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 – May 12, 2010**

DATE: May 6, 2010

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

Enclosed are the following items related to the May 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 Mozobil®, Nplate®, and Arcalyst® – See Appendix C.

30 Day Notice to Prior Authorize Ilaris®– See Appendix D.

30 Day Notice to Prior Authorize Besivance™ – See Appendix E.

30 Day Notice to Prior Authorize Requip XL™ and Mirapex ER™ – See Appendix F.

30 Day Notice to Prior Authorize Lovaza® – See Appendix G.

Action Item – Annual Review of Statin & Statin Combination Products and 30 Day Notice to Prior Authorize Livalo® – See Appendix H.

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

FDA and DEA Updates – See Appendix J.

Future Business

Adjournment

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Drug Utilization Review Board

(DUR Board)

Meeting – May 12, 2010 @ 6:00 p.m.

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

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

1. Call To Order

A. Roll Call – Dr. Graham

Items to be presented by Dr. Muchmore, Chairman:

2. Public Comment Forum

A. Acknowledgment of Speakers and Agenda Items

Items to be presented by Dr. Muchmore, Chairman:

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

A. February 10, 2010 DUR Minutes – Vote
B. February 11, 2010 DUR Recommendation Memorandum
C. Correspondence

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

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

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

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

5. Action Item – Vote to Prior Authorize Mozobil®, Nplate®, and Arcalyst® – See Appendix C.

A. COP Recommendations

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

6. 30 Day Notice to Prior Authorize Ilaris® – See Appendix D.

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

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

7. 30 Day Notice to Prior Authorize Besivance™ – See Appendix E.

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

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

8. 30 Day Notice to Prior Authorize Requip XL™ and Mirapex ER™ – See Appendix F.

A. Requip XL™ Product Summary
B. Mirapex ER™ Product Summary
C. Cost Comparison
D. COP Recommendations

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

9. 30 Day Notice to Prior Authorize Lovaza® – See Appendix G.

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

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

10. Action Item – Annual Review of Statins & Statin Combination Products and 30 Day Notice to Prior Authorize Livalo® – See Appendix H.

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

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

11. Action Item – Annual Review of Antidepressants and 30 Day Notice to Prior Authorize Oleptro™ – See Appendix I.

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

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

12. FDA and DEA Updates – See Appendix J.

13. Future Business

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

14. Adjournment

Appendix A

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

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

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

Janie Huff, Takeda	Robert Vik, Azor	John Seidenberger, Boehringer-Ingelheim
Rich Wardrop, Eisai	Mark DeClerk, Lilly	Richard Ponder, J&J
Brad Robertson, GSK	Randy McGinley, Bayer	Aylan Lane, Elan
Linda Cantu, BMS	Vanessa Papion, UCB	Jim Dunlap, Eli Lilly
Donna Erwin, BMS		

PRESENT FOR PUBLIC COMMENT:

Agenda Item No. 6	Jon Beaty, Ph.D.; Boehringer-Ingelheim
Agenda Item No. 8	Michael Gray, Genzyme Medical Affairs

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. 6 Jon Beaty, Ph.D.; Boehringer-Ingelheim

Agenda Item No. 8 Michael Gray, Genzyme Medical Affairs

ACTION: NONE REQUIRED

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

3A: February 10, 2010 DUR Minutes

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

ACTION: MOTION CARRIED

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

4A: Retrospective Drug Utilization Review: October 2009

4B: Medication Coverage Activity Audit: February 2010

4C: Help Desk Activity Audit: February 2010

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: **VOTE TO UPDATE ANXIOLYTIC PRIOR AUTHORIZATION CATEGORY**

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

Board members discussed amending criteria wording for members under 18 years of age; "No concurrent stimulant ADHD medications ~~(except Strattera)~~"; and "Quantity limits set a 3 units per day for all products unless it exceeds FDA recommendations. The Board also asked for a claims analysis within six months of date of criteria changes.

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE TWYNSTA™**

For Public Comment: Jon Beaty, Ph.D.: Thank you. Yes, I am Dr. Jon Beaty. I'm a research scientist and work with the medical affairs office at Boehringer-Ingelheim and I'm here to provide scientific support for your consideration of Twynsta in your agency. As you said, Twynsta is a combination of telmisartan and amlodipine. It's indicated for the treatment of hypertension alone or with other antihypertensive agents. Twynsta may also be used in initial therapy in patients who are likely to need multiple drugs to achieve their blood pressure goals. The usual starting dose of Twynsta is 40 mg telmisartan, 5 mg amlodipine once daily. Patients requiring larger blood pressure reductions may be started on Twynsta 80 plus 5 once daily. Initial therapy with Twynsta is not recommended in patients greater than 75 years of age or with hepatic impairment. An 8-week randomized double blind placebo controlled 4x4 factorial study in patients in patients with mild to severe hypertension was conducted to determine if treatment with Twynsta was more effective in reducing blood pressure compared to the respective monotherapies. The study randomized 1,461 patients to one of sixteen treatment arms. Subjects that were assigned to receive amlodipine 10 mg qd were started on 5 mg qd or combinations thereof for the first two weeks, and then stepped up. Patients assigned to receive, I'm sorry …… the four key treatment combinations that resulted in the approved label for Twynsta, including the combinations of telmisartan 40 or 80 and amlodipine 5 or 10, had statistically significant reduction in in-clinic, seated trough cuff systolic and diastolic blood pressure compared to the respective individual monotherapies. The majority of the antihypertensive effect of the telmisartan/amlodipine combination is obtained in the first two weeks after initiation of therapy. In patients receiving the combination, significantly large reductions in seated diastolic and systolic blood pressure compared to patients with respective monotherapies were observed in every assessment which occurred in weeks two, four, six and eight in the study. The antihypertensive effect of Twynsta tablets was similar in patients greater than 65 years of age compared to those younger, in male and female patients, and patients with and without diabetes. The magnitude of blood pressure lowering in black patients approached that observed in non-black patients. Note that the number in the study, out of 1,461 subjects, there were 237 of African American ethnic heritage. Automated ambulatory blood pressure monitoring was performed in a subset of 562 patients and this confirmed the results seen in the in-clinic systolic and diastolic blood pressure

cuff measurements that I just described. The incidence of peripheral edema during the 8-week randomized double blind treatment period was highest with amlodipine 10 mg monotherapy and was notably lower when telmisartan was used in combination with amlodipine 10 mg qd. So just quick safety information regarding Twynsta. Like all drugs that influence that are agonists to the angiotensin thoracic system, there's a boxed warning in the label to avoid the use during pregnancy. In patients with heart failure, renal artery stenosis or severe renal impairment, care should be exercised with dosing of Twynsta. In clinical trials, the most common reported adverse events with Twynsta that were more frequent than with placebo, were peripheral edema, dizziness, clinically meaningful orthostatic hypotension and back pain. I'd be happy to entertain any questions you have.
Materials included in agenda packet; presented by Dr. Keast.
Dr. Kuhls moved to approve as submitted; seconded by Dr. Bell.
ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: **VOTE TO PRIOR AUTHORIZE PENNSAID®**
Materials included in agenda packet; presented by Dr. Sipols.
Dr. Feightner moved to approve as submitted; seconded by Ms. Varalli-Claypool.
ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: **30-DAY NOTICE TO PRIOR AUTHORIZE MOZOBIL®, NPLATE®, AND ARCALYST®**
For Public Comment: Michael Gray: My name is Michael Gray. I'm with medical affairs of Genzyme and I'm here to actually address the prior authorization on Mozobil as well as I'd like to address the criteria for approval, number 6. Mozobil is an orphan status drug. It is used only in the setting of stem cell collection for autologous transplant for myeloma and non-Hodgkins lymphoma, so that's its only indication. That's already a very, very small population which is why it has the orphan status. In this state, looking at the two centers that do the transplants, which would be the University and then Tulsa, there's only going to be approximately 80 patients that undergo an autologous transplant in this state, and not all of those would really need Mozobil for their stem cell collection. So, you know, the prior authorization, it becomes very difficult in the setting of collection and autologous transplants. My background was in transplant at M.D. Anderson Cancer Center. If you, you know, look at how you do things, you're going to treat the patient, try to get them to as good a remission as possible and then immediately try to collect those stem cells so that you can give them the high dose chemotherapy and then their cells back. If you make it so that you have this 30-day window, essentially you have to almost guesstimate whether or not you would or wouldn't need the drug in order to file the pre-auth prior. Timing wise, that's going to be very difficult. Secondly, also would be criteria for approval; requiring that, number 6, requiring that the patient fail at collection or have heavy pre-treatment is not actually what is within our label. That's actually more restrictive than the label that we have, which is it can be used at the discretion of the transplant physician writing for it. To require that the patient fail means that they're going to get their induction chemotherapy, attempt a collection which would be here in this state, mainly a G-CSF, so they reach four or five days of G, go under aphaeresis and then they would fail and then you would have to file for the pre-auth and then wait for that to be authorized for them to restart another four to five days of G and then receive Mozobil in order to have their collection. So what I'd like you to consider is to simply restrict it to its use on the label, which is actually a very, very small population for orphan status drug. Like I said, here in total, the number of autos done in this state is only approximately 80 patients. And not all of those patients are going to need this drug. So I feel that the transplanters, hopefully, would not overuse this drug because there's really not a place for it. It's only indicated for one thing which is to collect stem cells for those patients.
Board members collectively approved removal of criteria number 6: "Must have either a prior stem cell collection failure or a history of heavy pre-treatment".
Board members discussed changes in criteria recommendations.
Materials included in agenda packet; presented by Dr. Sipols.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 9: **ANNUAL REVIEW OF XOPENEX® AND ALBUTEROL HFA PRODUCTS**
Materials included in agenda packet; presented by Dr. Chonlahan.
No action was required.
ACTION:

AGENDA ITEM NO. 10: **FDA & DEA UPDATES**
Materials included in agenda packet; presented by Dr. Graham.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 11: **FUTURE BUSINESS**

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

A: **Annual Review of Smoking Cessation Products**
B: **Annual Review of Growth Hormones**
C: **FY09 Annual Review**
D: **New Product Reviews**
ACTION: **NONE REQUIRED**

AGENDA ITEM NO. 12: **ADJOURNMENT**

The meeting was adjourned at 7:38 p.m.

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

Memorandum

Date: March 12, 2010

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

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

Subject: DUR Board Recommendations from Meeting of March 10, 2010

Recommendation 1: Vote to Update Anxiolytic Prior Authorization Category

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following changes:

Prior Authorization

- Remove current PA requirements for members greater than 18 years of age.
- Members ~~18~~ 12 or younger will require prior authorization. The criteria for approval would be as follows:
  - Chronic Behavioral Health Related Diagnosis:
    - Prescription originally written by a psychiatrist, AND
    - No concurrent stimulant ADHD medications ~~(except Strattera)~~, AND
    - No contraindicated indications, AND
    - Maximum dosing of 3 times daily.
  - Chronic Physical Diagnosis:
    - Up to TID dosing if a hypnotic is being used concurrently; up to QID otherwise.
  - Exceptions can be granted for administration prior to procedures.

- Members 13 through 18 years of age will require prior authorization. The criteria for approval would be as follows:
  - Chronic Behavioral Health Related Diagnosis:
    - No concurrent stimulant ADHD medications, AND
    - No contraindicated indications, AND
    - Maximum dosing of 3 times daily.
  - Chronic Physical Diagnosis:
    - Up to TID dosing if a hypnotic is being used concurrently; up to QID otherwise.
  - Exceptions can be granted for administration prior to procedures.

System Edits

- Quantity limits set at up to 3 units per day (less based on FDA maximums) for all products.
- No requests for dosing greater than 3 times daily will be approved unless a Chronic Physical Diagnosis exists; for these diagnoses the maximum allowed dosing would be 4 times daily.
- Current members will be given 2 months to taper dosing to no more than 3 doses daily
- A member may receive more than 3 units per day if the following criteria exist:
  - 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).
  - The member has a Chronic Physical Diagnosis and a clinical reason for excessive units has been provided.

~~**ProDUR Edits**~~

- ~~Therapeutic Duplication Module – currently set to notify pharmacies only (claims are suspended until pharmacy responds) of duplications of therapy for most major drug categories.~~
- ~~Can be limited to antianxiety medications (would include buspirone) and set to deny when more than one product was being filled. (Claims would pay when multiple products are prescribed by a single physician.)~~
- ~~A member may receive more than one anxiolytic concurrently if the following criteria exist:~~
  - ~~The duplicate therapy is an injection or sublingual product to be given as needed when oral therapy cannot be administered.~~
  - ~~The prescription is from a psychiatrist and a clinical reason for multiple products has been provided.~~
  - ~~The member has a Chronic Physical Diagnosis and a clinical reason for multiple products has been provided.~~

In addition the DUR Board requests follow up after six months to review potential issues with therapeutic duplication and to monitor use in members 18 years of age or less.

Recommendation 2: Vote to Prior Authorize Twynsta®

MOTION CARRIED by unanimous approval.

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

Recommendation 3: Vote to Prior Authorize Pennsaid®

MOTION CARRIED by unanimous approval.

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

Recommendation 4: Annual Review of HFA Products

No action required.

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

Dianne B. Gasbarra MD
4200 West Memorial Road, Suite 405
Oklahoma City, Oklahoma 73120
(405) 749-0210

March 9, 2010

Dr. Shellie Gorman Keast
DUR Manager
Pharmacy Management Consultants

Dear Dr. Keast,

I have been advised that decisions are currently being made regarding a formulary entry for Albuterol inhalers. I realize that there are a variety of preparations to choose from and for that reason I want to share some of my thoughts with you.

I have had a number of patients that either did not tolerate some component of the Proair HFA preparation, and/or did not recognize an appropriate response to the medication. The Proventil HFA preparation has not had that same level of negative patient feedback, however the Ventolin HFA has been the hands down winner among patients. They seem to be very appreciative of the counting mechanism that is built into the device. Teaching appropriate inhaler use technique is easier having the counting device in place. So often patients administer the two inhalations back to back without pausing between actuations. Having the counting device has helped to curb that habit, and therefore improve medication delivery and patient response. I think that patients are able to be more objective about how often they are using the inhaler and at the same time less anxious about running out of medication.

For these reasons I want to express my hope that Ventolin HFA will be your formulary choice for the inhaler form of Albuterol HFA. Thank-you for your consideration in this issue.

Sincerely,

DB Gasbarra MD

Dianne B. Gasbarra MD

Appendix B

RETROSPECTIVE DRUG UTILIZATION REVIEW REPORT
November 2009

MODULE	DRUG INTERACTION	DUPLICATION OF THERAPY	DRUG-DISEASE PRECAUTIONS	DOSING & DURATION
Total # of messages	44,991	56,765	1,053,512	28,988
Limits applied	Established, Major, Males and Females, Age 61-150	Males and Females, Narcotics, Age 34-35	Contraindicated, Diabetes Mellitus, Males and Females Age 19-35	High Dose Only,Benzodiazepines, Males and Females, Age 71-150
Total # of messages after limits were applied	31	194	83	44
Total # of members reviewed	31	144	65	44

LETTERS

Category	Prescribers	Pharmacies	Total Letters
Drug Interaction	18	0	18
Duplication of Therapy	100	21	121
Drug-Disease Precautions	6	0	6
Dosing & Duration	5	0	5
Total Letters Sent	129	21	150

RETROSPECTIVE DRUG UTILIZATION REVIEW REPORT
December 2009

MODULE	DRUG INTERACTION	DUPLICATION OF THERAPY	DRUG-DISEASE PRECAUTIONS	DOSING & DURATION
Total # of messages	47,153	59,119	1,128,838	29,598
Limits applied	Established, Major, Males and Females, Age 0-21	Males and Females, Narcotics, Age 36-37	Contraindicated, Diabetes Mellitus, Males and Females Age 36-45	High Dose & Low Dose, Ortho Evra, Males and Females, Age 0-150
Total # of messages after limits were applied	45	178	141	95
Total # of members reviewed	45	151	117	95

LETTERS

Category	Prescribers	Pharmacies	Total Letters
Drug Interaction	9	0	9
Duplication of Therapy	78	12	90
Drug-Disease Precautions	6	0	6
Dosing & Duration	0	10	10
Total Letters Sent	93	22	115

Retrospective Drug Utilization Review Report

Claims Reviewed for September 2009

Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
Limits which were applied	Established, Major, Males and Females, Age 36-50	Narcotics, Males and Females, Age 30-31	Contraindicated, Glaucoma, Males and Females, Age 0-150	High Dose, Benzodiazepines, Males and Females, Age 0-19

Response Summary (Prescriber)
Letters Sent: 215
Response Forms Returned: 97

The response forms returned yielded the following results:

4 (4%)	*Record Error—Not my patient.*
15 (15%)	*No longer my patient.*
2 (2%)	*Medication has been changed prior to date of review letter.*
29 (30%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
29 (30%)	*I am aware of this situation and will plan to continue monitoring therapy.*
18 (19%)	*Other*

Response Summary (Pharmacy)
Letters Sent: 39
Response Forms Returned: 22

The response forms returned yielded the following results:

2 (9%)	*Record Error—Not my patient.*
3 (14%)	*No longer my patient.*
0 (0%)	*Medication has been changed prior to date of review letter.*
7 (32%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
6 (27%)	*I am aware of this situation and will plan to continue monitoring therapy.*
4 (18%)	*Other*

Retrospective Drug Utilization Review Report

Claims Reviewed for October 2009

Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
Limits which were applied	Established, Major, Males and Females, Age 51-60	Narcotics, Males and Females, Age 32-33	Contraindicated, Diabetes Mellitus, Males and Females, Age 0-18	High Dose, Benzodiazepines, Males and Females, Age 20-70

Response Summary (Prescriber)
Letters Sent: 128
Response Forms Returned: 97

The response forms returned yielded the following results:

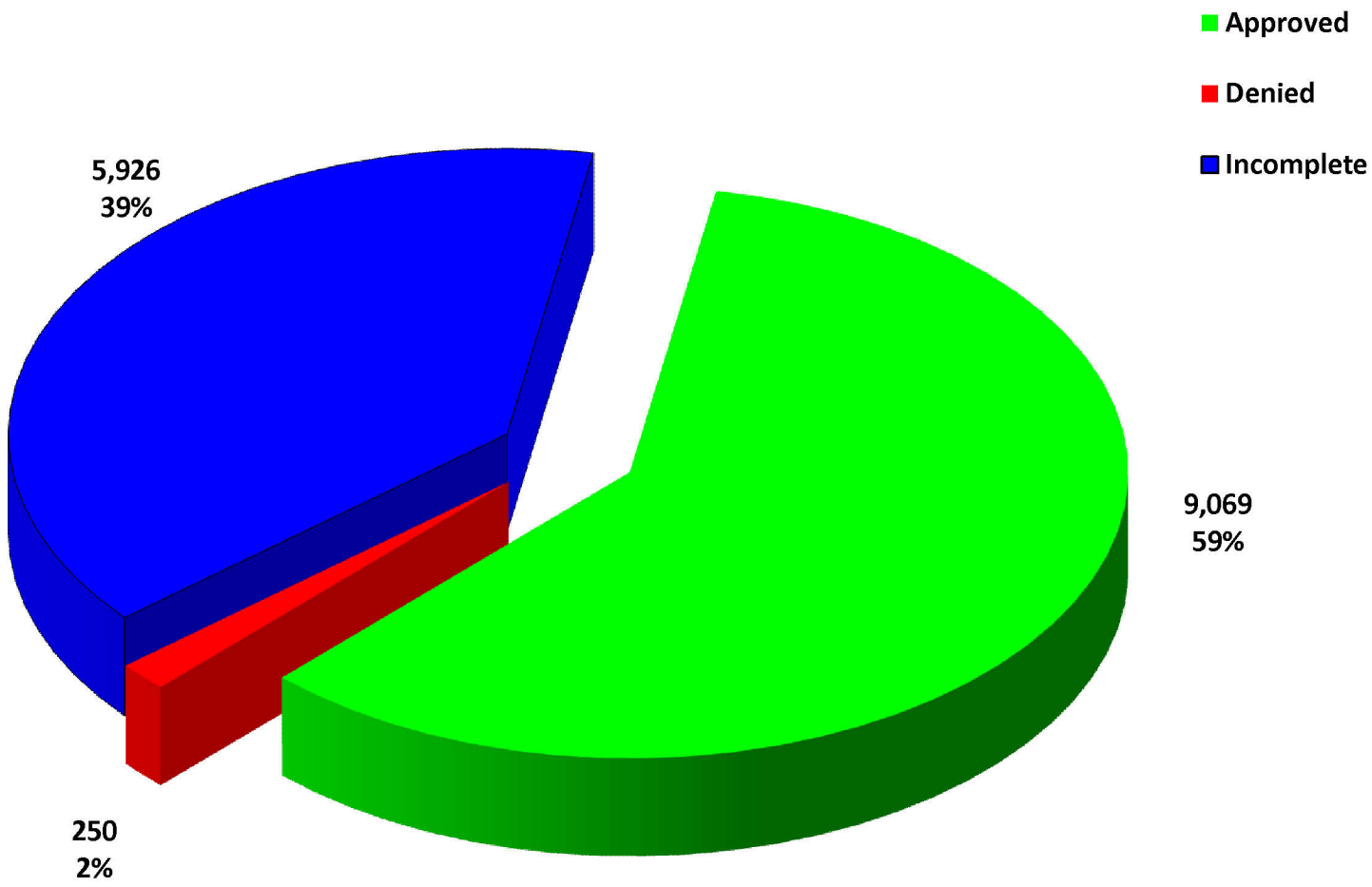
4 (4%)	*Record Error—Not my patient.*
14 (14%)	*No longer my patient.*
8 (8%)	*Medication has been changed prior to date of review letter.*
19 (20%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
36 (37%)	*I am aware of this situation and will plan to continue monitoring therapy.*
16 (16%)	*Other*

Response Summary (Pharmacy)
Letters Sent: 13
Response Forms Returned: 6

The response forms returned yielded the following results:

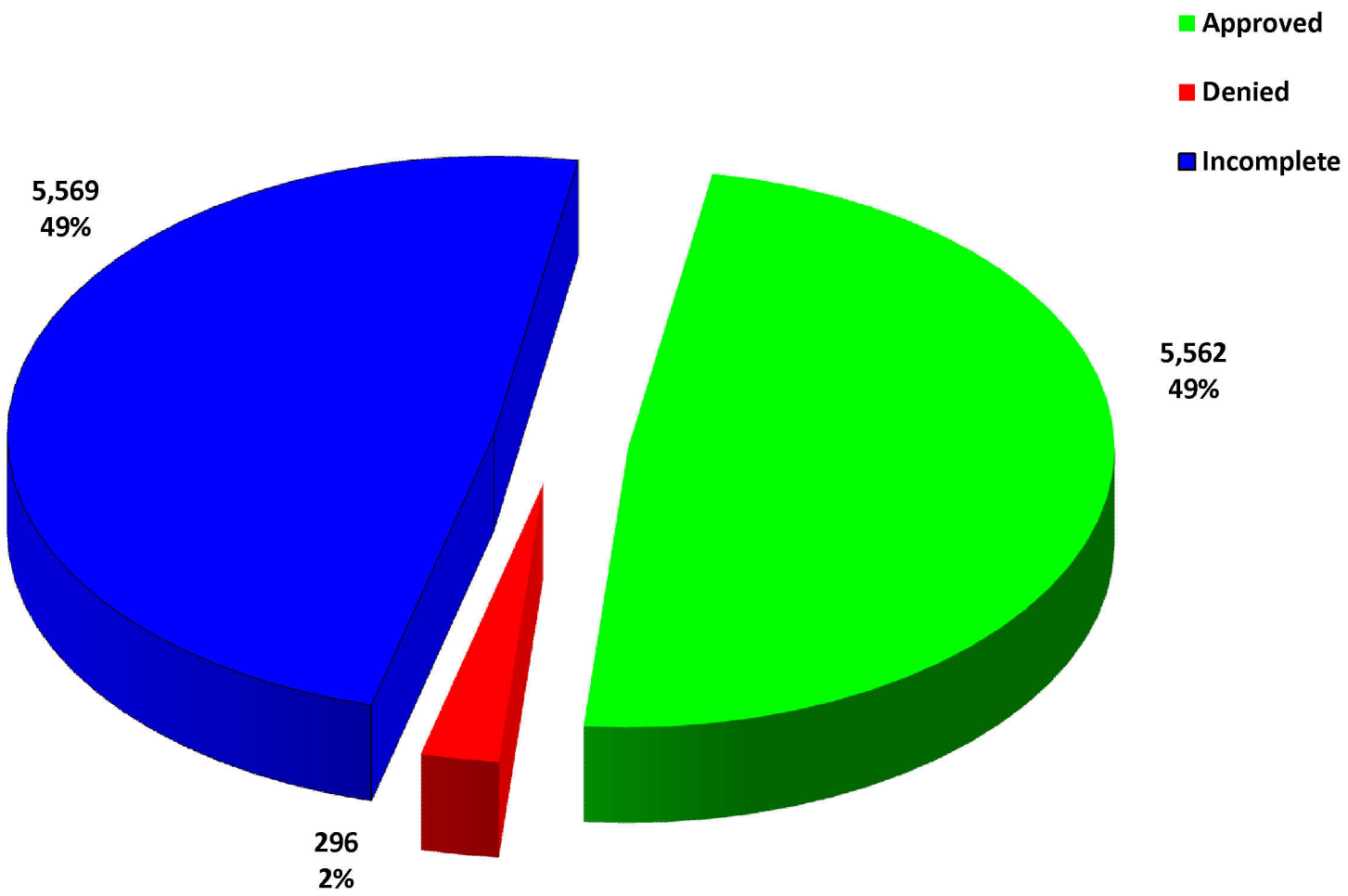
0 (0%)	*Record Error—Not my patient.*
1 (17%)	*No longer my patient.*
0 (0%)	*Medication has been changed prior to date of review letter.*
2 (33%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
1 (17%)	*I am aware of this situation and will plan to continue monitoring therapy.*
2 (33%)	*Other*

PRIOR AUTHORIZATION ACTIVITY REPORT: March 2010



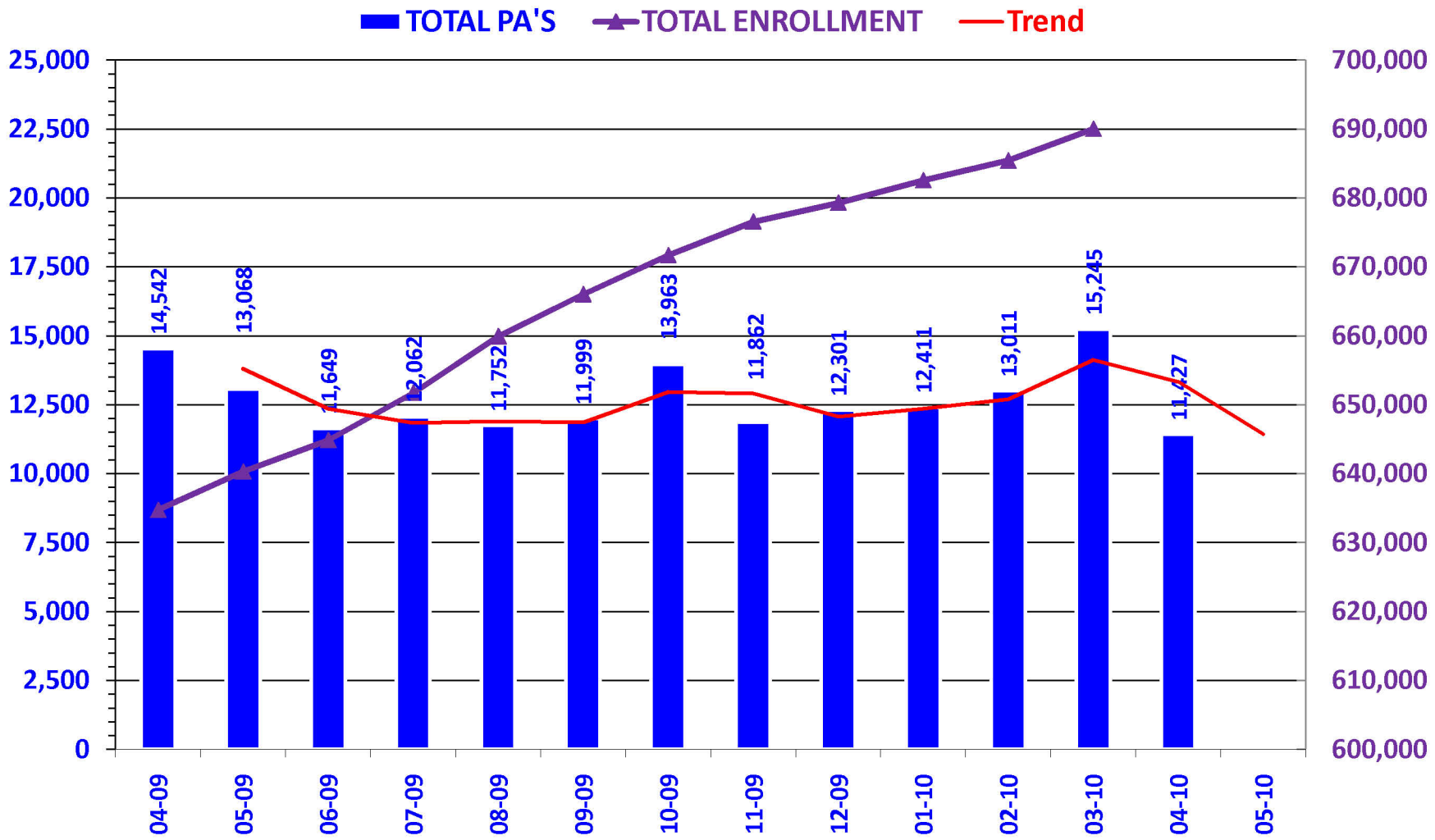
PA totals include overrides

PRIOR AUTHORIZATION ACTIVITY REPORT: April 2010



PA totals include overrides

PRIOR AUTHORIZATION REPORT: April 2009 – April 2010



PA totals include overrides

Prior Authorization Activity

March 2010

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort	597	265	3	329	360
Amitiza	19	8	0	11	155
Antidepressant	484	129	6	349	340
Antihistamine	442	246	2	194	300
Antihypertensives	165	60	0	105	341
Antimigraine	161	30	2	129	291
Atypical Antipsychotics	188	123	1	64	268
Benzodiazepines	4,824	4,141	14	669	91
Bladder Control	91	12	0	79	339
Brovana (Arformoterol)	2	1	0	1	361
Byetta	3	1	0	2	363
Elidel/Protopic	56	26	1	29	90
ESA	217	155	0	62	58
Fibric Acid Derivatives	10	1	0	9	364
Fibromyalgia	176	76	1	99	351
Fortamet/Glumetza	4	1	0	3	361
Forteo	4	1	0	3	362
Glaucoma	13	2	0	11	193
Growth Hormones	59	51	4	4	172
HFA Rescue Inhalers	109	47	5	57	269
Insomnia	130	37	3	90	112
Misc Analgesics	64	7	24	33	218
Muscle Relaxant	239	77	87	75	53
Nasal Allergy	596	68	8	520	141
NSAIDS	191	41	2	148	296
Ocular Allergy	21	0	0	21	0
Ocular Antibiotics	35	7	1	27	10
Opioid Analgesic	193	69	6	118	149
Other	685	242	24	419	162
Otic Antibiotic	177	88	0	89	17
Pediculicides	131	56	0	75	16
Plavix	565	398	2	165	312
Proton Pump Inhibitors	704	125	1	578	108
Singulair	881	490	2	389	259
Smoking Cessation	98	29	2	67	45
Statins	140	32	1	107	353
Stimulant	1,128	725	6	397	233
Symlin	1	0	0	1	0
Synagis	82	59	7	16	20
Topical Antibiotics	24	5	0	19	33
Topical Antifungals	32	1	0	31	12
Ultram ER and ODT	9	0	0	9	0
Xolair	2	0	2	0	0
Xopenex Nebs	49	26	0	23	263
Zetia (Ezetimibe)	26	16	0	10	361
Emergency PAs	4	4	0	0	
Total	**13,831**	**7,978**	**217**	**5,636**	

Overrides					
Brand	65	40	2	23	188
Dosage Change	499	454	8	37	12
High Dose	8	7	0	1	213
IHS - Brand	77	67	4	6	72
Ingredient Duplication	11	8	0	3	58
Lost/Broken Rx	89	82	4	3	10
Nursing Home Issue	102	96	0	6	5
Other	26	20	0	6	21
Quantity vs. Days Supply	535	315	15	205	237
Wrong D.S. on Previous Rx	2	2	0	0	105
Overrides Total	**1,414**	**1,091**	**33**	**290**	
Total Regular PAs + Overrides	**15,245**	**9,069**	**250**	**5,926**	

Denial Reasons

Lack required information to process request.	2,679
Unable to verify required trials.	2,645
Not an FDA approved indication/diagnosis.	237
Does not meet established criteria.	205
Considered duplicate therapy. Member has a prior authorization for similar medication.	137
Member has active PA for requested medication.	128
Requested dose exceeds maximum recommended FDA dose.	77
Medication not covered as pharmacy benefit.	48
Drug Not Deemed Medically Necessary	2

Duplicate Requests: 1,076

Changes to existing PAs: 988

Prior Authoriztion Activity

April 2010

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort	569	251	4	314	357
Amitiza	25	7	1	17	197
Antidepressant	455	145	5	305	340
Antihistamine	573	304	6	263	310
Antihypertensives	127	53	0	74	304
Antimigraine	121	20	5	96	253
Atypical Antipsychotics	527	249	1	277	340
Benzodiazepines	590	309	5	276	139
Bladder Control	96	11	5	80	313
Brovana (Arformoterol)	1	0	0	1	0
Byetta	4	1	0	3	360
Elidel/Protopic	46	26	1	19	94
ESA	207	157	0	50	57
Fibric Acid Derivatives	11	2	0	9	359
Fibromyalgia	173	51	4	118	347
Forteo	1	1	0	0	360
Glaucoma	24	8	0	16	324
Growth Hormones	60	47	0	13	168
HFA Rescue Inhalers	98	34	4	60	256
Insomnia	121	35	1	85	146
Misc Analgesics	51	5	17	29	270
Muscle Relaxant	206	84	63	59	67
Nasal Allergy	560	84	10	466	145
NSAIDS	193	38	12	143	315
Ocular Allergy	43	3	3	37	30
Ocular Antibiotics	76	20	0	56	17
Opioid Analgesic	199	88	5	106	172
Other	520	162	37	321	118
Otic Antibiotic	142	64	0	78	13
Pediculicides	162	82	3	77	13
Plavix	346	238	0	108	309
Proton Pump Inhibitors	570	101	17	452	101
Qualaquin (Quinine)	1	0	1	0	0
Singulair	1,074	571	11	492	258
Smoking Cessation	68	22	0	46	68
Statins	127	41	0	86	355
Stimulant	1,132	717	10	405	232
Symlin	8	4	1	3	360
Topical Antibiotics	21	4	0	17	16
Topical Antifungals	27	6	1	20	40
Ultram ER and ODT	14	1	0	13	30
Xolair	4	2	1	1	362
Xopenex Nebs	39	17	3	19	275
Zetia (Ezetimibe)	26	15	0	11	360
Emergency PAs	14	14	0	0	
Total	**9,452**	**4,094**	**237**	**5,121**	

Overrides					
Brand	68	42	2	24	259
Dosage Change	557	505	11	41	13
High Dose	6	5	0	1	87
IHS - Brand	28	23	0	5	143
Ingredient Duplication	7	5	1	1	15
Lost/Broken Rx	79	74	2	3	11
NDC vs Age	3	3	0	0	361
Nursing Home Issue	64	60	2	2	11
Other	40	29	1	10	49
Quantity vs. Days Supply	1,120	720	40	360	266
Stolen	5	5	0	0	81
Wrong D.S. on Previous Rx	1	0	0	1	0
Overrides Total	**1,975**	**1,468**	**59**	**448**	
Total Regular PA + Overrides	**11,427**	**5,562**	**296**	**5,569**	

Denial Reasons

Unable to verify required trials.	2,672
Lack required information to process request.	2,502
Does not meet established criteria.	266
Not an FDA approved indication/diagnosis.	157
Member has active PA for requested medication.	80
Considered duplicate therapy. Member has a prior authorization for similar medication.	66
Medication not covered as pharmacy benefit.	56
Requested dose exceeds maximum recommended FDA dose.	37
Drug Not Deemed Medically Necessary	5

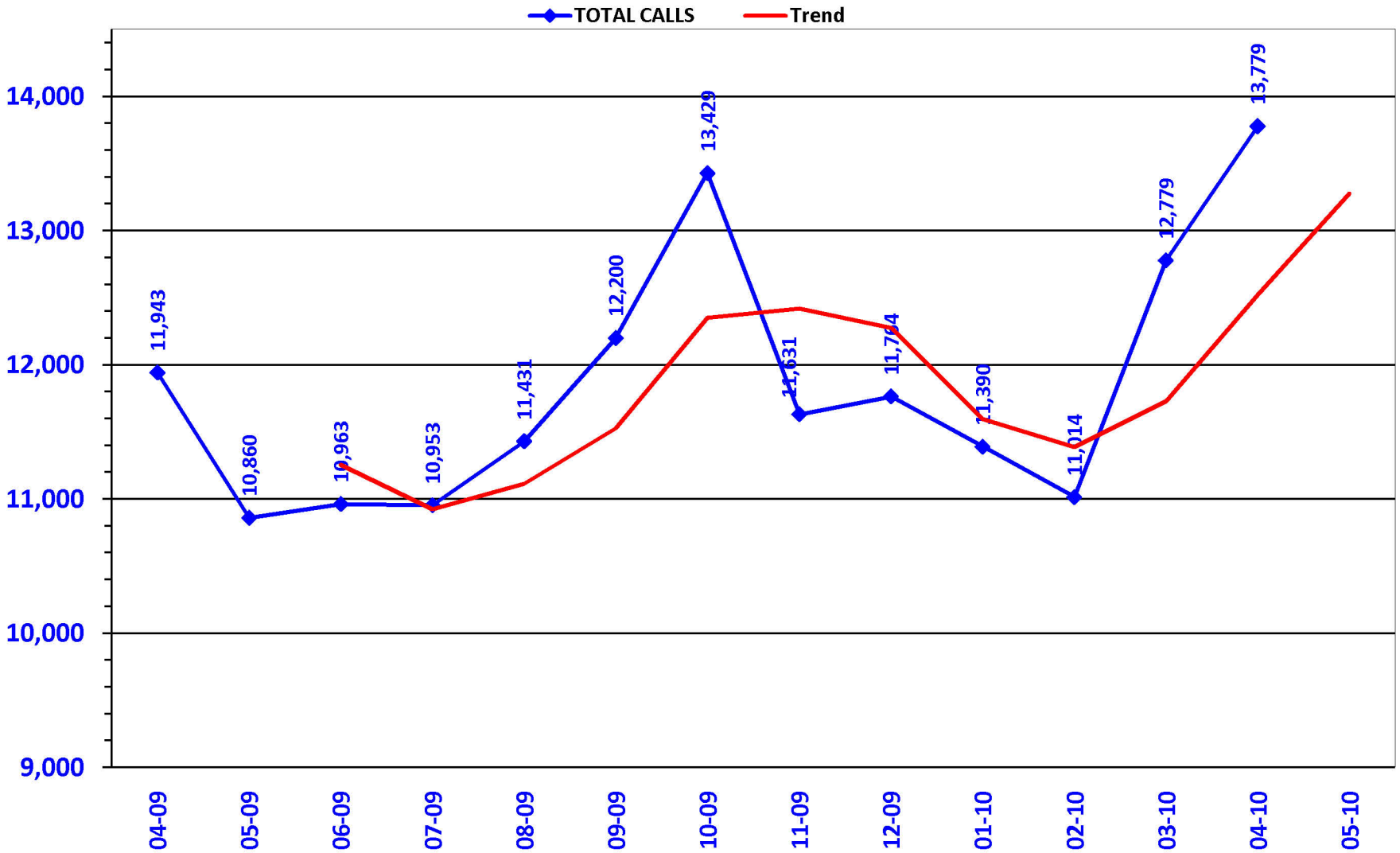
Duplicate Requests: 848

Letters: 1,420

No Process: 341

Changes to existing PAs: 650

CALL VOLUME MONTHLY REPORT:
April 2009 – April 2010



Appendix C

Vote to Prior Authorize Mozobil®, Nplate®, and Arcalyst®

Oklahoma Health Care Authority, May 2010

Recommendations:

The College of Pharmacy recommends pharmacy prior authorization of Mozobil® (plerixafor), Nplate® (romiplostim), and Arcalyst® (rilonacept) with the following criteria.

Mozobil® (plerixafor) criteria for approval:

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

Nplate® (romiplostim) criteria for approval:

1. FDA approved indication of chronic immune (idiopathic) thrombocytopenia purpura (ITP) in adults 18 and over.
2. Previous insufficient response with at least two of the following treatments: corticosteroids, immunoglobulins, or splenectomy
3. Recent platelet count of $< 50 \times 10^9/L$
4. Initial dosing of 1 mcg/kg once weekly as a subcutaneous injection with recent patient weight in kilograms provided

5. **Continuation criteria:**
    a. Weekly CBCs with platelet count and peripheral blood smears until stable platelet count (≥ 50 x 109/L for at least 4 weeks without dose adjustment) has been achieved; then obtain monthly thereafter
    b. Dosing adjustments:
        i. Platelets < 50 x 10^9/L, increase dose by 1 mcg/kg
        ii. Platelets > 200 x 10^9/L for 2 consecutive weeks, reduce dose by 1 mcg/kg
        iii. Platelets > 400 x 10^9/L, do not dose. Continue to assess platelet count weekly. When platelets < 200 x 10^9/L, resume at a dose reduced by 1 mcg/kg
6. **Discontinuation criteria:**
    a. Platelet count does not increase to a level sufficient to avoid clinically important bleeding after 4 weeks of therapy at the maximum weekly dose of 10 mcg/kg
7. Approval period will be for four weeks initially, and then quarterly.

Arcalyst® (rilonacept) criteria for approval:

1. FDA approved indication of Cryopyrin-Associated Periodic Syndromes (CAPS) verified by genetic testing. This includes Familial Cold Auto-inflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS) in adults and children 12 and older.
2. The member should not be using a tumor necrosis factor blocking agent (e.g. adalimumab, etanercept, and infliximab) or anakinra
3. Should not be initiated in patients with active or chronic infection including hepatitis B, hepatitis C, human immunodeficiency virus, or tuberculosis.
4. Dosing should not be more often than once weekly.
5. **Approved dosing schedule for adults 18 and over:**
    a. Initial treatment: loading dose of 320 mg delivered as two 2mL subcutaneous injections of 160 mg each given on the same day at two different injection sites.
    b. Continued treatment is one 160 mg injection given once weekly.
6. **Approved dosing schedule for pediatric patients aged 12-17 years (must have patient weight in kilograms):**
    a. Initial treatment: loading dose of 4.4 mg/kg, up to a maximum of 320 mg, delivered as one or two subcutaneous injections with a maximum single-injection volume of 2mL.
    b. Continued treatment is 2.2 mg/kg, up to a maximum of 160 mg, given once weekly.
7. Approval period is for one year.

Appendix D

30 Day Notice to Prior Authorize Ilaris® (canakinumab)

Oklahoma Health Care Authority, May 2010

Manufacturer	Novartis Pharma Stein AG
Classification	Immunological Agent/Interleukin-1β blocker
Status	Prescription Only

Canakinumab Summary

Canakinumab is an interleukin-1 blocker indicated for the treatment of Cryopyrin-Associated Periodic Syndromes (CAPS), including Familial Cold Auto-Inflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS), in adults and children 4 and older. CAPS refer to rare genetic syndromes, generally caused by mutations in the NLRP-3 gene, which encodes the protein cryopyrin. This protein is an important component of the inflammasome, which becomes overactive causing an excessive release of activated interleukin-1 beta (IL-1β) that drives inflammation. Symptoms include fever, urticaria-like rash, arthralgia, myalgia, fatigue, and conjunctivitis. Canakinumab is a recombinant, human anti-human-IL-1β monoclonal antibody. The drug binds to human IL-1β and neutralizes its activity by blocking interaction with IL-1 receptors. C-reactive protein (CRP) and serum amyloid A (SAA) are indicators of inflammatory disease that are elevated in patients with CAPS. Studies showed that following canakinumab treatment, CRP and SAA levels normalized within 8 days. Phase III data have shown sustained remission in more than 90% of CAPS patients (28 out of 31) treated with canakinumab.

Canakinumab is given by a healthcare provider as a subcutaneous injection every eight weeks in a single dose. Prior to initiation of therapy vaccination history should be reviewed. There is an increased risk of secondary transmission of infection by live vaccines and also the possibility of reduced effectiveness of immunization while taking canakinumab. There is an increased risk of developing a serious infection while taking canakinumab. For this reason, it is not recommended to combine canakinumab therapy with other medications that block IL-1 or TNF-blocking agents.

The most common adverse reactions reported with canakinumab were nasopharyngitis, diarrhea, influenza, headache, and nausea. Increased risk of infections has also been associated with canakinumab therapy. In clinical trials, a total of sixty-two patients were exposed to canakinumab for at least 6 months. A total of 9 serious adverse reactions were reported, including vertigo (2 patients), infections (3 patients), including intra-abdominal abscess following appendectomy (1 patient).

The current cost of a 180mg vial of canakinumab is $16,720. It is given every eight weeks as a weight-based dose, with a maximum dose of 150mg. For a year of therapy at the maximum dose, the cost would be approximately $117,040.

Canakinumab is currently being evaluated in clinical trials for treatment of several other conditions, including diabetes mellitus types I and II, juvenile idiopathic arthritis, and the prevention of gout exacerbations.

Recommendations

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

Criteria for approval:

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

Product Details

Indication- Canakinumab is indicated for treatment of Cryopyrin-Associated Periodic Syndromes (CAPS) which includes Familial Cold Autoinflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS) in patients 4 years of age and older.

Dosage Forms- Canakinumab is supplied as a lyophilized powder for injection (180mg per vial). It must be reconstituted with 1 mL of preservative-free sterile water resulting in a total volume of 1.2 mL reconstituted solution of 150 mg/mL.

Contraindications- as of April 30, 2010, no specific contraindications have been indicated for rilonacept.

Pregnancy Risk Category C

Warnings and Precautions

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

Common Adverse Reactions

- **Dermatologic-** injection site reactions (7-9%)- reported as mild
- **Gastrointestinal effects-** diarrhea (20%), gastroenteritis (11%), nausea (14%)
- **Musculoskeletal effects-** musculoskeletal pain (11%)
- **Neurologic effects-** headache (14%), vertigo (9-14%)
- **Respiratory effects-** bronchitis (11%), nasopharyngitis (34%), pharyngitis (11%), rhinitis (17%), upper respiratory infections have been reported
- **Endocrine/metabolic-** increased weight (11%)
- **Other-** influenza (17%)

Drug Interactions

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

Patient Information

How to Use This Injectable Medicine:

- Your doctor will prescribe your exact dose and tell you how often it should be given. This medicine is given as a shot under your skin.
- A nurse or other trained health professional will give you this medicine.

Drugs and Foods to Avoid:

- Ask your doctor or pharmacist before using any other medicine, including over-the-counter medicines, vitamins, and herbal products.
- Make sure your doctor knows if you or your child are using medicines that weaken your immune system, such as a steroid medicine (dexamethasone, prednisolone, prednisone, or Medrol®), cancer medicines, or adalimumab (Humira®), anakinra (Kineret®), etanercept (Enbrel®), infliximab (Remicade®), or rilonacept (Arcalyst™).
- Tell your doctor if you are also using a blood thinner such as warfarin (Coumadin®).
- Talk to your doctor before getting flu shots or other vaccines while you are receiving this medicine. Vaccines may not work as well, or they could make you ill while you are using this medicine.

Warnings While Using This Medicine:

- Make sure your doctor knows if you are pregnant or breastfeeding
- Tell your doctor if you have an infection, HIV or AIDS, hepatitis B, hepatitis C, tuberculosis (TB) or a history of TB, or if you have been in close contact with someone who has active TB.
- You or your child may get infections more easily while using this medicine. Avoid people who are sick or who have infections. Call your doctor right away if you or your child have a fever, chills, or cough.

Possible Side Effects While Using This Medicine:

- Call your doctor right away if you notice any of these side effects:
    - Allergic reaction: Itching or hives, swelling in your face or hands, swelling or tingling in your mouth or throat, chest tightness, trouble breathing.
    - Fever, chills, cough, sore throat, and body aches.
    - Shortness of breath or difficulty with breathing.
    - Stuffy or runny nose.
    - Trouble with swallowing.

- If you notice these less serious side effects, talk with your doctor:
    - Dizziness or lightheadedness.
    - Feeling of constant movement of self or surroundings.
    - Headache.
    - Nausea, diarrhea, loss of appetite, or stomach pain.
    - Pain, itching, burning, swelling, or a lump under your skin where the shot is given.
    - Weight gain.
- If you notice other side effects that you think are caused by this medicine, tell your doctor.

REFERENCE
Product Information: ILARIS (canakinumab subcutaneous injection). Novartis Pharma Stein AG, Stein, Switzerland, June 2009.
Canakinumab monograph. Lexi-Comp, Inc. (Lexi-Drugs) Lexi-Comp, Inc. Accessed April 30, 2010.

Appendix E

30 Day Notice to Prior Authorize Besivance™ (besifloxacin ophthalmic suspension 0.6%)

Oklahoma Health Care Authority

May 2010

Manufacturer	Bausch & Lomb
Classification	Ophthalmic Quinolone Antimicrobial
Status	Prescription Only

Besivance™ Summary

Besivance™ (besifloxacin ophthalmic suspension) is a quinolone antimicrobial suspension indicated for treatment of bacterial conjunctivitis caused by susceptible isolates of the following bacteria:

- CDC coryneform group G,
- *Corynebacterium pseudodiphtheriticum,*
- *Corynebacterium striatum,*
- *Haemophilus influenzae,*
- *Moraxella lacunata,*
- *Staphylococcus aureus,*
- *Staphylococcus epidermidis,*
- *Staphylococcus hominis,*
- *Staphylococcus lugdunensis,*
- *Streptococcus mitis* group,
- *Streptococcus oralis,*
- *Streptococcus pneumoniae,*
- *Streptococcus salivarius*

For topical ophthalmic use only.

Cost Comparison of Besivance™

Product	EAC (Brand Only) (Estimated Acquisition Cost)	SMAC (generic available) (State Maximum Allowable Cost)
Vigamox	3 ml – $23.95/ml = $71.85	
Zymar	5 ml – $14.74/ml = $73.70	
Azasite	2.5 ml – $30.16/ml = $75.40	
Quixin	5 ml – $13.82/ml = $69.10	
Besivance	5 ml - $14.64/ml = $73.20	
Ciproflaxacin		5 ml – $1.84/ml = $9.20
Ofloxacin		5 ml – $0.75/ml = $3.75
Gentamycin		5 ml – $0.63/ml = $3.15
Sulfacetamide(Bleph-10)		5 ml – $0.21/ml = $1.05
Polymyxin B/TMP		5 ml – $0.89/ml = $4.45

Recommendations

The College of Pharmacy recommends placement of Besivance™ in Tier 3 of the Ophthalmic Antibiotic Products Product Based Prior Authorization Category. The College also recommends moving Quixin® to Tier 3 from Tier 2. The existing criteria for this category will apply.

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

Mandatory Generic Plan applies.

Criteria for a Tier 2 medication:

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

Criteria for a Tier 3 medication:

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

Medication Product Details[1]

Indication

Besivance™ (besifloxacin) is a fluoroquinolone antibacterial indicated for the treatment of bacterial conjunctivitis

Dosage Forms: 5 ml dropper bottle

Dose: 1 drop 3 times a day, four to twelve hours apart, for 7 days.

Pregnancy Risk Category: C

Contraindications: Contraindicated in patients with known hypersensitivity to any of the components

Precautions

Microbial overgrowth – Prolonged use of topical antibiotics may cause overgrowth of nonsusceptible organisms including fungi. If super-infection occurs, discontinue use and institute alternative therapy.

Topical Ophthalmic Use Only –Besivance™ is for topical ophthalmic use only and should not be injected subconjunctivally, nor should it be introduced directly into the anterior chamber of the eye.

Contact Lenses – Patients should not wear contact lenses if they have signs or symptoms of bacterial conjunctivitis or during the course of therapy with Besivance™.

Common Adverse Effect

- ☑ Conjunctival redness
- ☑ Blurred vision
- ☑ Eye pain
- ☑ Eye irritation
- ☑ Eye pruritis
- ☑ Headache

Patient Information

- Besivance™ should not be used while wearing contact lenses.
- Avoid contaminating the applicator tip with material from the eye, fingers, or other source.
- Besivance™ should be discontinued at the first sign of a rash or allergic reaction.
- Wash hands thoroughly before administering dose.
- The medication should be used as directed. Skipping doses or not completing the full course of treatment may decrease the effectiveness of the immediate treatment and increase the likelihood that bacteria will develop resistance and will not be treatable by Besivance™ or other antibacterial drugs in the future.

REFERENCE

Besivance(TM) (besifloxacin) Product Information. Bausch & Lomb, Inc. April 2009.

Appendix F

30 Day Notice to Prior Authorize Requip XL™ (ropinirole extended release) And Mirapex ER™ (pramipexole extended release)

Oklahoma Health Care Authority
May 2010

Requip XL™ (ropinirole)

Manufacturer	GlaxoSmithKline
Classification	non-ergoline dopamine agonist
Status	Prescription Only

Requip XL™ Summary

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

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

Dosing and Administration:

- The starting dose is 2 mg taken once daily for 1 to 2 weeks, followed by increases of 2 mg/day at 1 week or longer intervals as appropriate, depending on therapeutic response and tolerability, up to a maximally recommended dose of 24 mg/day. Caution should be exercised during dose titration because too rapid a rate of titration can lead to dose selection that does not provide additional benefit, but that increases the risk of adverse reactions.
- If Requip XL™ must be discontinued, it should be tapered gradually over a 7-day period.
- Tablet must be swallowed whole with or without food.
- Tablet should not be chewed, crushed, or divided.
- Off-Label Uses: Restless Leg Syndrome (RLS)
- Patients may be switched directly from immediate-release ropinirole to Requip XL™. The initial switching dose of Requip XL™ should most closely match the total daily dose of immediate-release ropinirole as shown on the following table:

Immediate-Release Tablets Total Daily Dose (mg)	Requip XL™ Tablets Total Daily Dose (mg)
0.75 to 2.25	2
3 to 4.5	4
6	6
7.5 to 9	8
12	12
15 to 18	16
21	20
24	24

Mirapex ER™ (pramipexole extended release)

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

Mirapex ER™ Summary

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

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

Dosing and Administration:

- The starting dose is 0.375 mg given once per day. Dosages may be increased gradually, not more frequently than every 5 to 7 days, first to 0.75 mg per day and then by 0.75 mg increments up to a maximum recommended dose of 4.5 mg per day.
- Discontinuing therapy requires tapering the dose gradually over a period of one week.
- If a significant interruption in therapy with Mirapex ER™ tablets has occurred, re-titration of therapy may be warranted.
- May be taken with or without food; however, taking with food may reduce occurrence of nausea.
- Tablet must be swallowed whole. They should not be chewed, crushed, or divided.
- Moderate renal impairment (creatinine clearance between 30 and 50mL/min) should be initiated on every other day therapy. May increase dosages to once a day dosing in 0.375mg increments up to a recommended 2.25 mg per day.
- Mirapex ER™ tablets have not been studied in patients with moderate to severe renal impairment (creatinine clearance <50 mL/min) or on hemodialysis
- Off-Label Uses: Treatment of depression or fibromyalgia

Product Cost Comparison

Product	EAC*	SMAC**	Regimen, Max Dose	Monthly Cost#
Mirapex ER™ 4.5mg	$8.65		QD, 4.5mg	$259.50
Pramipexole@ 1.5 mg	$2.60		TID, 4.5mg	$234.00
Requip™(Ropinirole)@ 4mg	$2.94	$0.38	TID, 24mg	$68.40
Requip™ XL(Ropinirole) 12mg	$12.63		QD, 24mg	$757.80
Carbidopa/Levodopa ER@ 50-200mg	$1.59	$0.48	QD-BID, 8 tabs/day	$115.20
Carbidopa/Levodopa@ 25-250mg	$0.90	$0.30	BID-TID, 8 tabs/day	$72.00

*** EAC = Estimated Acquisition Cost, ** SMAC = State Maximum Allowable Cost (generic available), # Max Dose, Lowest Cost Used.**

Recommendations

The College of Pharmacy recommends prior authorization of Requip XL™ and Mirapex ER™ to ensure appropriate utilization of these medications. Approval will be granted only for the FDA approved indication of Parkinson's Disease.

Requip XL™ (ropinirole extended-release tablets) Product Details

Indication: indicated for the treatment of the signs and symptoms of idiopathic Parkinson's disease.

Dosage Forms 2 mg, 4 mg, 6 mg, 8 mg, and 12 mg

Contraindications: None

Pregnancy Risk Factor C

Precautions

- **Falling asleep** during activities of daily living may occur, including the operation of motor vehicles, which sometimes resulted in accidents. Sudden onset of sleep may occur without apparent warning or daytime drowsiness. Sedating medications (such as alcohol or CNS depressants), the presence of sleeping disorders, or other medications that increase plasma levels of ropinirole, may increase the risk of somnolence or falling asleep while engaged in activities of daily living. Before initiating treatment, patients should be advised of the potential of sudden onset of sleep or to develop drowsiness and asked about risk factors they may have. If a patient develops sudden onset of sleep during activities that require active participation (e.g., conversations, eating, etc.) and/or cannot avoid high-risk activities in the future, Requip XL™ should ordinarily be discontinued.
- **Syncope**, sometimes associated with bradycardia, may occur.
- **Symptomatic hypotension** (including postural/orthostatic hypotension) may occur, especially during dose escalation.
- **Elevation of blood pressure and changes in heart rate** may occur.
- **Hallucination** may occur.
- **Dyskinesi**a may be caused or exacerbated. Decreasing the L-dopa dose may lessen or eliminate this side effect.
- **May exacerbate psychosis**: Avoid use in patients with a major psychotic disorder.
- **Discontinuation of therapy**: Dopaminergic agents have been associated with a syndrome resembling neuroleptic malignant syndrome on abrupt withdrawal or significant dosage reduction after long-term use.
- Ropinirole inhibits prolactin secretion in humans and may potentially **inhibit lactation**.
- **Pleural/retroperitoneal fibrosis**: Risk of fibrotic complications (eg, pleural effusion/fibrosis, interstitial lung disease) has been reported in patients receiving ropinirole.
- **Melanoma**: Risk for melanoma development is increased in Parkinson's disease patients; drug causation or factors contributing to risk have not been established. Patients should be monitored closely and periodic skin examinations should be performed.

Common Adverse Effects

- Falling asleep during activities of daily living
- Syncope
- Symptomatic hypotension, hypotension, postural/orthostatic hypotension
- Elevation of blood pressure and changes in heart rate
- Hallucination
- Dyskinesia
- Major psychotic disorders
- Events with dopaminergic therapy
- Retinal pathology

Drug Interactions

- CYP1A2 is the major enzyme responsible for the metabolism of ropinirole. Thus inhibitors (e.g., ciprofloxacin, fluvoxamine) or inducers (e.g., omeprazole or smoking) of CYP1A2 may alter the clearance of ropinirole. Adjustment of dosage of REQUIP XL™ may be required.
- Higher doses of estrogens, usually associated with hormone replacement therapy (HRT), reduced oral clearance of ropinirole. Starting or stopping HRT treatment may require adjustment of dosage of Requip XL™.
- Dopamine antagonists, such as neuroleptics (e.g., phenothiazines, butyrophenones, thioxanthenes) or metoclopramide, may diminish effectiveness of ropinirole.
- Antipsychotics (Atypical): May diminish the therapeutic effect of Anti-Parkinson's Agents (Dopamine Agonist). Risk D: Consider therapy modification.
- Higher doses of estrogens, usually associated with hormone replacement therapy (HRT), reduced oral clearance of ropinirole. Starting or stopping HRT treatment may require adjustment of dosage of Requip XL™.

Patient Information

- **Falling asleep during normal activities.** You may fall asleep while doing normal activities such as driving a car, doing physical task, or using hazardous machinery while taking Requip™ or Requip XL™. You may suddenly fall asleep without being drowsy or without warning. This may result in having accidents. Your chances of falling asleep while doing normal activities while taking Requip™ or Requip XL™ is greater if you take other medicines that cause drowsiness. Tell your healthcare provider right away if this happens. Before starting Requip™ or Requip XL™, be sure to tell your healthcare provider if you take any medicines that make you drowsy.
- **Changes in blood pressure.** Requip™ and Requip XL™can decrease or increase your blood pressure. Lowering of your blood pressure is of special concern. If you faint, feel dizzy, nauseated, or sweaty when you stand up from sitting or lying down, this may mean that your blood pressure is decreased. If you notice this, you should contact your healthcare provider. Also, when changing position from lying down or sitting to standing up, you should do it carefully and slowly. Lowering of your blood pressure can happen especially when you start taking Requip™ or Requip XL™ or when your dose is increased.
- **Fainting.** Fainting can occur, and sometimes your heart rate may be decreased. This can happen especially when you start taking Requip™ or Requip XL™ or dose is increased. Tell your healthcare provider if you faint or feel dizzy.
- **Hallucinations** (unreal visions, sounds, or sensations) can occur in patients taking Requip™ or Requip XL™. The chances of having hallucinations are higher in patients with Parkinson's disease who are elderly, taking Requip™ or Requip XL™ with other Parkinson's disease drugs, or taking higher doses of Requip™ or Requip XL™. If you have hallucinations, talk with your healthcare provider.
- **Uncontrolled sudden movements.** Requip™ or Requip XL™ may cause uncontrolled sudden movements or make such movements you already have worse or more frequent.
- **Unusual urges.** Some patients taking Requip™ or Requip XL™ get urges to behave in a way unusual for them. Examples of this are an unusual urge to gamble or increased sexual urges and behaviors. Please notify your health care provider if unusual behaviors are occurring.
- **Do not suddenly stop taking Requip™ or Requip XL™** without talking to your healthcare provider. Sudden discontinuation may develop fever, confusion, or severe muscle stiffness.

Mirapex ER™ (pramipexole extended-release tablets) Product Details

Indication: indicated for the treatment of the signs and symptoms of idiopathic Parkinson's disease.

Dosage Forms 0.375mg, 0.75mg, 1.5mg, 3 mg, and 4.5mg extended release tablets
Note, when converting from immediate release to extended release, initiate extended release preparation the morning after the last immediate release evening tablet is taken. The total daily dose should remain the same.

Contraindications: None

Pregnancy Risk Factor C

Precautions

- **Falling Asleep during Activities of Daily Living**- Patients treated with pramipexole have reported falling asleep while engaged in activities of daily living, including the operation of motor vehicles, which sometimes resulted in accidents. Although many of these patients reported somnolence while on pramipexole tablets, some perceived that they had no warning signs such as excessive drowsiness, and believed that they were alert immediately prior to the event. Some events had been reported as late as one year after the initiation of treatment
- **Symptomatic Orthostatic Hypotension** -Dopamine agonists, in clinical studies and clinical experience, appear to impair the systemic regulation of blood pressure, with resulting orthostatic hypotension, especially during dose escalation.
- **Impulse control/Compulsive Behaviors-** patients can experience intense urges to gamble, increased sexual urges, intense urges to spend money, binge eating, and/or other intense urges, and the inability to control these urges while taking one or more of the medications, including Mirapex ER™, that increase central dopaminergic tone.
- **Hallucinations** -hallucinations (visual or auditory or mixed) were reported in 25 of 387 (6%) patients treated with Mirapex ER™ compared to 5 of 281 (2%) patients receiving placebo
- **Dyskinesia-** may potentiate the dopaminergic side effects of levodopa and may cause or exacerbate preexisting dyskinesia
- **Renal Impairment**- Patients with mild renal impairment (a creatinine clearance above 50 mL/min) require no reduction in daily dose. No data available in moderate to severe renal impairment.
- **Rhabdomyolysis** - a single case of rhabdomyolysis occurred in a 49-year-old male with advanced Parkinson's disease. The patient was hospitalized with an elevated CPK (10,631 IU/L). The symptoms resolved with discontinuation of the medication.
- **Events reported with dopaminergic therapy**: includes withdrawal-emergent hyperpyrexia and confusion, fibrotic complications, and melanoma. Dopaminergic agents have been associated with a syndrome resembling neuroleptic malignant syndrome on abrupt withdrawal or significant dosage reduction after long-term use.

Common Adverse Effect

- Nausea
- Constipation
- Dizziness
- Muscle Spasms
- Hallucination
- Somnolence
- Dry Mouth
- fatigue
- Peripheral edema

Drug Interactions

- **Dopamine antagonists**: May diminish the effectiveness of pramipexole.
- **Antipsychotics (Atypical)**: May diminish the therapeutic effect of Anti-Parkinson's Agents (Dopamine Agonist). Risk D: Consider therapy modification.
- **Antipsychotics (Typical)**: Anti-Parkinson's Agents (Dopamine Agonist) may diminish the therapeutic effect of Antipsychotics (Typical). Antipsychotics (Typical) may enhance the therapeutic effect of Anti-Parkinson's Agents (Dopamine Agonist). Avoid concomitant therapy if possible and monitor for decreased effects of both agents when these combinations cannot be avoided. Atypical antipsychotics such as clozapine and quetiapine may be less likely to reduce the effects of anti-Parkinson's agents. Risk D: Consider therapy modification.

Patient Information

- Do not drive a car, operate a machine, or do anything that needs you to be alert until you know how Mirapex ER™ affects you. Sleepiness caused by Mirapex ER™ may first occur as late as one year after initiation of treatment.
- Do not drink alcohol while taking Mirapex ER™ tablets. It can increase your chances of feeling sleepy or falling asleep when you should be awake.

REFERENCE

1. Requip XL™) (ropinirole extended-release) Product Information. GlaxoSmithKline. July, 2008.
2. Mirapex ER™ (pramipexole dihydrochloride) extended-releasetablets. Product Information. Boehringer Ingelheim Pharmaceuticals Inc. March 2010

Appendix G

30 Day Notice to Prior Authorize Lovaza® (omega-3-acid ethyl esters)

Oklahoma Health Care Authority
May 2010

Manufacturer	GlaxoSmithKline
Classification	Anti-Hypertriglyceridemia
Status	Prescription Only

Lovaza® Summary

Lovaza® was approved by the FDA in 2004 and initially marketed by Reliant Pharmaceuticals in the Fall of 2005 under the brand name Omacor®. The name was changed in 2007 to Lovaza® because Omacor® was too similar to Amacar® (aminocaproic acid).

Lovaza® is a purified form of omega-3 acid extracted from marine fish. It has been approved by the FDA as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe hypertriglyceridemia (≥500 mg/dL). The mechanism of action is not completely understood; however, it is believed that Lovaza® exerts its TG lowering properties by inhibiting substrates that are responsible for TG synthesis, specifically acyl CoA: 1,2-diacylglycerol acyltransferase.

Lovaza® is supplied as 1-gram transparent soft-gelatin capsules filled with light-yellow oil. The daily dose of Lovaza® is 4 grams per day and is taken as a single 4-g dose (4 capsules) or as two 2-g doses (2 capsules given twice daily.)

Lovaza® is marketed as the better alternative to fish oil capsules available over the counter due to the FDA regulated manufacturing process. The 5 step purification process is said to help remove mercury and environmental toxins that can be present in fish oil. Lovaza® is also marketed as a concentrated formulation, requiring only 4 capsules a day, while it could take up to 14 capsules per day of other fish oil supplements to provide the same amount of active fatty acids to lower very high trigycerides.

Lovaza® treatment to reduce very high TG levels may result in elevations in LDL-C and non-HDL-C in some individuals. Patients should be monitored to ensure that the LDL-C level does not increase excessively. The effects of Lovaza® on cardiovascular outcomes, such as mortality and morbidity, have not been determined.

Recommendations

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

1. Laboratory documentation of hypertriglyceridemia that is greater than 500 mg/dL.
2. Previous failure with both nicotinic acid and fibric acid medications.

Medication Product Details

Indication

Lovaza® is indicated as an adjunct to diet to reduce triglyceride levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia.

Dosage Forms

1-gram soft-gelatin capsules

Contraindications

Lovaza® is contraindicated in patients with known hypersensitivity (e.g., anaphylactic reaction) to Lovaza® or any of its components.

Pregnancy Risk Factor C

Monitoring: Laboratory Tests

- In patients with hepatic impairment, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels should be monitored periodically during therapy with Lovaza®.
- In some patients, increases in ALT levels without a concurrent increase in AST levels were observed.
- In some patients, Lovaza® increases LDL-C levels. LDL-C levels should be monitored periodically during therapy with Lovaza®.
- Laboratory studies should be performed periodically to measure the patient's TG levels during therapy with Lovaza®.

Fish Allergy

Lovaza® contains ethyl esters of omega-3 fatty acids (EPA and DHA) obtained from the oil of several fish sources. It is not known whether patients with allergies to fish and/or shellfish, are at increased risk of an allergic reaction to Lovaza®. Lovaza® should be used with caution in patients with known hypersensitivity to fish and/or shellfish.

Common Adverse Effects

- ☑ Eructation
- ☑ Infection
- ☑ Flu Syndrome
- ☑ Dyspepsia

Less Common Adverse effects

- ☑ Back Pain
- ☑ Pain
- ☑ Angina
- ☑ Rash
- ☑ Taste Perversion

Drug Interactions

Some studies with omega-3-acids demonstrated prolongation of bleeding time. The prolongation of bleeding time reported in these studies has not exceeded normal limits and did not produce clinically significant bleeding episodes. Clinical studies have not been done to thoroughly examine the effect of Lovaza® and concomitant anticoagulants. Patients receiving treatment with Lovaza® and an anticoagulant or other drug affecting coagulation should be monitored periodically (e.g., aspirin, NSAIDS, warfarin, coumarin).

Patient Information

- Take Lovaza® at the same time or times each day.
- Take Lovaza® with or without food. You may find it easier to take Lovaza® with food.
- Do not take more than 4 capsules a day. Taking more than 4 capsules per day may increase the chance of side effects.
- Take Lovaza® capsules whole. Do not break, crush, dissolve, or chew Lovaza® capsules before swallowing. If you cannot swallow Lovaza® capsules whole, tell your doctor. You may need a different medicine.
- Your doctor should start you on a low-fat and low-cholesterol diet before giving you Lovaza®. Stay on this low-fat and low-cholesterol diet while taking Lovaza®.
- Your doctor should do blood tests to check your triglyceride and cholesterol levels during treatment with Lovaza®.
- If you have liver disease, your doctor should do blood tests to check your liver function during treatment with Lovaza®.

REFERENCE

Lovaza(TM) (omega-3-acid ethyl esters) Package Insert. GlaxoSmithKline. September, 2009.

Appendix H

Annual Review of HMG-CoA Reductase Inhibitors (Statins) And Statin Combination Products - Fiscal Year 2009

Oklahoma Health Care Authority

May 2010

Current Prior Authorization Criteria

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

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

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

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

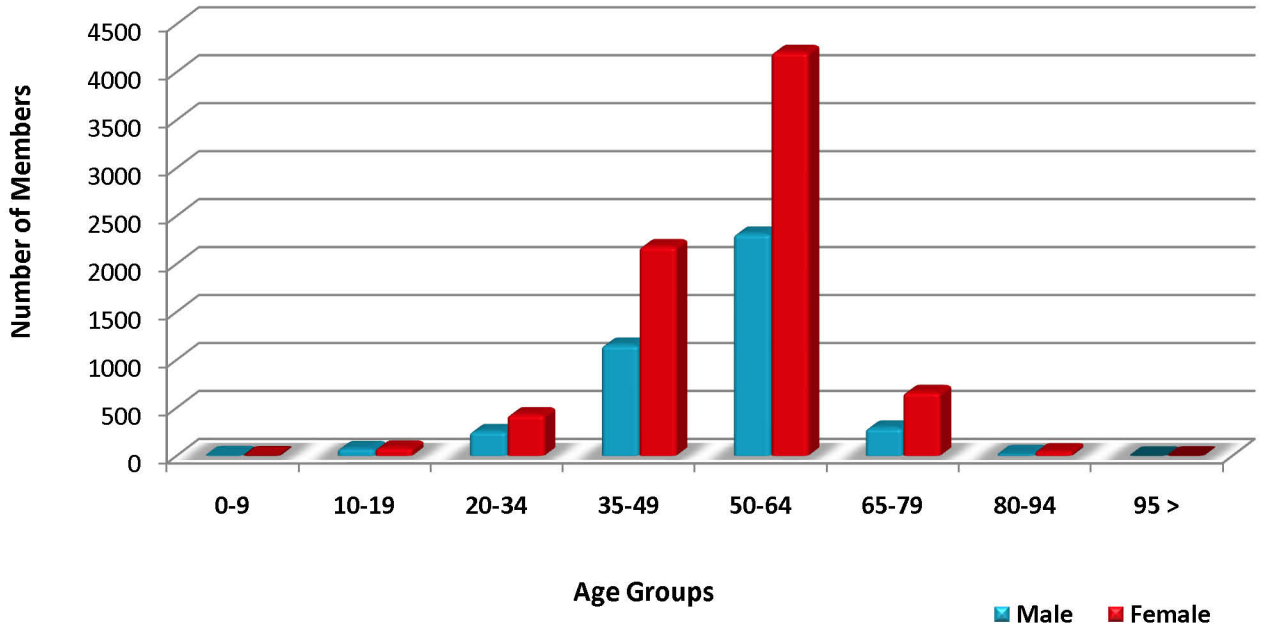
HMG-CoA Reductase Inhibitors (Statins)		
Tier One	***Tier Two***	***Tier Three***
Fluvastatin (Lescol® & Lescol® XL)	Atorvastatin (Lipitor®)	Lovastatin (brand Altoprev®)
Lovastatin (Mevacor®)	Rosuvastatin (Crestor®)	Simvastatin/Ezetimibe (Vytorin®)
Pravastatin (Pravachol®)		Ezetemibe (Zetia®)
Simvastatin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

Utilization of Medication or Class

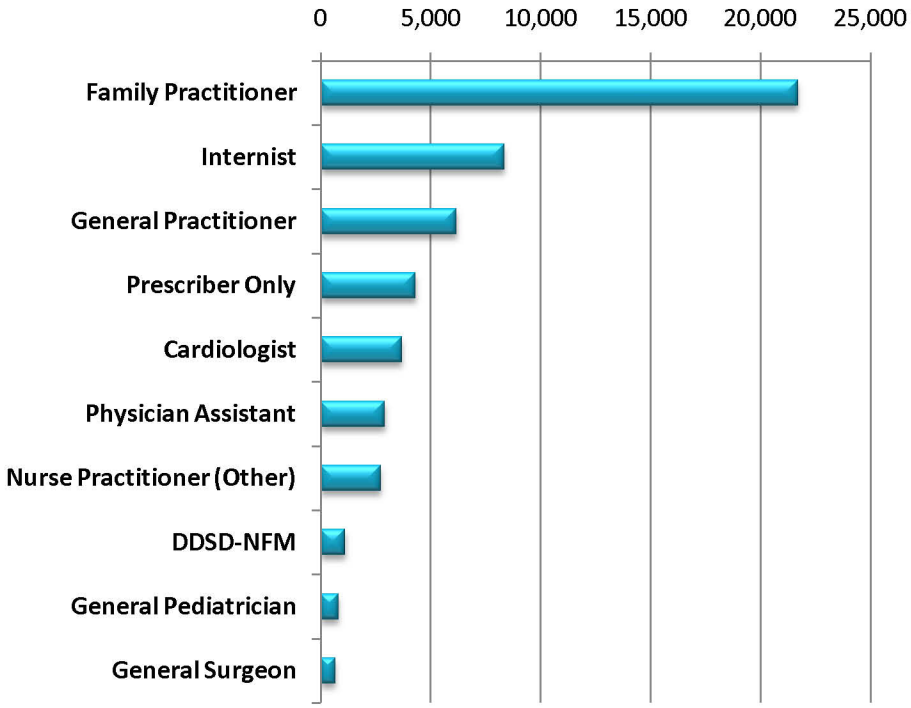
Trends in Utilization of Statins and Statin Combination Products

Fiscal Year	Members	Claims	Paid	Paid/Claim	Perdiem	Units	Days
2008	11,044	51,808	$4,585,167.82	$88.50	$2.17	2,103,148	2,109,298
2009	12,140	55,901	$4,558,744.79	$81.55	$2.02	2,270,562	2,256,495
Percent Change	9.90%	7.90%	-0.60%	-7.90%	-6.90%	8.00%	7.00%
Change	1,096	4,093	-$26,423.03	-$6.95	-$0.15	167,414	147,197

Demographics of Members Utilizing Statins and Statin Combination Products



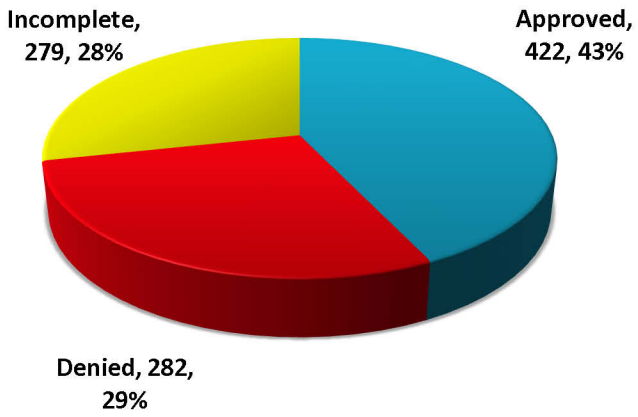
Prescribers of Statins and Statin Combination Products by Number of Claims



Prior Authorization of Statins and Statin Combination Products

There were a total of 785 petitions submitted for this PBPA category during fiscal year 2009. Computer edits are in place to look for Tier 1 medications, and if detected, the medication will not require a petition. The following chart shows the status of the submitted petitions.

Status of Petitions for Statins and Statin Combination Products



Market News and Update

- On August 3, 2009, the FDA approved **pitavastatin (Livalo®)** for the treatment of hyperlipidemia and mixed dyslipidemias. The LDL reduction capability of pitavastatin demonstrated in clinical trials[1] ranged from 31% to 44% from baseline, which is comparable to atorvastatin 10mg and 20mg and slightly superior to simvastatin 20mg, but not 40mg. One benefit of pitavastatin is that it is only minimally metabolized by the liver through the cytochrome P-450 pathway, the means by which many other medications are metabolized. This product is not yet available.

- AstraZeneca and Abbott announced in June of 2009 that the companies have submitted a New Drug Application (NDA) to the FDA for an investigational compound for the treatment of mixed dyslipidemia, a combination of two or more lipid abnormalities including high LDL cholesterol, high triglycerides, and low HDL-cholesterol. The investigational new drug consists of a combination of **rosuvastatin and fenofibric acid**, currently marketed as Crestor® and Trilipix®. Pending approval by the FDA, the new product will be marketed as **Certriad™.**

- **The ACCORD Lipid Trial[2],** presented at the American College of Cardiology conference in March of 2010, was funded by the National Institutes of Health (NIH) to evaluate the occurrence of major cardiovascular events (nonfatal heart attack, nonfatal stroke, cardiovascular death) in patients receiving **simvastatin plus fenofibrate, compared to simvastatin alone**. All patients in the study had a history of type 2 diabetes mellitus, were at high risk for cardiovascular disease, and were followed on average for 4.7 years. The trial found that there was **no difference in cardiovascular outcomes between the two groups**. At this time, FDA has made no new conclusions or recommendations regarding the combination use of simvastatin or other statin

drugs and fenofibrate. The agency will conduct a thorough review of the primary ACCORD data as soon as they become available.

- Follow-Up to the August 2008 Early Communication About an Ongoing Safety Review of Ezetimibe/Simvastatin **(Vytorin®),** Simvastatin **(Zocor®)** and Ezetimibe **(Zetia®)[3]-** FDA has now completed its review of the data from the SEAS trial as well as a review of interim data from two large-scale ongoing cardiovascular trials with Vytorin - the SHARP and IMPROVE-IT trials. Based on the currently available information the FDA believes it is **unlikely that Vytorin® or Zetia® increases the risk of cancer or cancer-related death.** The FDA is not advising healthcare professionals or consumers to stop using these medications, but to continue to evaluate the clinical benefits and potential risks of Vytorin or Zetia compared to other FDA-approved cholesterol lowering medications.

Conclusion and Recommendation

The College of Pharmacy recommends the addition of Livalo® to Tier 2 of the Statin PBPA Category. The existing criteria for this category will apply.

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

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

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

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

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

Utilization Details of Statins and Statin Combination Products: FY 2009

Medication	Claims	Members	Units	Days	Amount Paid	Claims/ Member	Perdiem	% Paid
LIPITOR TAB 20MG	8,260	1,990	342,270	342,302	$1,402,888.62	4.15	$4.10	30.77%
SIMVASTATIN TAB 20MG	7,858	1,966	297,970	296,130	$62,737.70	4	$0.21	1.38%
SIMVASTATIN TAB 40MG	7,623	1,950	302,874	302,065	$75,098.88	3.91	$0.25	1.65%
LIPITOR TAB 40MG	6,015	1,479	251,059	249,797	$1,032,730.09	4.07	$4.13	22.65%
LIPITOR TAB 10MG	5,761	1,332	238,161	236,761	$688,425.24	4.33	$2.91	15.10%
PRAVASTATIN TAB 40MG	3,058	961	126,995	121,801	$31,372.06	3.18	$0.26	0.69%
SIMVASTATIN TAB 80MG	2,515	626	92,420	98,137	$23,919.30	4.02	$0.24	0.52%
LIPITOR TAB 80MG	1,856	470	78,627	80,134	$322,774.47	3.95	$4.03	7.08%
LOVASTATIN TAB 20MG	1,764	488	70,994	67,210	$14,711.95	3.61	$0.22	0.32%
PRAVASTATIN TAB 20MG	1,558	537	62,064	61,202	$14,381.72	2.9	$0.23	0.32%
SIMVASTATIN TAB 10MG	1,371	375	50,958	50,414	$10,093.08	3.66	$0.20	0.22%
LOVASTATIN TAB 40MG	1,289	328	59,077	52,049	$15,995.24	3.93	$0.31	0.35%
CRESTOR TAB 10MG	1,153	261	49,645	49,861	$178,695.37	4.42	$3.58	3.92%
VYTORIN TAB 10-40MG	993	205	43,400	43,400	$143,727.56	4.84	$3.31	3.15%
ZETIA TAB 10MG	960	220	43,704	43,912	$142,932.85	4.36	$3.25	3.14%
CRESTOR TAB 20MG	660	165	28,760	29,054	$104,575.13	4	$3.60	2.29%
VYTORIN TAB 10-20MG	615	118	26,532	26,737	$87,358.51	5.21	$3.27	1.92%
VYTORIN TAB 10-80MG	436	98	19,393	20,041	$63,942.26	4.45	$3.19	1.40%
LOVASTATIN TAB 10MG	414	113	16,362	16,042	$3,407.93	3.66	$0.21	0.07%
PRAVASTATIN TAB 10MG	404	126	14,359	14,329	$3,026.17	3.21	$0.21	0.07%
PRAVASTATIN TAB 80MG	372	119	15,590	16,205	$12,321.49	3.13	$0.76	0.27%
CRESTOR TAB 40MG	226	57	8,610	8,985	$31,266.06	3.96	$3.48	0.69%
CRESTOR TAB 5MG	143	43	6,550	6,580	$22,736.90	3.33	$3.46	0.50%
SIMCOR TAB 500-20MG	132	67	4,472	4,141	$9,810.85	1.97	$2.37	0.22%
LESCOL XL TAB 80MG	114	21	5,100	5,130	$16,880.32	5.43	$3.29	0.37%
VYTORIN TAB 10-10MG	99	20	4,911	4,911	$16,208.65	4.95	$3.30	0.36%
ADVICOR TAB 500-20MG	59	13	2,220	2,010	$6,862.73	4.54	$3.41	0.15%
SIMVASTATIN TAB 5MG	45	17	1,690	1,690	$346.28	2.65	$0.20	0.01%
LESCOL CAP 40MG	36	7	1,530	1,260	$3,947.38	5.14	$3.13	0.09%
LESCOL CAP 20MG	31	6	1,385	1,385	$3,630.63	5.17	$2.62	0.08%
SIMCOR TAB 1000-20	24	13	780	750	$2,989.00	1.85	$3.99	0.07%
ALTOPREV TAB 60MG ER	20	3	720	720	$3,856.29	6.67	$5.36	0.08%
ADVICOR TAB 1000-40	16	3	510	510	$2,099.09	5.33	$4.12	0.05%
ADVICOR TAB 1000-20	13	1	390	390	$1,395.74	13	$3.58	0.03%
SIMCOR TAB 750-20MG	5	3	390	360	$1,174.24	1.67	$3.26	0.03%
ALTOPREV TAB 40MG ER	3	1	90	90	$425.01	3	$4.72	0.01%
Totals	**55,901**	**12,140***	**2,270,562**	**2,256,495**	**$4,558,744.79**	**4.6**	**$2.02**	**100.00%**

*Total number of unduplicated members

[1] Livalo® Product Information. Kowa Pharmaceuticals America, Inc. 2009. Accessed at: http://cardiobrief.files.wordpress.com/2009/08/pitavastatinapfinal080309.pdf

[2] http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm203681.htm

[3] http://www.fda.gov/drugs/drugsafety/postmarketdrugsafetyinformationforpatientsandproviders/drugsafetyinformationforheathcareprofessionals/ucm194964.htm

Appendix I

Fiscal Year 2009 Annual Review of Antidepressants and 30 Day Notice to Prior Authorization Oleptro™ (trazodone extended release)

Oklahoma Health Care Authority
May 2010

Current Prior Authorization of Antidepressants

Tier-2 Authorization Criteria

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

Tier-3 Authorization Criteria

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

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

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

Quantity Limits

The following is a table of quantity limits that apply:

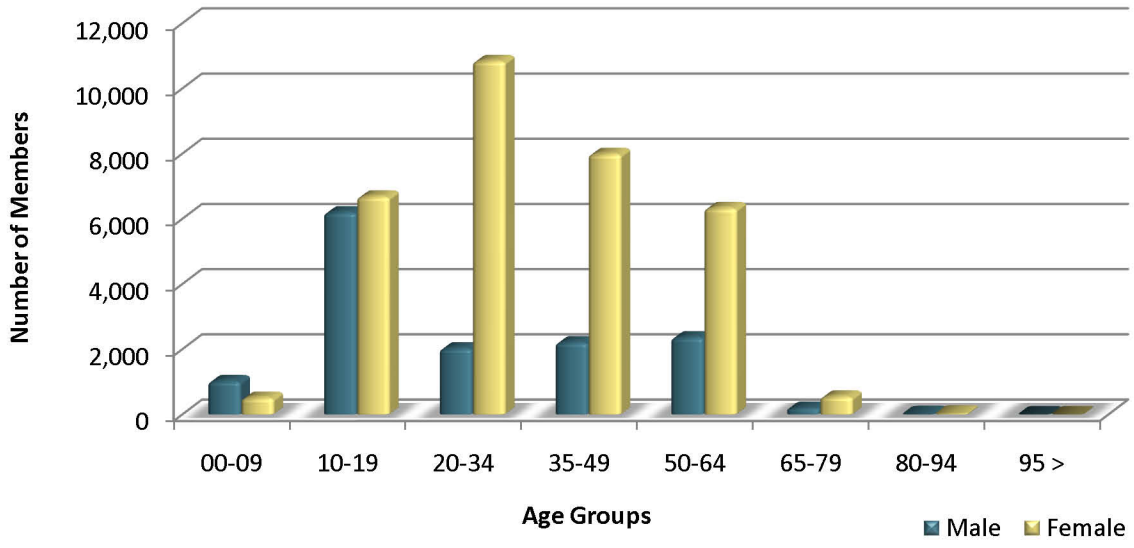
Quantity Limits on Antidepressants			
Drug	**Quantity Limits**	**Comments**	**FDA Daily Max**
Fluoxetine (**Prozac**®) Caps/ Tabs	100 capsules/tablets per 34 days	20mg-80mg QD	80mg
Fluoxetine (**Prozac Weekly**®)	4 caps (1 pack) per 28 days	Half life ~ 7 days	90mg weekly
Paroxetine (**Paxil**®**, Pexeva**®) Tabs	10, 20mg - 100 tabs per 100 days 30mg – 100 tabs per 50 days 40mg – 100 tabs per 66 days	20mg-50mg QD	50mg
Paroxetine (**Paxil CR**®) Tabs	100 tablets per 100 days	12.5mg-75mg QD	75mg
Sertraline (**Zoloft**®) Tabs	100 tablets per 50 days	25mg-200mg QD	200mg
Fluvoxamine (**Luvox**®) tablets	25mg – 100 tablets per 100 days 50mg – 100 tablets per 50 days 100mg - 102 tablets per 34 days	50mg-300mg QD	300mg
Fluvoxamine (**Luvox**® **CR**) tablets	100, 150mg - 100 tablets or 34 days	50mg-300mg QD	300mg
Citalopram (**Celexa**®) Tabs	10mg – 100 tabs per100 days 20mg – 100 tabs per 66 days 40mg – 100 tabs per 100 days	20mg-40mg QD	60mg
Escitalopram (**Lexapro**®) Tabs	100 tablets per 66 days	10mg-20mg QD	20mg
Bupropion (**Wellbutrin**®) Tabs	75, 100mg –102 tablets per 34 days	100mg-150mg BID-TID	450mg
Bupropion (**Wellbutrin SR**®) Tabs	100, 150, 200mg - 100 tabs per 50 days	150mg - 200mg BID	400mg
Bupropion (**Wellbutrin XL**®) sustained release Tabs	150, 300mg - 100 tabs per 100 days	150mg – 300mg QD	450mg
Bupropion (**Aplenzin**®) Tabs	174, 348, 522mg – 30 tabs per 30 days	174mg-522mg QD	522mg
Mirtazapine (**Remeron**®) Tabs and SolTabs	15, 30, 45mg - 100 tabs per 100 days	15-45mg QD	45mg
Trazodone (**Desyrel®**) Tabs	100 tabs or 34 days supply	100-375mg per day	600mg
Venlafaxine (**Effexor**®**)** Tabs	102 tablets per 34 days	25mg -200mg QD	200mg
Venlafaxine ER Tabs	37.5, 75mg – 100 tabs per 100 days 150, 225mg – 100 tabs per 50 days	37.5-225mg QD	225mg
Venlafaxine (**Effexor XR**®) Caps	100 capsules per 100 days	37.5mg -225 mg QD	225mg
Venlafaxine (**Pristiq**®) Caps	50, 100mg – 100 tabs per 100 days	50-100mg QD	100mg
Duloxetine (**Cymbalta**®) Caps	20, 30mg - 100 tabs per 50 days 60mg - 100 tabs per 100 days	20mg-60mg QD	60mg
Nefazodone (**Serzone®**) Tabs	100 tabs or 34 days supply	100 – 200mg BID	600mg

Utilization of Antidepressants

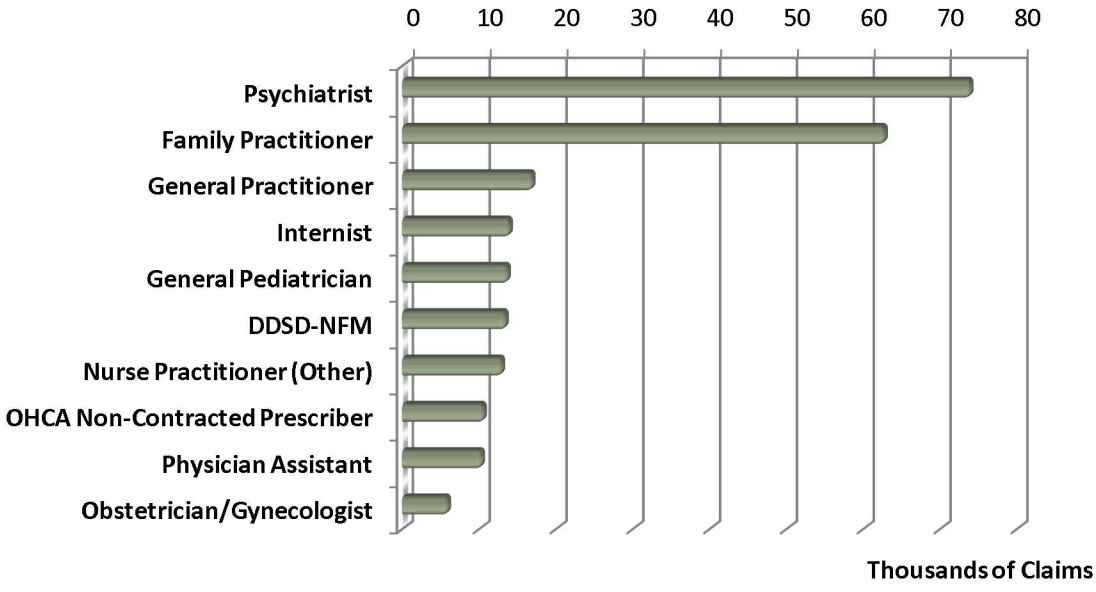
Comparison of Fiscal Year Utilization

Fiscal Year	Members	Claims	Paid	Paid/Claim	Perdiem	Units	Days
2008	44,018	238,368	$9,858,577.54	$41.36	$1.25	9,470,573	7,904,868
2009	47,146	246,578	$9,148,190.97	$37.10	$1.13	9,808,348	8,130,414
Change	3,128	8,210	-$710,386.57	-$4.26	$0.12	337,775	225,546
% Change	7.10%	3.40%	-7.20%	-10.30%	-9.60%	3.60%	2.90%

Demographics of Members Utilizing Antidepressant Medications: FY 2009



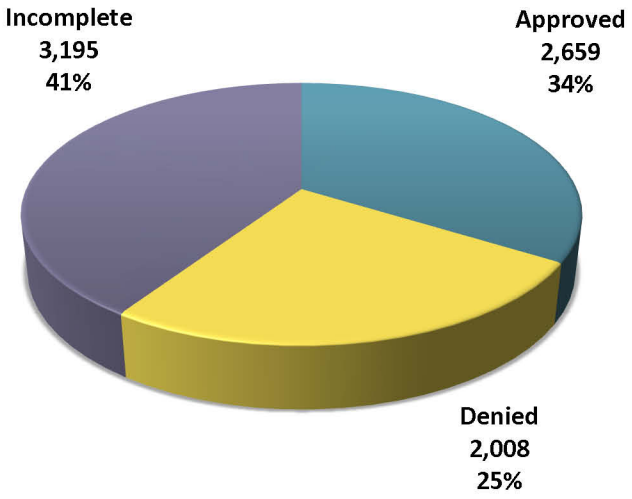
Prescribers of Antidepressant Medications by Number of Claims: FY 2009



Prior Authorization of Antidepressants

There are two types of computer edits implemented at the point of sale for the antidepressant category. One edit detects stabilization on a Tier 2 medication via recent continuous claims for the Tier 2 medication, in which case, the medication would be grandfathered for that member. The other edit detects a Tier 1 medication in the claims history according to criteria, in which case, a prior authorization is automatically generated for that member, and the claim is paid. If the edits detects neither, then a manual prior authorization is required. There were a total of 7,862 petitions submitted for this PBPA category during fiscal year 2009.

Status of Petitions for Antidepressant Medications: FY 2009



Market News and Update

- Labopharm, Inc. received FDA approval in February of 2010 for an extended release formulation of trazodone[1]. **Oleptro™ (trazodone extended release)** is indicated for the treatment of major depressive disorder. The starting dose is 150mg once daily and may be increased by 75mg per day every three days up to a maximum dose of 375mg per day. The medication should be taken preferably at bedtime on an empty stomach. The tablet may be taken whole or broken in half along the score-line, however it should not be chewed or crushed. Oleptro™ is availabe as bisectable tablets of 150mg and 300mg.
- In a recent of *Biological Psychiatry*, researchers from the National Institutes of Health report that **scopolamine** appears to produce replicable rapid improvement in mood[2]. Scopolamine was found to reduce symptoms of depression within three days of the first administration. Participants reported that they experienced relief from their symptoms by the morning after the first administration of drug. Moreover, one-half of participants experienced full symptom remission by the end of the treatment period. Participants remained well during a subsequent placebo period, indicating that the antidepressant effects persist for at least two weeks in the absence of further treatment.
- **Vilazodone** is a novel dual-acting treatment for MDD that combines serotonin reuptake inhibition with a partial 5-hydroxytryptamine1A receptor agonist. On June 2009, Clinical Data, Inc. announced the completion of two phase III trials for with positive results[3]. Clinical Data, Inc. plans to file a New Drug Application in the near future.

Patent Expirations

- **Escitalopram (Lexapro®)** - anticipated to expire 2012
- **Venlafaxine ER Caps (Effexor XR®)** - anticipated to expire 2013
- **Duloxetine (Cymbalta®)** - anticipated to expire 2013

Conclusion and Recommendations

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

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

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

Medication Product Details

Indication
Oleptro™ is indicated for the treatment of major depressive disorder.

Dosage Forms
Bisectable tablets of 150 mg or 300 mg.

Contraindications
None listed

Pregnancy Risk Factor C

Precautions

- **Clinical Worsening/Suicide Risk**: Monitor for clinical worsening and suicidal thinking and behavior.
- **Serotonin Syndrome or Neuroleptic Malignant Syndrome-like Reactions**: Have been reported with antidepressants. Discontinue Oleptro™ and initiate supportive treatment.
- **Activation of Mania/Hypomania**: Screen for bipolar disorder and monitor for mania/hypomania.
- **QT Prolongation**: Increases the QT interval. Avoid use with drugs that also increase the QT interval and in patients with risk factors for prolonged QT interval.
- **Use in Patients with Heart Disease**: Use with caution in patients with cardiac disease.
- **Orthostatic Hypotension and Syncope**: Warn patients of risk and symptoms of hypotension.
- **Abnormal Bleeding**: May increase the risk of bleeding. Use with NSAIDs, aspirin, or other drugs that affect coagulation may compound this risk.
- **Interaction with MAOIs**: Do not use concomitantly or within 14 days of monoamine oxidase inhibitors.
- **Priapism**: Warn male patients of this risk and how/when to seek medical attention.
- **Hyponatremia**: Can occur in association with SIADH.
- **Potential for Cognitive and Motor Impairment**: Has potential to impair judgment, thinking, and motor skills. Advise patients to use caution when operating machinery.
- **Discontinuation Symptoms**: May occur with abrupt discontinuation and include anxiety and sleep disturbance. Upon discontinuation, taper Oleptro™ and monitor for symptoms.

Common Adverse Effects

- Sedation
- Dizziness
- Constipation
- Somnolence
- Blurred Vision

Less Common Adverse effects

- Sexual dysfunction
- Vomiting
- Headache
- Dry mouth
- Vertigo
- Abnormal Coordination
- Agitation

Drug Interactions

- **Monoamine Oxidase Inhibitors**: Should not be used concomitantly with Oleptro™
- **CNS Depressants**: Trazodone may enhance effects of alcohol, barbiturates, or other CNS depressants
- **CYP3A4 Inhibitors**: May necessitate lower dose of Oleptro™
- **CYP3A4 Inducers** (e.g., carbamazepine): May necessitate higher dose of Oleptro™
- **Digoxin or Phenytoin**: Monitor for increased serum levels
- **Warfarin:** Monitor for increased or decreased prothrombin time
- **Serotonergic Medications**: Serotonin syndrome has been reported
- **NSAIDs, Aspirin or other Anticoagulants**: Potential for increased risk of bleeding

Patient Information

- Oleptro™ should be swallowed whole or broken in half along the score line.
- In order to maintain its controlled-release properties, it should not be chewed or crushed.
- Oleptro™ should be taken at the same time every day, in the late evening preferably at bedtime, on an empty stomach.
- Oleptro™ may cause somnolence or sedation and may impair the mental and/or physical ability required for the performance of potentially hazardous tasks. Patients should be cautioned about operating hazardous machinery, including automobiles until they are reasonably certain that the drug treatment does not affect them.
- Trazodone may enhance the response to alcohol, barbiturates, and other CNS depressants.
- Women who intend to become pregnant or who are breastfeeding should discuss with a physician whether they should continue to use Oleptro™, since use in pregnant and nursing women is not recommended.

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[1] Oleptro(TM) (trazodone extended-release) Product Information. LaboPharm. January 20, 2010.

[2] Drevets et al. **Replication of Scopolamine's Antidepressant Efficacy in Major Depressive Disorder: A Randomized, Placebo-Controlled Clinical Trial**. *Biological Psychiatry*, 2010; 67 (5): 432

[3] Clinical Data, Inc. Pharhttp://www.pgxhealth.com/development/pipeline.cfm

Appendix J

U.S. Food and Drug Administration

News & Events

NOTE TO CORRESPONDENTS

For Immediate Release: April 7, 2010
Contact: Sandy Walsh, 301-796-4669, sandy.walsh@fda.hhs.gov

FDA Approves First Generic Versions of Two Drugs for the Treatment of Hypertension

On April 6, the U.S. Food and Drug Administration approved the first generic versions of two drugs used for the treatment of hypertension. Losartan potassium tablets and losartan potassium and hydrochlorothiazide tablets (a combination drug) are the generic equivalents of Cozaar and Hyzaar tablets, respectively.

Cozaar and Hyzaar tablets are widely-used antihypertensive drugs. Both generic losartan products will carry the same safety warnings as their brand counterparts. These warnings include a boxed warning against the use of these products during the second and third trimesters of pregnancy.

Losartan potassium tablets are approved in 25 milligram, 50 mg, and 100 mg strengths, and Losartan potassium and hydrochlorothiazide tablets are approved in 50 mg/12.5 mg, 100mg/12.5 mg, and 100 mg/25 mg strengths. Both products are manufactured by TEVA Pharmaceuticals USA in North Wales, Pa.

In related actions, the FDA also approved applications from several other companies for losartan potassium and hydrochlorothiazide tablets for the 10(mg/12.5 mg strength only. These companies include Mylan Pharmaceuticals Inc., Roxane Laboratories Inc., and Torrent Pharmaceuticals Ltd.

For more information:

Consumer Information: Generic Drugs [1]

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

Links on this page:

1. http://www.fda.gov/Drugs/ResourcesForYou/ucm167906.htm
2. http://www.fda.gov/AboutFDA/ContactFDA/StayInformed/RSSFeeds/PressReleases/rss.xml
3. http://www.fda.gov/AboutFDA/ContactFDA/StayInformed/RSSFeeds/ucm144575.htm

U.S. Food and Drug Administration

News & Events

FDA NEWS RELEASE

For Immediate Release: Apr. 13, 2010
Media Inquiries: Erica Jefferson, 301-796-4988, erica.jefferson@fda.hhs.gov
Consumer Inquiries: 888-INFO-FDA

Asthma and COPD Inhalers That Contain Ozone-depleting CFCs to be Phased Out; Alternative Treatments Available

The U.S. Food and Drug Administration today announced, in accordance with longstanding U.S. obligations under the Montreal Protocol on Substances that Deplete the Ozone Layer, seven metered-dose inhalers (MDI) used to treat asthma and chronic obstructive pulmonary disease (COPD) will be gradually removed from the U.S. marketplace. These inhalers contain ozone-depleting chlorofluorocarbons (CFCs), which are propellants that move medication out of the inhaler and into the lungs of patients. Alternative medications that do not contain CFCs are available.

The affected products and their phase out schedule include:

Inhaler Medication	Last Date to be manufactured, sold or dispensed in U.S.	Manufacturer
Tilade Inhaler (nedocromil)	June 14, 2010	King Pharmaceuticals
Alupent Inhalation Aerosol (metaproterenol)	June 14, 2010	Boehringer Ingelheim Pharmaceuticals
Azmacort Inhalation Aerosol (triamcinolone)	Dec. 31, 2010	Abbott Laboratories
Intal Inhaler (cromolyn)	Dec. 31, 2010	King Pharmaceuticals
Aerobid Inhaler System (flunisolide)	June 30, 2011	Forest Laboratories
Combivent Inhalation Aerosol (albuterol and ipratropium in combination)	Dec. 31, 2013	Boehringer Ingelheim Pharmaceuticals
Maxair Autohaler (pirbuterol)	Dec. 31, 2013	Graceway Pharmaceuticals

Patients using the inhalers scheduled to be phased out should talk to their health care professional about switching to one of several alternative treatments currently available. Until then, patients should continue using their current inhaler medication.

CFCs are harmful because they deplete the ozone layer miles above the Earth that absorb some of the sun's harmful ultraviolet rays. The United State has banned the general use of CFCs in consumer aerosols for decades, and eliminated the production of CFCs in the United States as of Jan. 1, 1996, except for certain limited uses, such as MDIs.

"During this transition, FDA wants to ensure that patients have access to safe and effective alternative medications to treat their asthma or COPD," said Badrul Chowdhury, M.D., Ph.D., director of the Division of Pulmonary, Allergy, and Rheumatology Products in FDA's Center for Drug Evaluation and Research. "We are currently working with professional societies and patient organizations to make sure patients understand which products will nc longer be available and have information on which alternative medication might work best for them."

The CFC phase out is part of an international agreement to ban substances that deplete the Earth's ozone layer. The Montreal Protocol on Substances that Deplete the Ozone Layer and the U.S. Clean Air Act aim to protect the public health and the environment from the potentially negative effects of ozone depletion. Bans on products containing CFCs began in the late 1970s.

The decision to phase out the products is the latest in a series of decisions related to the removal of CFC inhaler products from the market as required by the Clean Air Act. The agency proposed to phase-out the seven remaining products in 2007 and reached a final decision after reviewing more than 4,000 public comments and information submitted as part of a public meeting.

For more information:

- Seven Inhalers That Use CFCs Being Phased Out [1]
- Phase Out of CFC Metered-Dose Inhalers [2]
- Metered-Dose Inhalers Clean Air Act Information [3]
- Drug Treatments for Asthma and Chronic Obstructive Pulmonary Disease that Do Not Use Chlorofluorocarbons [4]

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RSS Feed for FDA News Releases [5] [what is RSS? [6]]

Links on this page:

1. http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm207864.htm
2. http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm193896.htm
3. http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/LawsActsandRules/ucm071523.htm
4. http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm082370.htm
5. http://www.fda.gov/AboutFDA/ContactFDA/StayInformed/RSSFeeds/PressReleases/rss.xml

KHN
KAISER HEALTH NEWS

States' Medicaid Funds Tapped For Federal Health Overhaul

TOPICS: MEDICAID, HEALTH REFORM

By CHRISTOPHER WEAVER
KHN Staff Writer
APR 20, 2010

The new health care law could shift billions of dollars from cash-strapped states to the federal government by changing the way Medicaid prescription drug rebates are treated, according to state and industry officials and an examination of Medicaid spending data.

Democrats included a provision in the health law designed to raise $38 billion over 10 years by requiring greater discounts from drugmakers selling to Medicaid, the joint federal-state health insurance program for the poor. Previously, the rebates were divided between the states and the federal government. Under the law, a significant portion of the rebates will go solely to Washington beginning this year.

Regan Lachapelle, a spokeswoman for Senate Majority Leader Harry Reid, D-Nev., said the change was necessary to help pay for a $434 billion, 10-year increase in federal Medicaid funding. "Federalizing the rebate was a small piece compared to the many things we did to help states," she said in an e-mail.

In addition, for some states, the rebate losses may be offset by another part of the law. That provision would require drugmakers to provide discounts to states for drugs sold to Medicaid managed care plans hired by the states. Yet even with those new discounts, some states project that they will see overall losses in the rebate programs

California, for instance, stands to lose $50 million next year alone because of the changes, according to Toby Douglas, the state's deputy Medicaid director. Douglas said that estimate was "very preliminary." He expects firmer numbers after the federal government provides more details about the change, which could come as soon as Wednesday.

Anne Murphy, Indiana's secretary of the Family and Social Services Administration, circulated a memo predicting losses of $400 million over 10 years because the federal government plans to "confiscate" a portion of its rebates. A spokesperson added that the estimate is based on state officials' reading of the law and that they are awaiting guidance, too.

The new law will increase the minimum rebates that drug firms must offer Medicaid programs from 15.1 percent to 23.1 percent for most brand name medications. Minimum rebates would also be increased for other drugs, including generics.

Under the old policy, states sent Washington a proportion equal to the share of Medicaid funding the federal government paid. The law says that the federal government now will get 100 percent of the rebate funding "attributable" to the increase from 15.1 to 23.1 percent. (Any rebates above 23.1 percent will still be shared.)

Industry analysts have suggested that wording may give the agency overseeing Medicaid some leeway in how it administers the rebate change to soften the impact on states.

The federal Medicaid agency refused to discuss the effects the provision could have on states. But, a spokeswoman said the agency would release guidelines "very soon."

State officials worry that since states already were getting rebates well above the previously required 15 percent, the change will cost nearly all of them millions of dollars a year. Based on 2009 Medicaid data, states received average rebates of 38.5 percent.

Officials "are very unhappy that their money is being taken away at a time when the states cannot afford this," said Ann Kohler, the director of the National Association of State Medicaid Directors.

As of December, 44 states had exceeded Medicaid spending projections for the fiscal year that ends Sept. 30, according to a survey released in February by the Kaiser Family Foundation. And at least 29 states had either recently made reductions in benefits and physician pay to their programs or expected to do so soon. (KHN is a project of the Kaiser Family Foundation.)

All but three states, Arizona, Massachusetts and New Mexico, would stand to lose money, in many cases millions of dollars a year, because of the drug rebate changes, according to a state-by-state examination of 2009 Medicaid spending records by Kaiser Health News. The 47 other states and the

District of Columbia had negotiated average rebates from drugmakers that are better than required and in many cases far surpass the 23.1 percent requirement. For example, Georgia's rebates average about 50 percent.

The analysis compared total rebates received by federal and state governments with total drug spending for each state's Medicaid program for 2009, according to data from the federal agency that oversees Medicaid.

Drugmakers did not return calls asking for comment, and state officials were reluctant to discuss rebates, which are protected by confidentiality agreements with the firms.

One caveat in trying to determine a state's losses is that each state negotiates rebates on a drug-by-drug basis and lower rebates apply to generics and other classes of drugs.

Some state lawmakers are already calling on federal officials to back away from the proposal. "Some things may need to be changed," said Sharon Treat, a Democratic Maine legislator. "For those of us that have been working hard to get health care passed, it would be a slap in the face if we lose money."

Maine could face particularly steep losses under the change because the state does not use managed care for any of its Medicaid enrollees and would not benefit from the provision offering discounts for managed care programs.

Forty-one states use managed care plans to cover about 70 percent of Medicaid enrollees nationwide. However, only 16 of them depend on the managed care programs to administer drug benefits, while others have opted to pay for many drugs directly to get rebates. Those 16 states would have the most to gain from the new managed care policy.

The provision might encourage additional states to use managed care plans for drug coverage. That could lead to a reduction in drug spending and is raising concerns among some pharmaceutical makers.

Arizona is one of the states that will see a major benefit. It runs the entire Medicaid program through managed care plans, so the state did not benefit in the past from the federally required rebates. Because of the change, the program will likely gain significant new funding.