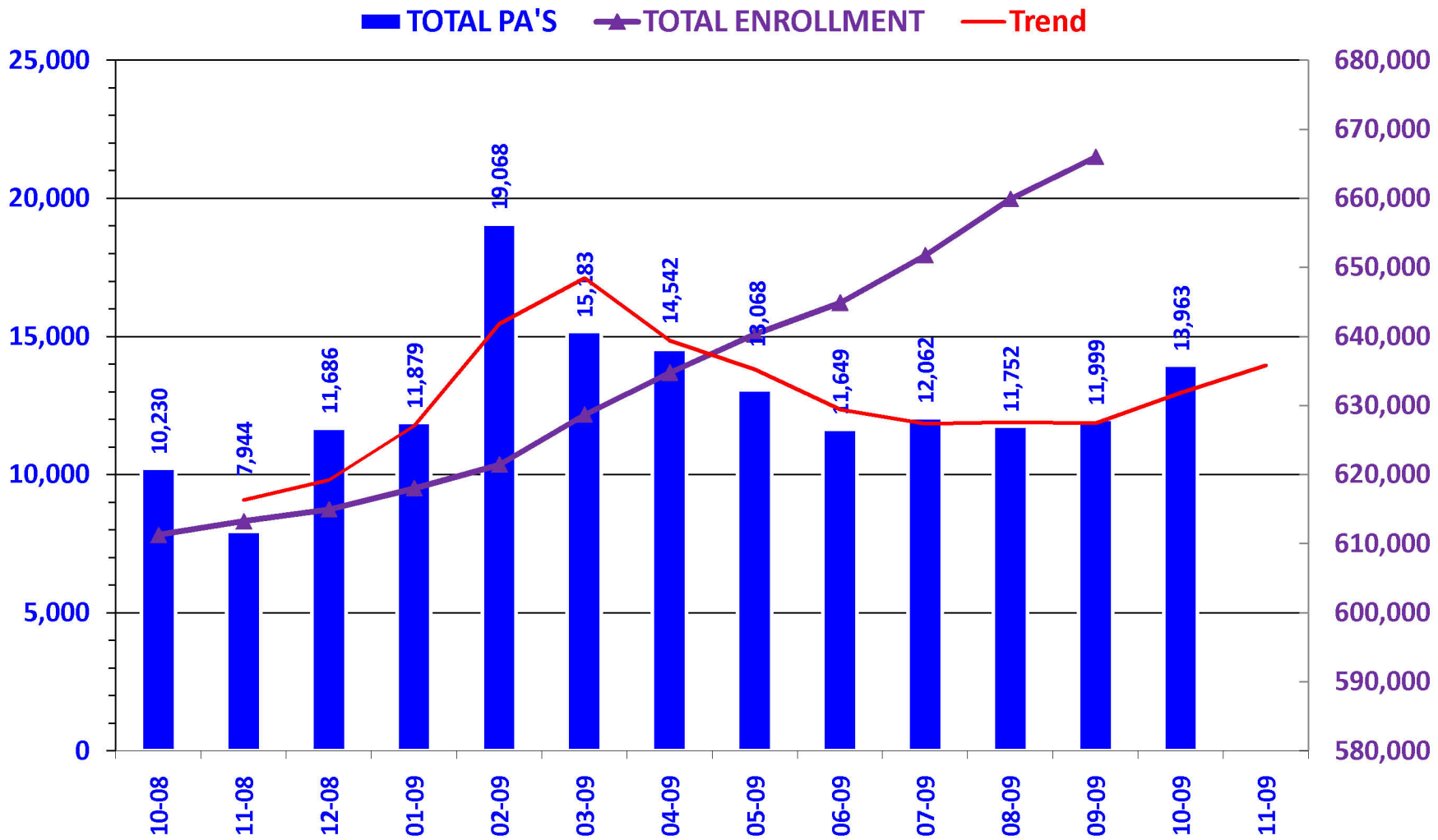
0 (0%)	*Record Error—Not my patient.*
0 (0%)	*No longer my patient.*
0 (0%)	*Medication has been changed prior to date of review letter.*
0 (0%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
0 (0%)	*I am aware of this situation and will plan to continue monitoring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

PRIOR AUTHORIZATION ACTIVITY REPORT: October 2009



PA totals include overrides

PRIOR AUTHORIZATION REPORT: October 2008 – October 2009



PA totals include overrides

Prior Authorization Activity

10/1/2009 Through 10/31/2009

	Average Length of	Approved	Denied	Incomplete	Total
Advair/Symbicort	355	345	3	485	833
Amitiza	193	8	0	9	17
Antidepressant	337	194	1	416	611
Antihistamine	315	178	1	231	410
Antihypertensives	353	67	2	113	182
Benzodiazepines	102	3,788	20	778	4,586
Bladder Control	336	10	0	11	21
Brovana (Arformoterol)	365	1	0	0	1
Byetta	363	7	0	10	17
Elidel/Protopic	91	19	0	36	55
ESA	62	124	1	45	170
Fibric Acid Derivatives	271	3	0	7	10
Fortamet/Glumetza	360	1	0	0	1
Forteo	359	1	0	2	3
Glaucoma	363	8	0	6	14
Growth Hormones	175	36	3	7	46
HFA Rescue Inhalers	258	68	1	97	166
Insomnia	135	50	4	129	183
Misc Analgesics	128	14	18	17	49
Muscle Relaxant	41	71	52	62	185
Nasal Allergy	215	9	45	128	182
NSAIDS	325	49	2	99	150
Nucynta	0	0	1	5	6
Ocular Allergy	170	5	0	36	41
Ocular Antibiotics	16	5	1	17	23
Opioid Analgesic	153	70	7	119	196
Other	140	179	16	310	505
Pediculicides	18	35	0	56	91
Plavix	352	110	0	65	175
Proton Pump Inhibitors	115	124	5	311	440
Qualaquin (Quinine)	0	0	1	0	1
Singulair	272	476	3	543	1,022
Smoking Cessation	52	20	4	57	81
Statins	346	18	2	35	55
Stimulant	227	719	4	365	1,088
Symlin	92	1	0	5	6
Synagis	163	379	143	227	749
Topical Antibiotics	28	9	0	39	48
Topical Antifungals	16	5	0	24	29
Ultram ER and ODT	0	0	0	1	1
Xolair	361	1	0	2	3
Xopenex Nebs	254	39	0	36	75
Zetia (Ezetimibe)	347	20	0	7	27
Emergency PAs		0	0	0	0
Total		**7,266**	**340**	**4,948**	**12,554**

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

Overrides					
Brand	173	53	2	16	71
Dosage Change	20	494	7	35	536
High Dose	128	3	1	1	5
IHS - Brand	60	53	0	7	60
Ingredient Duplication	29	13	0	6	19
Lost/Broken Rx	18	94	1	1	96
Nursing Home Issue	14	74	0	5	79
Other	20	31	1	8	40
Quantity vs. Days Supply	198	328	14	158	500
Stolen	31	3	0	0	3
Overrides Total		**1,146**	**26**	**237**	**1,409**
Regular PAs + Overrides Total		**8,412**	**366**	**5,185**	**13,963**

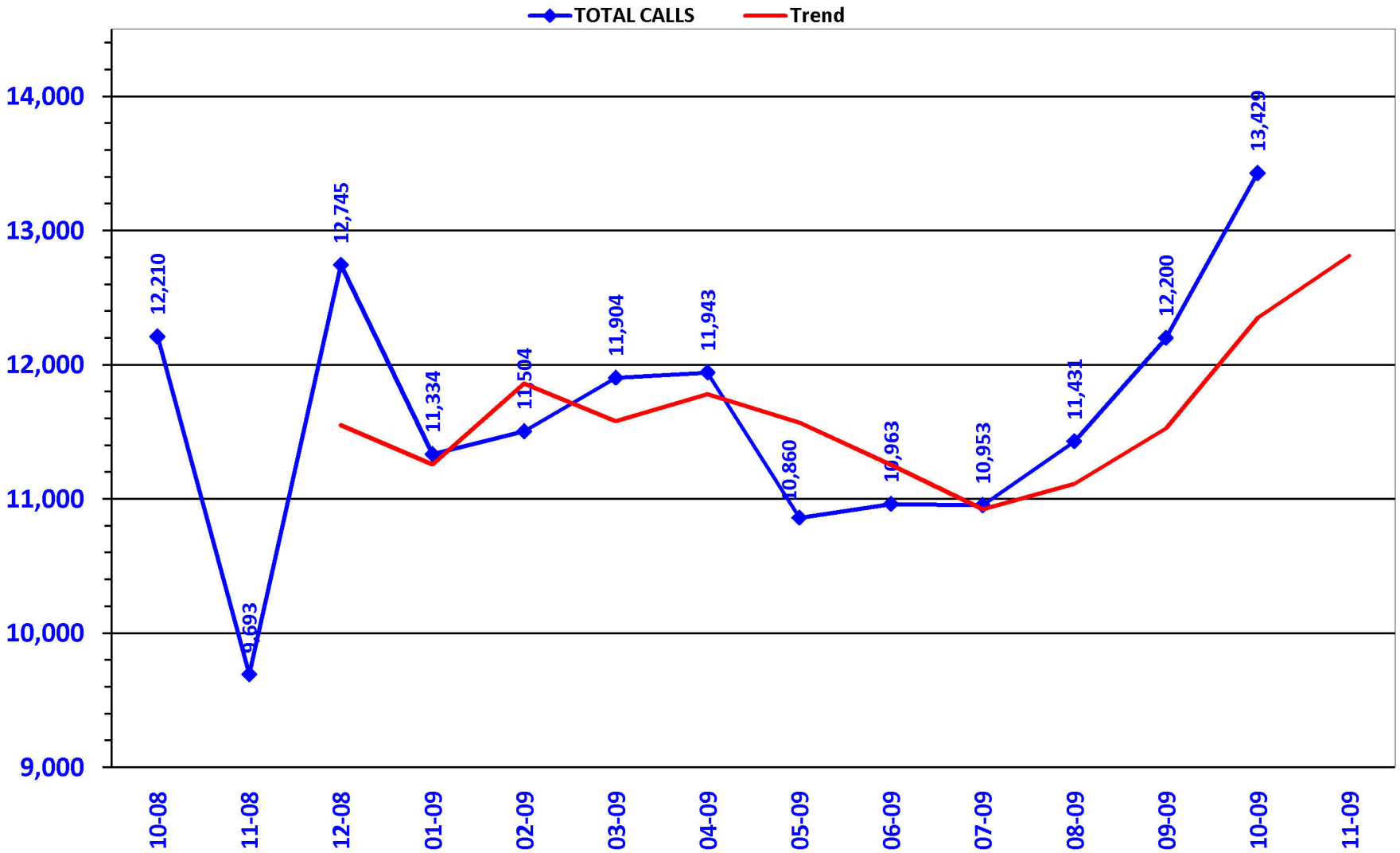
Denial Reasons	
Lack required information to process request.	3,000
Unable to verify required trials.	1,927
Does not meet established criteria.	208
Member has active PA for requested medication.	110
Considered duplicate therapy. Member has a prior authorization for similar medication.	105
Not an FDA approved indication/diagnosis.	74
Requested dose exceeds maximum recommended FDA dose.	64
Medication not covered as pharmacy benefit.	20
Drug Not Deemed Medically Necessary	2

Duplicate Requests: 1,103

Changes to existing PAs: 885

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

CALL VOLUME MONTHLY REPORT:
October 2008 – October 2009



Appendix C

VOTE TO PA EFFIENT™

OKLAHOMA HEALTH CARE AUTHORITY
NOVEMBER 2009

RECOMMENDATIONS

The College of Pharmacy recommends placing a prior authorization on Effient™ after 90 days of therapy.

The approval criteria for Effient™ would be as follows:

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

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

Appendix D

Vote to Prior Authorize Ulesfia™

Oklahoma Health Care Authority

November 2009

Recommendations

The College of Pharmacy recommends the addition of Ulesfia in Tier 3 of the Topical Antiparasitic Product Based Prior Authorization Category as voted on by the DUR Board previously. The authorization criteria and tier chart is as follows:

Approval of Tier 2 medication requires a recent trial of one Tier 1 medication with inadequate response or adverse effect.

Approval of Tier 3 medication requires recent trial(s) with all available Tier 2 medication(s) with inadequate response or adverse effect.

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

The following restrictions would also apply:

Ulesfia™ (benzoyl alcohol) Lotion

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

REFERENCE

1. Ulesfia(TM) (benzyl alcohol) Product Information. Sciele Pharma, Inc. April 2009.
2. Benzyl Alcohol Product Information. Lexi-Comp, Inc. (Lexi-Drugs) Lexi-Comp, Inc. Accessed October 2, 2009.

Appendix E

Vote to Prior Authorize Edluar™ and Intermezzo®
(Zolpidem Sublingual Tablets)

Oklahoma Health Care Authority
November 2009

Summary

Edluar™ (Zolpidem Sublingual Tablets)

- Edluar™ sublingual tablets should be placed under the tongue where it will disintegrate. The tablet should not be swallowed nor be taken with water.
- Edluar™ offers no additional advantage for hepatically impaired patients. It is recommended that the dose be reduced in this population as is also recommended for zolpidem tablets.

Intermezzo® (Zolpidem Sublingual Tablets)

- Transcept Pharmaceuticals, Inc. has filed an NDA for their version of zolpidem sublingual tablets for as-needed treatment of insomnia when a middle of the night awakening is followed by difficulty returning to sleep. Transcept is in the process of providing the FDA with additional requested safety data.

Recommendations

The College of Pharmacy recommends placement of Edluar™ and Intermezzo® in Tier 3 of the Hypnotics Category with a manual prior authorization. The existing prior authorization criteria for this category will apply. In addition, the petition should also include information regarding why member must have the sublingual formulation of zolpidem. A Quantity Limit similar to all other hypnotic medications will apply.

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

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

Current Prior Authorization of Hypnotic Medications

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

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

Appendix F

30 Day Notice to Prior Authorize Atypical Anti-Emetics

Oklahoma Healthcare Authority

November 2009

Atypical Anti-Emetics

Chemical Name	Trade Name	FDA Indications	Dosage Forms	Dosing	Quantity Limits
Ondansetron	Zofran®	- CINV - RINV - PONV	Tabs*, ODT* Oral Sol* IV*	Q 8 hrs, up to 2 days post tx	Sol: 50 mLs per 30 days 4mg, 8mg: 12 tabs per 30 days
Granisetron	Kytril®	- CINV - RINV - PONV	Tabs* IV* Oral Sol	Q 12 hrs, up to 1 day post tx	20 tabs per 30 days
Dolasetron	Anzemet®	- CINV - PONV	Tabs IV	One hr prior to tx or given IV at onset of nausea during tx	10 tabs per 30 days
Palonosetron	Aloxi®	- CINV - PONV	IV	One hr prior to or immediately before tx.	4 vials per 28 days
Aprepitant	Emend®	- CINV (adjunctive) - PONV	Caps	Dose up to 3 hrs prior to tx or up to 4 days post.	2 Packs per 30 days 80mg: 4 caps per 30 days 120mg: 2 caps per 30 days
Dronabinol	Marinol®	- CINV - AIDS (loss of appetite)	Caps*	3 hrs prior to tx or Q 2-4 hrs after tx up to 4-6 doses.	none
Nabilone	Cesamet®	- CINV+	Caps	Night before tx and BID-TID up to 48 hrs post tx.	none

*Generic Available with SMAC Pricing Applied

+ (in patients who fail to respond adequately to other antiemetic agents)

Utilization of 5-HT3 Receptor Antagonists

Utilization of 5-HT3 Receptor Antagonist for FY 2009

Fiscal Year	Members*	Claims	Amount Paid	Paid/Claim	Perdiem	Units	Days
2009	12,909	18,901	$380,414.05	$20.12	$1.12	254,793	338,785

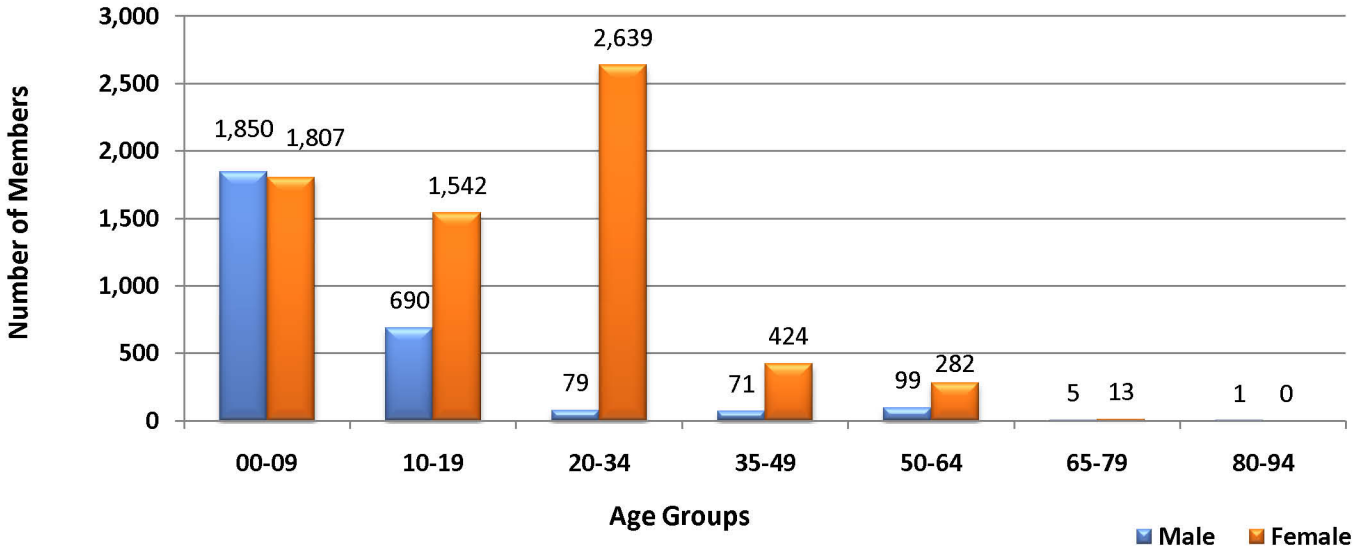
*Total number of unduplicated members

Trends in Utilization of 5-HT3 Receptor Antagonists

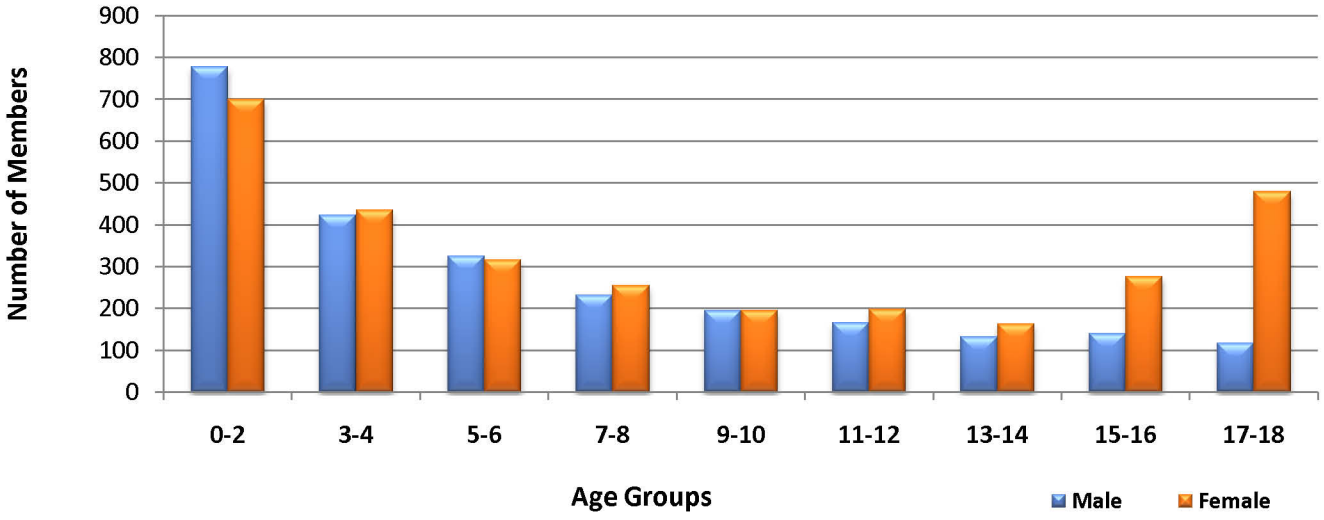
Calendar Year	Members*	Claims	Amount Paid	Paid/Claim	Perdiem	Units	Days
2006	2,733	5,039	$1,722,324.59	$341.80	$14.00	63,385	123,021
2007	4,652	8,200	$1,264,455.45	$154.20	$6.21	106,438	203,637
2008	9,559	15,421	$420,784.37	$27.29	$1.99	240,495	211,858
Percent Change	249%	206%	-75.6%	-92.0%	-85.8%	279%	72.2%
Change	6,826	10,382	-$1,301,540.22	-$314.51	-$12.01	177,110	88,837

*Total number of unduplicated members

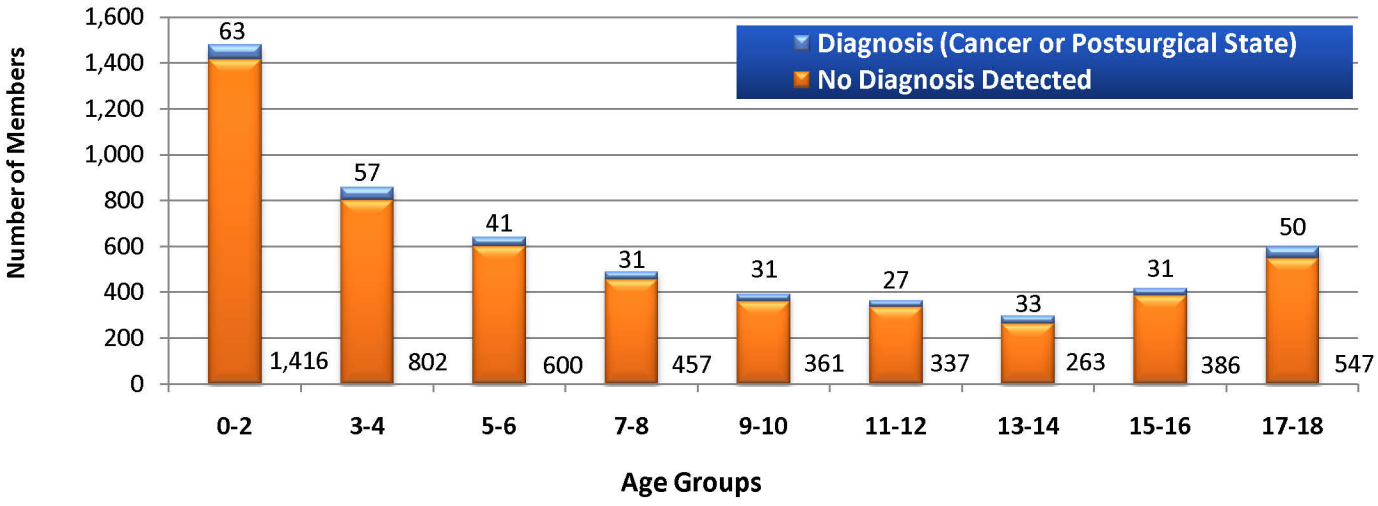
Demographics of Members Utilizating 5-HT3 Receptor Antagonists: CY 2008



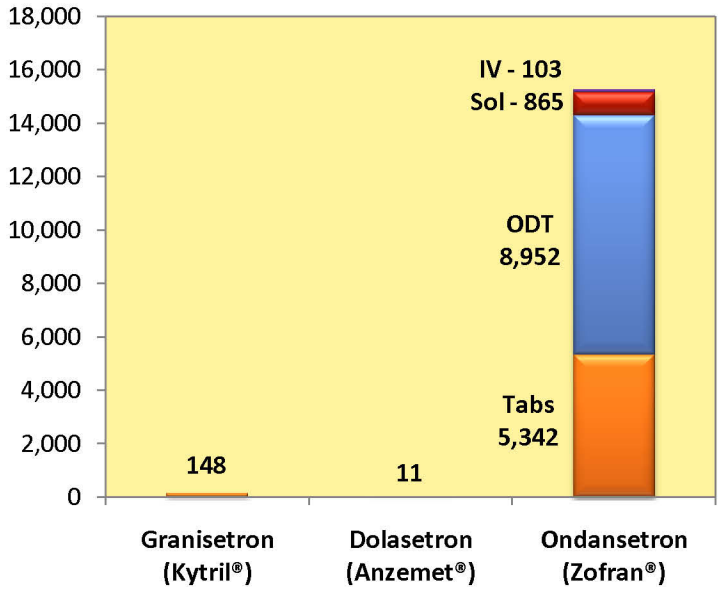
Demographics of Pediatric Members Utilizating 5-HT3 Receptor Antagonists: CY 2008



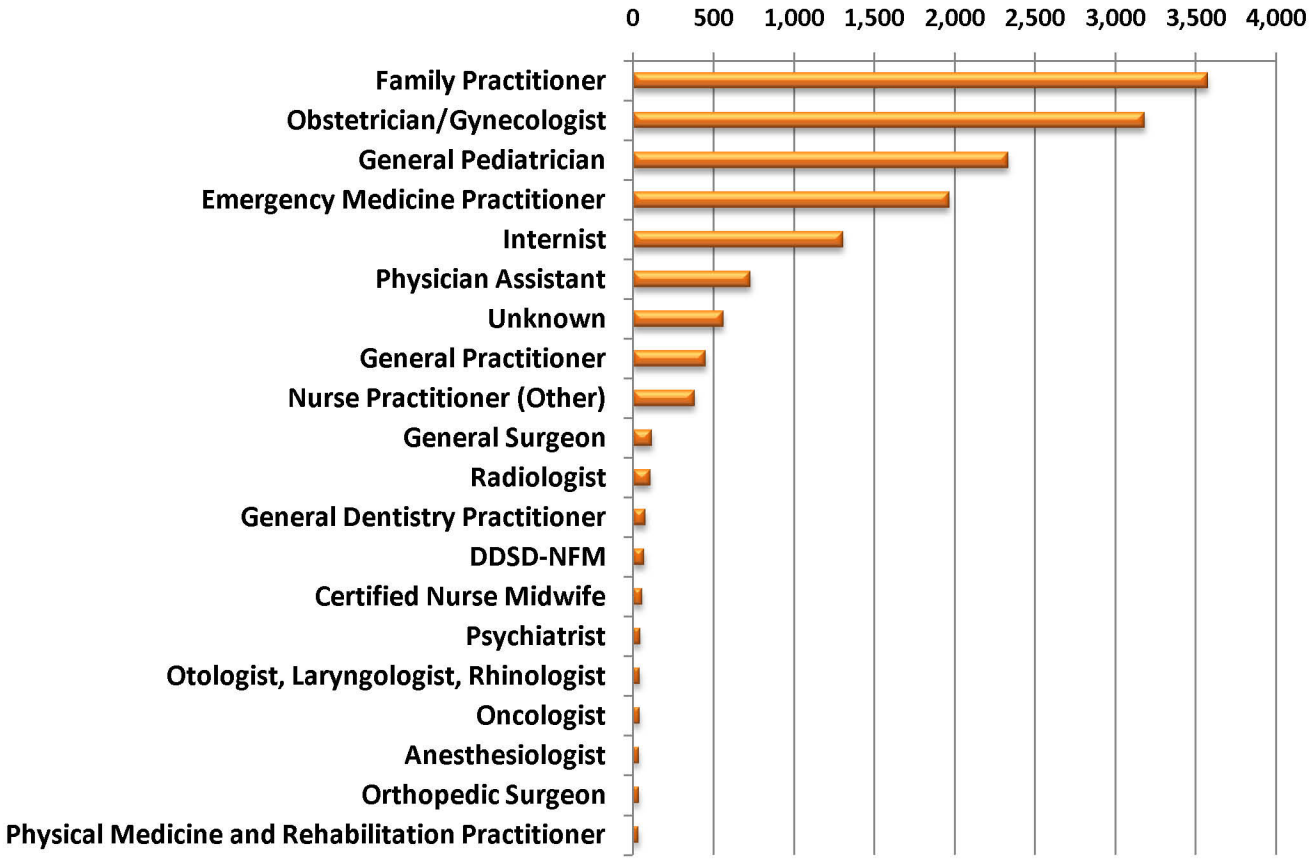
Demographics of Pediatric Members with Select Diagnosis: CY 2008



MarketShare of 5-HT3 Receptor Antagonists by Claims



Top Prescribers of 5-HT3 Receptor Antagonists by Claims



Utilization of Substance P/Neurokinin Antagonist: Aprepitant (Emend®)

Utilization of 5-HT3 Receptor Antagonist for FY 2009

Fiscal Year	Members*	Claims	Amount Paid	Paid/Claim	Perdiem	Units	Days
2009	114	327	$110,743.36	$338.66	$36.62	1,013	3,024

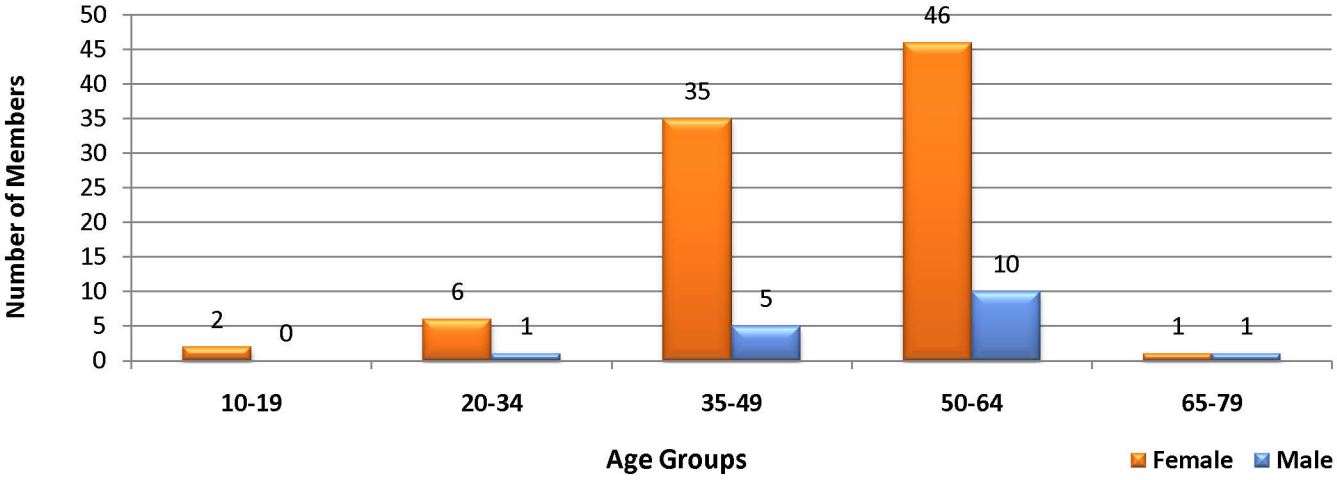
*Total number of unduplicated members

Trends in Utilization of Aprepitant (Emend®)

Calendar Year	Members*	Claims	Amount Paid	Paid/Claim	Perdiem	Units	Days
2006	72	222	$67,375.70	$303.49	$46.43	691	1,451
2007	94	290	$103,146.70	$355.68	$50.46	997	2,044
2008	111	336	$106,444.16	$316.80	$53.90	1,020	1,975
Percent Change	54.20%	51.40%	58.00%	4.40%	16.10%	47.60%	36.10%
Change	39	114	$39,068.46	$13.31	$7.47	329	524

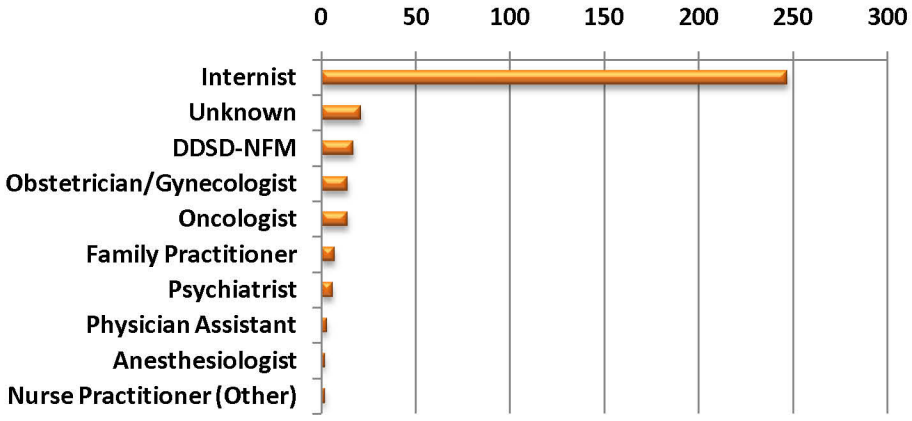
*Total number of unduplicated members

Demographics of Members* Utilizating Aprepitant (Emend®): CY 2008



*Total of 111 Members, 96% (104) of the members has a diagnosis of cancer or postsurgical state.

Top Prescriber Specialties of Aprepitant (Emend®) by Claims



Utilization of Cannabinoids (Marinol® and Cesamet®)

Utilization of Cannabinoids FY 2009

Fiscal Year	Members*	Claims	Amount Paid	Paid/Claim	Perdiem	Units	Days
2009	139	550	$310,829.31	$565.14	$20.05	35,935	15,504

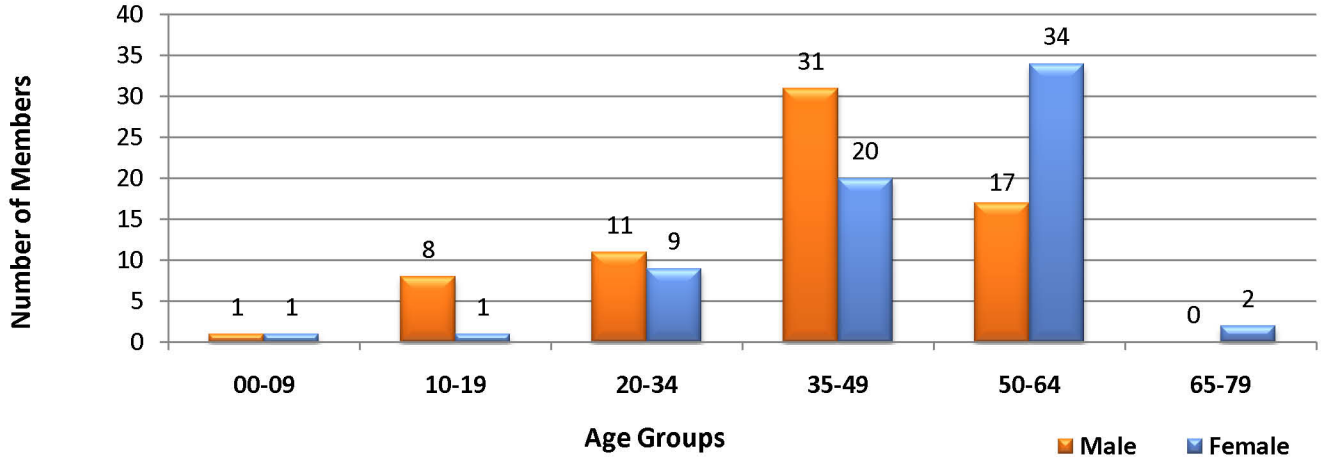
*Total number of unduplicated members

Utilization Trends of Cannabinoids

Calendar Year	Members*	Claims	Amount Paid	Paid/Claim	Perdiem	Units	Days
2006	109	432	$255,623.17	$591.72	$21.02	28,653	12,161
2007	134	504	$333,237.51	$661.19	$24.03	30,326	13,870
2008	135	554	$397,582.42	$717.66	$25.95	35,001	15,322
Percent Change	23.90%	28.20%	55.50%	21.30%	23.50%	22.20%	26.00%
Change	26	122	$141,959.25	$125.94	$4.93	6,348	3,161

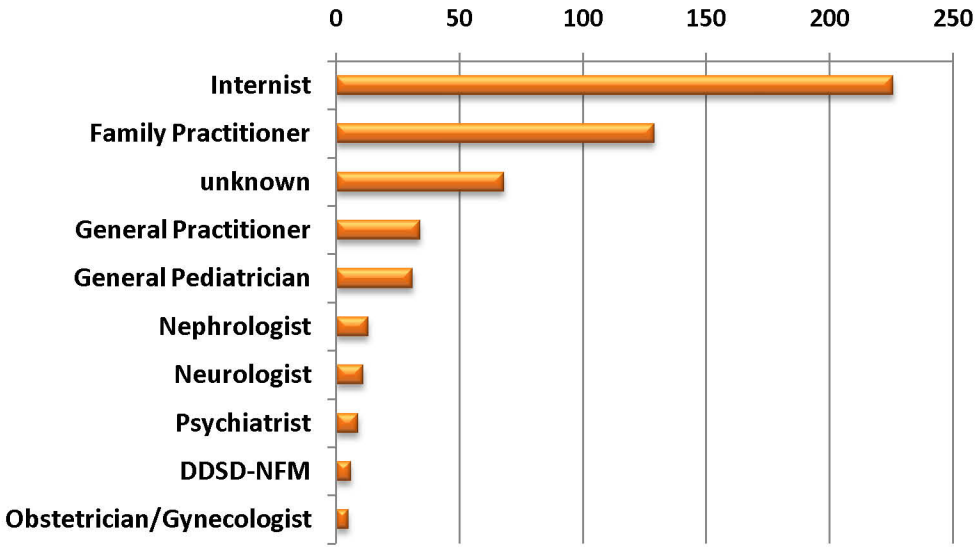
*Total number of unduplicated members

Demographics of Members* Utilizating Cannabinoids: CY 2008



*Total of 135 Members, 70% (95) of the members has a diagnosis of cancer or HIV.

Top Prescriber Specialties of Cannabinoids by Claims



Market Update

- **The patent for Zofran®** (ondansetron) expired in 2007. Numerous manufacturers of ondansetron entered the market after the exclusivity period ended and as a result the SMAC price was greatly reduced for this product which resulted in a paradigm shift in both utilization and cost for this class of medication.
- **The patent for Kytril®** (granisetron) has also expired but due to the low utilization of this product there are not as many manufacturers to increase competition enough to lower the price of granisetron as low as ondansetron.
- **The patent for Anzemet®** (dolasetron) is anticipated to expire in 2011.
- **There was not an increased in utilization of the remaining branded products** after ondansetron was available as generic. The generic ondansetron continued to increase in marketshare as Kytril® and Anzemet® decreased in marketshare through calendar years 2006, 2007, and 2008.
- **Granisetron is now available in a transdermal patch delivery system**. Sancuso® (granisetron) transdermal patch is indicated for the prevention of nausea and vomiting in patients receiving moderately and/or highly emetogenic chemotherapy for up to 5 consecutive days.
- **The patent for dronabinol (Marinol®)** has recently expired and currently there are two manufacturers of the generic.

Recommendations

The College of Pharmacy recommends the current quantity limit on ondansetron tablets and orally disintegrating tablets (**Zofran®)** be increased to #30 per 30 days. The College also recommends prior authorization of granisetron, dolasetron, aprepitant, and cannabinoids. The following are the proposed approval criteria.

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

- Approved Diagnosis
- 14 day trial of ondansetron with inadequate response.
- Approval length based on duration of need.
- Existing quantity limits apply.

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

- For the diagnosis of HIV related loss of apetite: approve for 6 months
- For chemotherapy induced nausea and vomiting a 14 day trial of ondansetron with inadequate response.
- Approval length based on duration of need.
- A quantity limit of 60 per 30 days also applies.

Utilization Details of 5-HT3 Receptor Antagonists: FY 2009

Chemical Name	Product Name	Claims	Members	Units	Days	Amount Paid	Claims/ Member	Perdiem	% Paid
Ondansetron	ONDANSETRON TAB 4MG **ODT**	8,595	7,149	74,991	144,524	$84,501.13	1.2	$0.58	22.21%
Ondansetron	ONDANSETRON TAB 4MG	3,772	2,641	53,626	69,080	$53,762.52	1.43	$0.78	14.13%
Ondansetron	ONDANSETRON TAB 8MG **ODT**	2,951	1,726	35,330	58,660	$44,859.67	1.71	$0.76	11.79%
Ondansetron	ONDANSETRON TAB 8MG	2,128	1,294	34,099	43,810	$32,810.26	1.64	$0.75	8.62%
Ondansetron	ONDANSETRON SOL 4MG/5ML	1,215	1,003	48,964	20,261	$124,202.31	1.21	$6.13	32.65%
Ondansetron	ONDANSETRON INJ 2MG/ML	47	12	456	105	$416.53	3.92	$3.97	0.11%
Ondansetron	ONDANSETRON INJ 40/20ML	36	12	4,461	559	$1,760.60	3	$3.15	0.46%
Ondansetron	ONDANSETRON INJ 4MG/2ML	16	10	246	48	$178.02	1.6	$3.71	0.05%
Ondansetron	ONDANSETRON TAB 4MG	2	2	22	8	$33.66	1	$4.21	0.01%
	Subtotals	**18,762**		**252,195**	**337,055**	**$342,524.70**	**1.86**	**$1.02**	**90.03%**
Granisetron	GRANISETRON TAB 1MG	114	40	2,135	1,359	$24,595.36	2.85	$18.10	6.47%
Granisetron	GRANISETRON INJ 1MG/ML	16	5	94	138	$5,946.77	3.2	$43.09	1.56%
Granisetron	GRANISOL SOL 2MG/10ML	5	2	330	110	$3,638.54	2.5	$33.08	0.96%
Granisetron	SANCUSO PATCH 3.1MG	1	1	4	30	$1,256.15	1	$41.87	0.33%
	Subtotals	**136**		**2,563**	**1,637**	**$35,436.82**	**2.39**	**$21.65**	**9.32%**
Dolasetron	ANZEMET TAB 100MG	3	2	35	93	$2,452.53	1.5	$26.37	0.64%
	Subtotals	**3**		**35**	**93**	**$2,452.53**	**1.5**	**$26.37**	**0.64%**
	Totals	**18,901**	**12,909***	**254,793**	**338,785**	**$380,414.05**	**1.46**	**$1.12**	**100.00%**

***Total Unduplicated Members**

Utilization Details of Aprepitant (Emend®): FY 2009

Brand Name	Claims	Members	Units	Days	Amount Paid	Claims/ Member	Perdiem	% Paid
EMEND CAP 80-125MG	261	84	846	2,644	$95,764.72	3.11	$36.22	86.47%
EMEND CAP 80MG	61	31	149	333	$13,824.75	1.97	$41.52	12.48%
EMEND CAP 125MG	3	3	8	8	$896.31	1	$112.04	0.81%
EMEND CAP 40MG	2	2	10	39	$257.58	1	$6.60	0.23%
Totals	**327**	**114***	**1,013**	**3,024**	**$110,743.36**	**2.87**	**$36.62**	**100.00%**

***Total Unduplicated Members**

Utilization Details of Cannabinoids: FY 2009

Chemical Name	Product Name	Claims	Members	Units	Days	Amount Paid	Claims/ Member	Perdiem	% Paid
Dronabinol	DRONABINOL CAP 5MG	218	66	13,754	6,360	$113,958.48	3.3	$17.92	36.66%
Dronabinol	DRONABINOL CAP 2.5MG	161	65	11,207	4,456	$45,671.38	2.48	$10.25	14.69%
Dronabinol	DRONABINOL CAP 10MG	69	16	4,575	1,960	$71,552.81	4.31	$36.51	23.02%
Dronabinol	MARINOL CAP 5MG	43	22	2,750	1,146	$33,492.55	1.95	$29.23	10.78%
Dronabinol	MARINOL CAP 2.5MG	38	24	2,316	1,058	$14,110.98	1.58	$13.34	4.54%
Dronabinol	MARINOL CAP 10MG	21	8	1,333	524	$32,043.11	2.63	$61.15	10.31%
	Totals	**550**	**139***	**35,935**	**15,504**	**$310,829.31**	**3.96**	**$20.05**	**100.00%**

***Total Unduplicated Members**

Appendix G

30 Day Notice to Prior Authorize Valturna™ (aliskiren and valsartan)

Oklahoma Health Care Authority
November 2009

Manufacturer	Novartis Pharmaceuticals, Inc.
Classification	Direct Renin Inhibitor (DRI) and Angiotensin II Receptor Blocker (ARB)
Status	Prescription Only

Vlaturna™ Summary

Valturna™ (aliskiren and valsartan) is a combination of aliskiren, a direct renin inhibitor, and valsartan, an angiotensin II receptor blocker (ARB), indicated for the treatment of hypertension:

- in patients not adequately controlled with monotherapy
- may be substituted for titrated components
- as initial therapy in patients likely to need multiple drugs to achieve their blood pressure goals

The following products are currently available:

- Aliskiren (Tekturna™)
- Aliskiren/Hydrochlorathiazide (Tekturna HCT™)
- Valsartan (Diovan®)
- Valsartan HCT (Diovan HCT®)

Recommendations

The College of Pharmacy recommends placement of Valturna™ in Tier 3 of the Direct Renin Inhibitors Product Based Prior Authorization Category. The existing criteria for this category will apply.

Approval Criteria

- FDA approved indication
- Recent trial, within the previous 6 months and at least 4 weeks in duration, of an ACE Inhibitor (or an ARB if previous trial of an ACEI) and a diuretic, used concomitantly at recommended doses, that did not yield adequate blood pressure control.
- Clinical exceptions will be granted for members already currently on aliskiren and valsartan at the available doses of Valturna™.

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

Medication Product Details

Indication

Valturna™ (aliskiren and valsartan) is a combination of aliskiren, a direct renin inhibitor, and valsartan, an angiotensin II receptor blocker (ARB), indicated for the treatment of hypertension:

- In patients not adequately controlled with monotherapy
- May be substituted for titrated components
- As initial therapy in patients likely to need multiple drugs to achieve their blood pressure goals

Dosage Forms: 150/160, 300/320mg tablets (aliskiren/valsartan)

Contraindications: Patients with a history of hypersensitivity to aliskiren or valsartan.

Pregnancy Risk Category: D

Precautions

- **Fetal/Neonatal Morbidity and Mortality**- can cause fetal harm when administered to a pregnant woman; when given during the 2^{nd} or 3^{rd} trimester, drugs that act on the renin-angiotensin-aldosterone system can cause fetal and neonatal morbidity and death when administered to pregnant women; No reproductive toxicity studies have been conducted with the combination of aliskiren and valsartan but have been with them alone.
- **Head and Neck Angioedema**- Angioedema of the face, extremities, lips, tongue, glottis and/or larynx has been reported in patients treated with aliskiren and has necessitated hospitalization and intubation. Discontinue aliskiren immediately in patients who develop angioedema and do not readminister.
- **Hypotension-** An excessive fall in blood pressure (hypotension) was rarely seen (<0.5%) in patients with uncomplicated hypertension treated with Valturna™ in controlled trials
- **Severe Renal Impairment**- Patients with severe renal impairment were excluded from clinical trials with Valturna in hypertension; Adjustment of the starting dose is not required in patients with mild-to-moderate renal impairment.
- **Hepatic Impairment-** Adjustment of the starting dose of valturna is not necessary with mild or moderate hepatic impairment and dosing Valturna™ in patients with severe hepatic impairment is limited; slower clearance of valsartan (higher AUC's) may be observed in patients with mild-to-moderate hepatic impairment, including patients with biliary obstructive disorders.
- **Congestive Heart Failure and Post-Myocardial Infarction-** Some patients with heart failure have developed increases in blood urea nitrogen, serum creatinine, and potassium on valsartan; these effects are usually minor and transient, and they are more likely to occur in patients with pre-existing renal impairment thus include assessment of renal function when evaluating patients with heart failure or post-myocardial infarction.
- **Hyperkalemia**- 1%-2% higher in the combination treatment group compared with the monotherapies aliskiren and valsartan, or with placebo; Caution is advised with concomitant use of Valturna™ with potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium, or other drugs that increase potassium levels may lead to increases in serum potassium.

- **Renal Artery Stenosis-** No data are available on the use of aliskiren in patients with unilateral or bilateral renal artery stenosis or stenosis of the artery to a solitary kidney; there has been no long-term use of valsartan in patients with unilateral or bilateral renal artery stenosis, but an effect similar to that seen with ACE inhibitors (increase in serum creatinine or blood urea nitrogen) should be anticipated.
- **Geriatric patients**- Adjustment of the starting dose is not required for elderly patients.
- **Pediatric patients-** Has not been studied in children under 18 years of age.

Common Adverse Effect

- Fatigue
- Nasopharyngitis
- Sore throat
- Diarrhea
- Dizziness
- Urinary Tract Infection
- Flu or Flu-like symptoms
- Upper Respiratory Tract Infection

Less Common Adverse effects

- Angioedema
- Impotence
- Sinusitis
- Rash/Allergic Reaction
- Muscle cramps

Drug Interactions

- No drug interaction studies have been conducted with Valturna and other drugs but there are studies on its components.
- Coadministration of irbesartan reduced aliskiren Cmax up to 50% after multiple dosing.
- Coadministration of atorvastatin resulted in about a 50% increase in aliskiren Cmax and AUC after multiple dosing.
- Coadministration of 200mg twice-daily ketoconazole, with aliskiren resulted in approximate 80% increase in plasma levels of aliskiren. A 400mg once-daily dose was not studied but would be expected to increase aliskiren blood levels further.
- Concomitant use of aliskiren with cyclosporine is not recommended: coadministration of 200mg and 600mg cyclosporine, with 75mg aliskiren resulted in an approximately 2.5-fold increase in Cmax and 5-fold increase in AUC of aliskiren.
- Concomitant use of potassium sparing diuretics (e.g., spironolactone, triamterene, amiloride), potassium supplements, or salt substitutes containing potassium with valsartan may lead to increases in serum potassium and in heart failure patients to increases in serum creatinine.

Patient Information

- Take Valturna™ once each day, about the same time each day with or without food.
- Valturna™ should start to work within 2 weeks.

- Valturna™ may harm an unborn baby, causing injury and death. If you get pregnant, stop taking Valturna™ and call your doctor right away. If you plan to become pregnant, talk to your doctor about other treatment options for your high blood pressure.
- Do not take Valturna™ if you are allergic to any of its components.
- Valturna™ may cause angioedema.
- Some common side effects are fatigue, sore throat, dizziness, diarrhea, and upper respiratory tract or urinary tract infections.
- Store Valturna™ tablets at room temperature between 59ºF-86ºF in a dry place.

REFERENCE

Valturna™ (aliskiren and valsartan tablets) Product Information. Novartis Pharmaceuticals Corporation. September 2009.

Appendix H

30 Day Notice to Prior Authorize Intuniv™ (guanfacine)

Oklahoma Health Care Authority
November 2009

Manufacturer	Shire US Inc.
Classification	Selective Alpha$_{2A}$ Receptor Agonist
Status	Prescription Only

Intuniv™ Summary

Intuniv™ is a selective alpha$_{2A}$ adrenergic receptor agonist indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD). Intuniv™ is an extended-release tablet and should be dosed once daily. Guanfacine is not a central nervous system (CNS) stimulant. The mechanism of action of guanfacine in ADHD is not known. The effectiveness of Intuniv™ for longer-term use (more than 9 weeks) has not been systematically evaluated in controlled trials.

Begin at a dose of 1mg/day, and adjust in increments of no more than 1mg/week. Maintain the dose within the range of 1-4mg once daily, depending on clinical response and tolerability.

A mean increase in systolic and diastolic blood pressure and heart rate, as well as, infrequent transient elevations in blood pressure above original baseline (i.e., rebound) have been reported to occur upon abrupt discontinuation of guanfacine. To minimize these effects, the dose should generally be tapered in decrements of no more than 1mg every 3 to 7 days.

Recommendations

The College of Pharmacy recommends placement of Intuniv™ in Tier 2 of the ADHD Product Based Prior Authorization Category. The existing criteria for this category will apply.

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

Mandatory Generic Plan applies.
*** Immediate release products do not count as adequate tier-1 trials**
Blue Color indicates Supplemental Rebate Participation

Product Details

Indication

Intuniv™ is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD). The efficacy of Intuniv™ was studied for the treatment of ADHD in two controlled clinical trials (8 and 9 weeks in duration) in 669 children and adolescents ages 6-17 who met DSM-IV® criteria for ADHD. The effectiveness of Intuniv™ for longer-term use (more than 9 weeks) has not been systematically evaluated in controlled trials.

Dosage Forms: Extended-release tablets: 1mg, 2mg, 3mg and 4mg

Contraindications

Patients with a history of hypersensitivity to Intuniv™, its inactive ingredients, or other products containing guanfacine (e.g.Tenex®) should not take Intuniv™.

Pregnancy Risk Category: B

Precautions

Hypotension, Bradycardia, and Syncope - Treatment with Intuniv™ can cause decreases in blood pressure and heart rate. These changes were dose dependent. Decreases in blood pressure and heart rate were usually modest and asymptomatic; however, hypotension and bradycardia can occur. Measure heart rate and blood pressure prior to initiation of therapy, following dose increases, and periodically while on therapy. Use Intuniv™ with caution in patients with a history of hypotension, heart block, bradycardia, or cardiovascular disease, because it can decrease blood pressure and heart rate. Use caution in treating patients who have a history of syncope or may have a condition that prediposes them to syncope, such as hypotension, orthostatic hypotension, bradycardia, or dehydration. Use Intuniv™ with caution in patients treated concomitantly with antihypertensives or other drugs that can reduce blood pressure or heart rate or increase the risk of syncope. Advise patients to avoid becoming dehydrated or overheated.

Sedation and Somnolence - Somnolence and sedation were commonly reported adverse reactions in clinical studies (38% for Intuniv™ vs. 12% for placebo) in children and adolescents with ADHD, especially during initial use. Before using Intuniv™ with other centrally active depressants (such as phenothiazines, barbiturates, or benzodiazepines), consider the potential for additive sedative effects. Caution patients against operating heavy equipment or driving until they know how they respond to treatment with Intuniv™. Advise patients to avoid use with alcohol.

Other Guanfacine-Containing Products - Guanfacine, the active ingredient in Intuniv™, is also approved as an antihypertensive. Do not use Intuniv™ in patients concomitantly taking other guanfacine-containing products (e.g., Tenex®).

Common Adverse Effect

- ☑ Somnolence
- ☑ Headache
- ☑ Fatigue
- ☑ Abdominal pain (upper)
- ☑ Nausea
- ☑ Lethargy
- ☑ Dizziness
- ☑ Irritability
- ☑ Constipation
- ☑ Hypotension/Decreased Blood Pressure
- ☑ Decreased Appetite
- ☑ Dry mouth

Less Common Adverse effects

- ☑ AV Block
- ☑ Tachycardia
- ☑ Sinus Arrhythmia
- ☑ Dyspepsia
- ☑ Asthenia
- ☑ Chest pain
- ☑ Increased ALT
- ☑ Increased Blood Pressure
- ☑ Increased weight
- ☑ Postural Dizziness
- ☑ Increased urinary frequency
- ☑ Enuresis
- ☑ Asthma
- ☑ Orthostatic hypotension
- ☑ Pallor

Drug Interactions

CYP3A4/5 Inhibitors

Use caution when Intuniv™ is administered to patients taking ketoconazole and other strong CYP3A4/5 inhibitors, since elevation of plasma guanfacine concentration increases the risk of adverse events such as hypotension, bradycardia, and sedation. There was a substantial increase in the rate and extent of guanfacine exposure when administered with ketoconazole; the guanfacine exposure increased 3-fold.

CYP3A4 Inducers

When patients are taking Intuniv™ concomitantly with a CYP3A4 inducer, an increase in the dose of Intuniv™ within the recommended dose range may be considered. There was a significant decrease in the rate and extent of guanfacine exposure when co-administered with rifampin, a CYP3A4 inducer. The exposure to guanfacine decreased by 70% (AUC).

Valproic Acid

Co-administration of guanfacine and valproic acid can result in increased concentrations of valproic acid. The mechanism of this interaction is unknown, although both guanfacine and valproic acid are metabolized by glucuronidation, possibly resulting in competitive inhibition. When Intuniv™ is co-administered with valproic acid, monitor patients for potential additive CNS effects, and consider monitoring serum valproic acid concentrations. Adjustments in the dose of valproic acid may be indicated when co-administered with Intuniv™.

Antihypertensive Drugs

Use caution when Intuniv™ is administered concomitantly with antihypertensive drugs, due to the potential for additive pharmacodynamic effects (e.g., hypotension, syncope)

CNS Depressant Drugs

Caution should be exercised when Intuniv™ is administered concomitantly with CNS depressant drugs (e.g. alcohol, sedative/hypnotics, benzodiazepines, barbiturates, and antipsychotics) due to the potential for additive pharmacodynamic effects (e.g., sedation, somnolence)

Patient Information

- Take Intuniv™ exactly as your doctor tells you. Your doctor may change your dose. Do not change your dose of Intuniv™ without talking to your doctor.
- Do not stop taking Intuniv™ without talking to your doctor.
- Intuniv™ should be swallowed whole with a small amount of water, milk, or other liquid.
- Do not crush, chew, or break Intuniv™.
- Do not take Intuniv™ with a high-fat meal.

REFERENCE

Intuniv(TM) (guanfacine) Product Information. Shire Pharmaceuticals. August 2009.
Guanfacine monograph. Lexi-Comp, Inc. (Lexi-Drugs) Lexi-Comp, Inc. Accessed October 7, 2009.

Appendix I

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Useful Links

- Nearly 7 million Americans are abusing prescription drugs*—more than the number who are abusing cocaine, heroin, hallucinogens, Ecstasy, and inhalants, combined. That 7 million was just 3.8 million in 2000, an 80 percent increase in just 6 years.
- Prescription pain relievers are new drug users' drug of choice, vs. marijuana or cocaine.
- Opioid painkillers now cause more drug overdose deaths than cocaine and heroin combined.
- Nearly 1 in 10 high school seniors admits to abusing powerful prescription painkillers. A shocking 40 percent of teens and an almost equal number of their parents think abusing prescription painkillers is safer than abusing "street" drugs.
- Misuse of painkillers represents three-fourths of the overall problem of prescription drug abuse; hydrocodone is the most commonly diverted and abused controlled pharmaceutical in the U.S.
- Twenty-five percent of drug-related emergency department visits are associated with abuse of prescription drugs.
- Methods of acquiring prescription drugs for abuse include "doctor-shopping," traditional drug-dealing, theft from pharmacies or homes, illicitly acquiring prescription drugs via the Internet, and from friends or relatives.
- DEA works closely with the medical community to help them recognize drug abuse and signs of diversion and relies on their input and due diligence to combat diversion. Doctor involvement in illegal drug activity is rare—less than one tenth of one percent of more than 750,000 doctors are the subject of DEA investigations each year—but egregious drug violations by practitioners unfortunately do sometimes occur. DEA pursues criminal action against such practitioners.
- DEA Internet drug trafficking initiatives over the past 3 years have identified and dismantled organizations based both in the U.S. and overseas, and arrested dozens of conspirators. As a result of major investigations such as Operations Web Tryp, PharmNet, Cyber Rx, Cyber Chase, and Click 4 Drugs, Bay Watch, and Lightning Strike, tens of millions of dosage units of prescription drugs and tens of millions of dollars in assets have been seized.

* Prescription drugs refers to abuseable pharmaceuticals controlled under federal law enforced by the DEA.

Useful Links:

- DEA Testimony on Prescription Drug Abuse

- ONDCP's Prescription Drug Abuse Fact Sheets
- SAMHSA's Brochure on Prescription Drug Abuse
- NIDA InfoFacts: Prescription Pain and Other Medications
- Prescription Drug Monitoring Project
- The Silent Epidemic - Kids and Pharmaceutical Abuse
- MedLine Plus: Prescription Drug Abuse
- National Drug Threat Assessment

Drugs

Information for Healthcare Professionals: Reports of Altered Kidney Function in patients using Exenatide (Marketed as Byetta)

[11/02/2009] FDA has approved revisions to the drug label for Byetta (exenatide) to include information on post-marketing reports of altered kidney function, including acute renal failure and insufficiency.

Byetta, an incretin-mimetic, is approved as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

From April 2005 through October 2008, FDA received 78 cases of altered kidney function (62 cases of acute renal failure and 16 cases of renal insufficiency), in patients using Byetta. Some cases occurred in patients with pre-existing kidney disease or in patients with one or more risk factors for developing kidney problems. From April 2005 through September 2008, more than 6.6 million prescriptions[1] for Byetta were dispensed. Therefore, the 78 reported cases of altered renal function represent a small percentage of the total number of patients who have used the drug.

Some of the 78 patients reported nausea, vomiting, and diarrhea--the most common side effects associated with Byetta in clinical trials. These side effects may have contributed to the development of altered kidney function in the reported cases.

The revisions to the drug label allow healthcare professionals to better weigh the known benefits of Byetta with the potential risks that exist for certain patients. Changes include:

- **Information regarding post-market reports of acute renal failure and insufficiency, highlighting that Byetta should not be used in patients with severe renal impairment (creatinine clearance <30 ml/min) or end-stage renal disease.**
- **Recommendations to healthcare professionals that caution should be applied when initiating or increasing doses of Byetta from 5 mcg to 10 mcg in patients with moderate renal impairment (creatinine clearance 30 to 50 ml/min).**
- **Recommendations that healthcare professionals monitor patients carefully for the development of kidney dysfunction, and evaluate**

the continued need for Byetta if kidney dysfunction is suspected while using the product.
- **Information about kidney dysfunction in the patient Medication Guide to help patients understand the benefits and potential risks associated with Byetta.**

This information reflects FDA's current analysis of data available to FDA concerning this drug. FDA intends to update this sheet when additional information or analyses become available.

To report any unexpected adverse or serious events associated with the use of this drug, please contact the FDA MedWatch program using the information at the bottom of the page.

Considerations for Healthcare Professionals:

- Discuss with patients the possibility of developing altered kidney function with Byetta, taking into account the clinical utility of Byetta, the risks/benefits of other antidiabetic therapies, and the risks associated with uncontrolled diabetes mellitus.
- Monitor for the emergence of signs and symptoms of altered kidney function, such as increased serum creatinine, changes in urination (color, frequency, amount), unexplained swelling in the extremities, increases in blood pressure, lethargy, changes in appetite or digestion, or dull ache in the mid to lower back.
- Consider discontinuation of Byetta if kidney dysfunction cannot be explained by other causes.
- Understand that altered kidney function can be a consequence of diabetes, independent of any risk associated with Byetta.
- Discuss with patients that chronic conditions such as hypertension and pancreatitis as well as medications, such as non-steroidal anti-inflammatory drugs (NSAIDs), diuretics, and antihypertensives, can increase the risk of developing altered renal function.
- Inform patients of the signs and symptoms of altered kidney function so they are aware of and able to notify their healthcare professional if they experience any unusual signs or symptoms.
- Tell patients to report nausea, vomiting, or dehydration, as these symptoms may contribute to altered kidney function.

Information for Patients:

- Altered kidney function, including acute kidney failure and renal insufficiency, has been reported in patients using Byetta. Some cases have been associated with dehydration from nausea, vomiting, and diarrhea, which are known side effects of Byetta.

- Reported cases of altered kidney function represent a very small percentage of the total number of patients who have used Byetta.
- Pay close attention for any signs or symptoms of altered kidney function, such as changes in urination (color, frequency, amount), unexplained swelling in the extremities, changes in blood pressure, lethargy, changes in appetite or digestion, or dull ache in mid to lower back.
- Contact your healthcare professional if you experience nausea, vomiting, diarrhea, or dehydration while using Byetta, as these symptoms may increase the likelihood of developing altered kidney function.
- Do not stop or change medicines that have been prescribed without first talking with your healthcare professional.
- Review the Medication Guide that accompanies each prescription of Byetta. It is provided to help patients understand the benefits and potential risks associated with Byetta.

Data Summary:
FDA has completed a review of 78 cases of altered kidney function reported in patients with diabetes using Byetta. The cases were reported to FDA's Adverse Event Reporting System (AERS) between April 28, 2005 and October 29, 2008. Sixty-two of the cases were classified as acute renal failure and 16 cases were classified as renal insufficiency. Cases of acute renal failure or insufficiency occurred as soon as 3 days and up to 2 years after initiation of Byetta. The patient ages ranged from 23 to 83 years, with an average age of 60 years.

The majority of patients, 74/78 (95%), had at least one contributory risk factor for altered kidney function, such as cardiac insufficiency, hypertension, pancreatitis, rhabdomyolysis, and urinary tract infection, as well as concomitant medications such as antiretrovirals, antihypertensives, diuretics, and non-steroidal anti-inflammatory drugs (NSAIDs). These factors could independently increase the risk for developing altered kidney function. Forty-two patients (54%) reported symptoms associated with volume depletion, such as diarrhea, and/or vomiting, which are also known risk factors for altered kidney function and are the most commonly reported adverse events associated with the use of Byetta.

Hospitalization was required in 71 of 78 (91%) patients and there were 4 deaths reported in the cases reviewed. Eighteen patients required dialysis and two patients required kidney transplantation after initiation of Byetta. Of those patients who required dialysis, six had no prior history of altered kidney function, two had a prior history of altered kidney function, and the remaining 10 patients reported no information regarding prior renal history.

Byetta was discontinued in 63 of 78 (80%) patients, with 39 (50%) patients reporting improved signs and symptoms after discontinuation of the drug. One patient experienced recurrent altered kidney function after re-initiation of Byetta.

Notably, 14 of the cases had past medical histories of chronic kidney disease, including four with chronic renal failure, despite recommendations against the use of Byetta in these patients in the current prescribing information.

Due to the serious potential consequences of altered kidney function and temporal relationship between the development of renal effects and initiation of Byetta, FDA has approved revisions to the drug label for Byetta to describe this risk.

References:

[1.] SDI Vector One®: National (VONA). clearance # C100003-2008-1392. received 10/15/2009.

Related Information

- Exenatide (marketed as Byetta) Information

Contact Us

- 1-800-332-1088
- 1-800-FDA-0178 Fax

- **Report a Serious Problem**

  MedWatch Online

  Regular Mail: Use postage-paid FDA Form 3500

  Mail to: MedWatch 5600 Fishers Lane

  Rockville, MD 20852-9787