Drug Utilization Review Board

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

Wednesday
July 8, 2009
6:00 p.m.

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

MEMORANDUM

TO: Drug Utilization Review Board Members

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

SUBJECT: **Packet Contents for Board Meeting – July 8, 2009**

DATE: July 2, 2009

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

Enclosed are the following items related to the July 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 Anti-Migraine Products – See Appendix C.

30 Day Notice to Apply Quantity Restrictions to Hydrocodone Products – See Appendix D.

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

Utilization Review of Fibromyalgia Products – See Appendix F.

Utilization Review of Otic Antibiotics – See Appendix G.

FDA and DEA Updates – See Appendix H.

Future Business

Adjournment

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Drug Utilization Review Board

(DUR Board)

Meeting – July 8, 2009 @ 6:00 p.m.

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

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

1. Call To Order

A. Roll Call – Dr. Graham

Items to be presented by Dr. Muchmore, Chairman:

2. Public Comment Forum

A. Acknowledgment of Speakers and Agenda Items

Items to be presented by Dr. Muchmore, Chairman:

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

A. June 10, 2009 DUR Minutes – Vote
B. June 11, 2009 DUR Recommendation Memorandum

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

4. Update on DUR / MCAU Program – See Appendix B.

A. Retrospective Drug Utilization Review for March 2009
B. Medication Coverage Activity Audit for June 2009
C. Help Desk Activity Audit for June 2009

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

5. Action Item – Vote to Prior Authorize Anti-Migraine Products – See Appendix C.

A. COP Recommendations

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

6. 30 Day Notice to Apply Quantity Restrictions to Hydrocodone Products – See Appendix D.

A. Utilization Review
B. Current Restrictions
C. COP Recommendations

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

7. 30 Day Notice to Prior Authorize Gelnique™ and Update of Bladder Control Products Product Based Prior Authorization Criteria – See Appendix E.

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

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

8. Utilization Review of Fibromyalgia Products – See Appendix F.

A. Fibromyalgia Overview
B. Utilization Review
C. COP Recommendations
D. Product Summaries

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

9. Utilization Review of Otic Antibiotics – See Appendix G.

A. Diagnosis and Etiology
B. Treatment Options
C. Utilization Review
D. COP Recommendations

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

10. FDA and DEA Updates – See Appendix H.

11. Future Business

A. Proton Pump Inhibitors Annual Review
B. Anxiolytic Criteria Review
C. New Product Reviews
D. Annual Reviews

12. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES of MEETING of JUNE 10, 2009

BOARD MEMBERS:	PRESENT	ABSENT
Brent Bell, D.O., D.Ph.	X	
Mark Feightner, Pharm.D.	X	
Dorothy Gourley, D.Ph.	X	
Evelyn Knisely, Pharm.D.		X
Thomas Kuhls, M.D.	X	
Dan McNeill, Ph.D., PA-C; Chairman	X	
Clif Meece, D.Ph.; Vice-Chairman	X	
John Muchmore, M.D., Ph.D.	X	
Paul Preslar, D.O.	X	
James Rhymer, 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.; 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	
Visiting Pharmacy Student(s): Brittany Lang	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:

John Harris, Abbott	Sam Smothers, MedImmune	Rob Baxter, MedImmune
David Williams, Forest Labs	James Lieurance, Endo Pharmaceuticals	John Seidenberger, Boehringer-Ingelheim
Holly Turner, Merck	Lon Lowrey, Novartis	Jim Graham, Ortho McNeil Janssen
Laura Stewart, Merck	Aaron Mays, Alcon	Jim Fowler, Astra Zeneca
Lance Buchanan, MedImmune	Sandra Brazil, Sanofi-Aventis	Tracy Copeland, Daiichi Sankyo
Michael Jones, GlaxoSmithKline	Bobby White, UCB	Pat Trahan, Taro
Kelly Rogers, Taro	Jim Dunlap, Eli Lilly	William Dozier, Gilead
Ron Schnare, Shire	Donna Erwin, BMS	Min Tranh, MSII

PRESENT FOR PUBLIC COMMENT:

Agenda Item No. 5	David L. Gordon, M.D.; OU Dept. of Neurology	(Did not appear before Board.)

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

1A: Roll Call

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

ACTION: NONE REQUIRED

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

Dr. McNeill recognized the speaker for public comment:
For Agenda Item no. 5: David L. Gordon, M.D.; OU Dept. of Neurology.
Speaker signed in but did not address DUR Board at Public Comment Section

ACTION: NONE REQUIRED

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

3A: April 8, 2009 DUR Minutes

Dr. Meece moved to approve as submitted; seconded by Dr. Gourley.

ACTION: MOTION CARRIED

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

4A: Retrospective Drug Utilization Review: February 2009
4B: Retrospective Drug Utilization Review Responses: January 2009
4C: Retrospective Drug Utilization Review Responses: February 2009
4D: Medication Coverage Activity Audit: April, May 2009
4E: Help Desk Activity Audit: April, May 2009

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: **30-DAY NOTICE TO PRIOR AUTHORIZE ANTI-MIGRAINE PRODUCTS AND VOTE TO PRIOR AUTHORIZE TREXIMET®**

Materials included in agenda packet; presented by Dr. Keast.
Dr. Gourley moved to approve as submitted; seconded by Dr. Muchmore.

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE NEW PROTON PUMP INHIBITORS**

Materials included in agenda packet; presented by Dr. Keast.
Dr. Muchmore moved to approve as submitted; seconded by Dr. Bell.

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: **VOTE TO PRIOR AUTHORIZE RYZOLT®**

Materials included in agenda packet; presented by Dr. Keast.
Dr. Muchmore moved to approve as submitted; seconded by Dr. Preslar.

ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: **VOTE PRIOR AUTHORIZE APLENZIN®**

Materials included in agenda packet; presented by Dr. Le.
Dr. Meece moved to approve as submitted; seconded by Dr. Feightner.

ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: **VOTE TO PRIOR AUTHORIZE ACETASOL® HC**

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

Dr. Meece moved to approve recommendations submitted by the College of Pharmacy, with the addition of "Allergy to all available products and failure of acetic acid alone"; seconded by Dr. Gourley.

ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: **VOTE TO PRIOR AUTHORIZE EXFORGE HCT®**

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

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 11: **ELECTION OF OFFICERS**

Dr. Meece made a motion to nominate Dr. Muchmore for Chair..

ACTION: MOTION CARRIED BY UNANIMOUS APPROVAL BY VOICE ACCLAMATION

Dr. Meece made a motion to nominate Dr. Bell for Vice-Chair.

ACTION: MOTION CARRIED BY UNANIMOUS APPROVAL BY VOICE ACCLAMATION

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

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

ACTION: NONE REQUIRED

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

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

13A: Hydrocodone Utilization Proposal
13B: Utilization Review of Fibromyalgia Products
13C: Utilization Review of Otic Antibiotics
13D: New Product Reviews

ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: **ADJOURNMENT**

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

Memorandum

Date: June 11, 2009

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

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

Subject: DUR Board Recommendations from Meeting of June 10, 2009

Recommendation 1: Vote to Prior Authorize Treximet®

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends immediate prior authorization of Treximet® with a quantity limit of 9 tabs per 30 days. Approval of this product would require a reason why the member cannot take separate generic products.

Recommendation 2: Vote to Prior Authorize Kapidex™ and Prilosec Suspension™

MOTION CARRIED by majority approval.

The College of Pharmacy recommends placement of Kapidex™ and Prilosec Suspension™ in Tier 2 of the Anti-Ulcer PBPA Category. The existing prior authorization criteria will apply. The College also recommends that quantity limits of one dosage unit per day be applied, consistent with other products in this category.

Recommendation 3: Vote to Prior Authorize Ryzolt™

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends placement of both Ryzolt™ and Ultram® ER into Tier 3 of the Narcotic Analgesic Category. The existing prior authorization criteria for this category will apply. (The previous prior authorization criteria for Ultram® ER will no longer apply.)

Recommendation 4: Vote to Prior Authorize Aplenzin®

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends placement of Aplenzin® (bupropion hydrobromide) in Tier 3 of the Anti-Depressants PBPA Category with quantity limits of one tablet per day per dosage strength. The existing prior authorization criteria will apply.

Recommendation 5: Vote to Prior Authorize Acetasol® HC

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends prior authorization of Acetasol® HC. The approval criteria are as follows:

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

Recommendation 6: Vote to Prior Authorize Exforge HCT®

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends placement of Exforge HCT in Tier-3 of the ARB Combination Anti-hypertensives PBPA Category. The existing prior authorization criteria for this category will apply.

Recommendation 7: Vote to Elect New Chair and Vice-Chair

A Motion was made by Dr. Meece to elect John Muchmore, M.D., Ph.D. to Chair and Brent Bell, D.O., D.Ph. as Vice-Chair by acclamation.

Appendix B

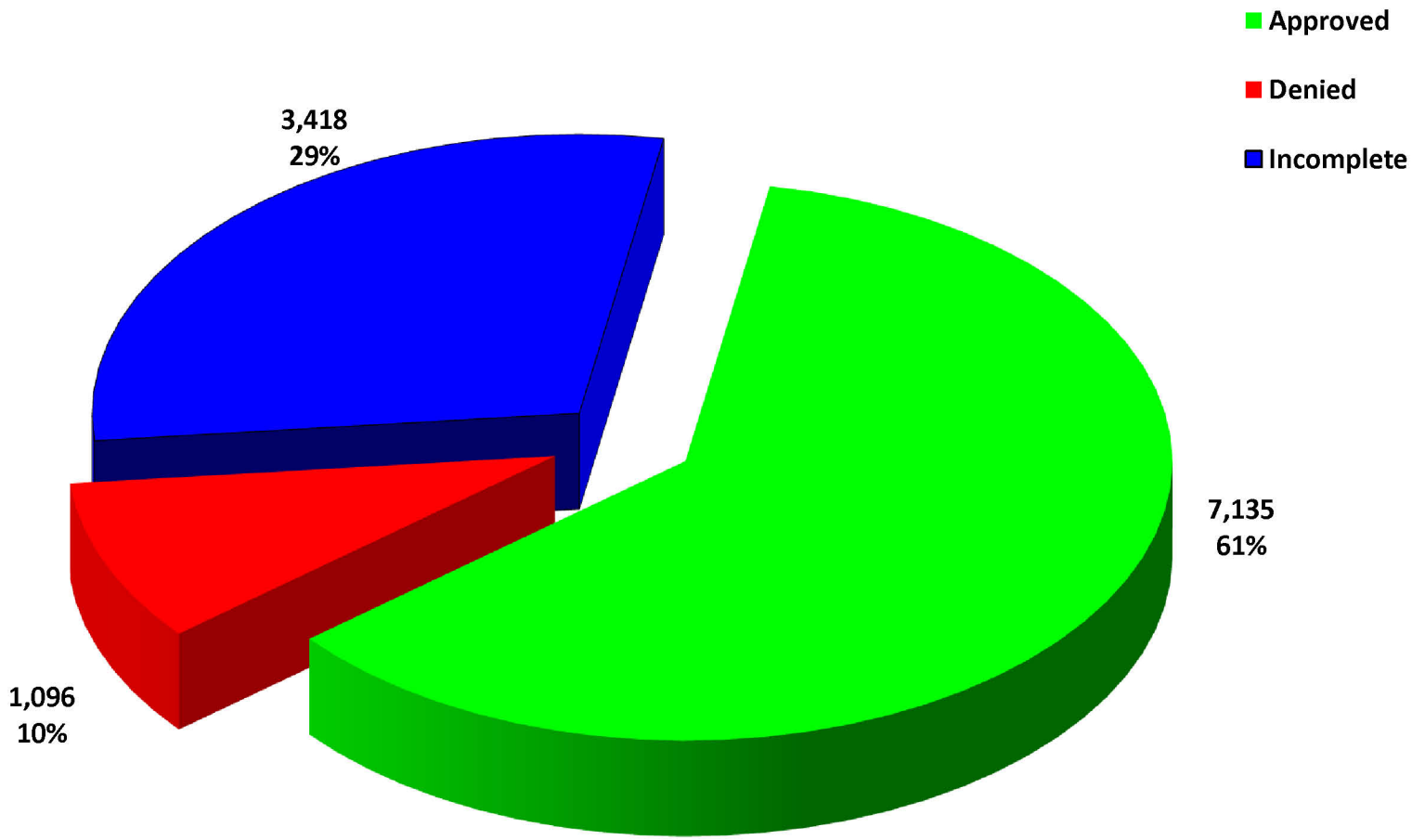
Retrospective Drug Utilization Review Report

Claims Reviewed for March 2009

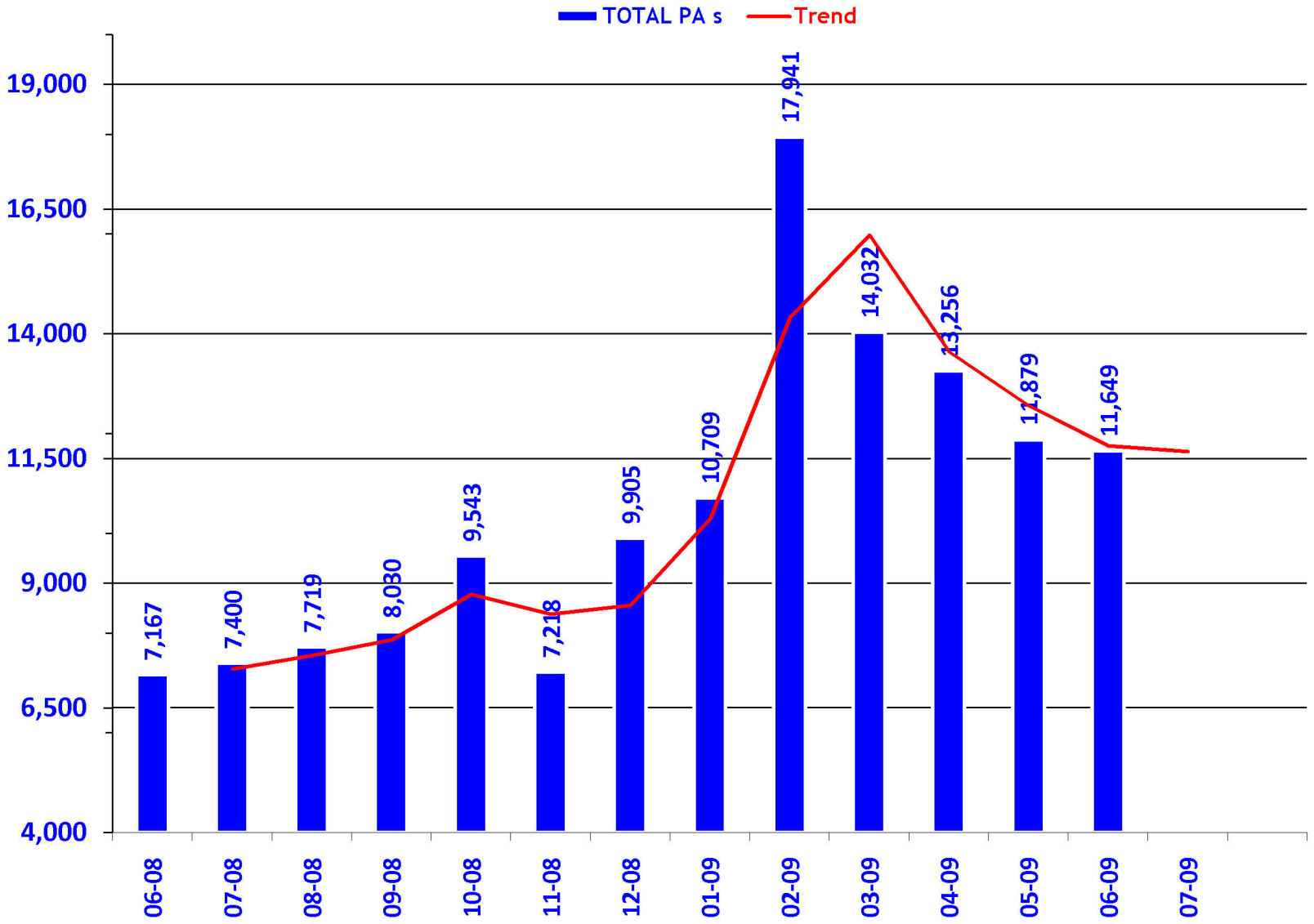
Module	**Drug Interaction**	**Duplication of Therapy**	**Drug-Disease Precautions**	**Dosing & Duration**
Total # of messages returned by system when no limits were applied	44,160	54,788	961,254	33,815
Limits which were applied	Established, Major, Males and Females, Age 31-51	Males and Females, Benzodiazepine Anticonvulsants, Age 0-50	Contraindicated, Asthma, Males and Females, Age 51-75	High dose and Duration , Benzodiazepines, Males and Females, Age 0-25
Total # of messages after limits were applied	110	133	200	28
Total # of members reviewed after limits were applied	110	123	146	28

LETTERS			
Prescribers		**Pharmacies**	
Sent	**Responded**	**Sent**	**Responded**
79		4	

PRIOR AUTHORIZATION ACTIVITY REPORT: June 2009



PRIOR AUTHORIZATION REPORT: June 2008 – June 2009



Activity Audit for

6/1/2009 Through 6/30/2009

	Avg Length of Approval	Approved	Denied	Incomplete	Total
Amitiza	162	7	2	10	19
Antidepressant	342	173	66	277	516
Antihistamine	325	216	66	189	471
Antihypertensives	344	61	31	68	160
Benzodiazepines	93	3,574	115	559	4,248
Bladder Control	341	8	2	11	21
Brovana (Arformoterol)	92	1	0	1	2
Byetta	362	3	0	4	7
Elidel/Protopic	89	28	7	34	69
ESA	61	166	2	70	238
Fibric Acid Derivatives	301	3	1	5	9
Fortamet/Glumetza	353	1	0	2	3
Forteo	365	1	0	1	2
Glaucoma	296	11	0	7	18
Growth Hormones	180	31	4	4	39
HFA Rescue Inhalers	214	54	10	66	130
Insomnia	138	48	40	95	183
Misc Analgesics	110	10	31	22	63
Muscle Relaxant	60	55	82	77	214
Nasal Allergy	227	6	107	73	186
NSAIDS	306	34	24	50	108
Ocular Allergy	75	4	6	30	40
Ocular Antibiotics	15	5	0	16	21
Opioid Analgesic	158	114	29	131	274
Other	99	183	43	258	484
Pediculicides	12	5	16	12	33
Plavix	355	127	1	57	185
Proton Pump Inhibitors	116	101	73	251	425
Qualaquin (Quinine)	0	0	3	0	3
Singulair	281	485	113	436	1,034
Smoking Cessation	79	25	5	59	89
Statins	328	25	10	24	59
Stimulant	235	509	72	221	802
Symlin	362	2	0	1	3
Synagis	0	0	1	0	1
Topical Antibiotics	39	6	35	77	118
Topical Antifungals	53	6	7	18	31
Ultram ER and ODT	223	4	3	6	13
Xolair	359	1	0	0	1
Xopenex Nebs	223	33	8	22	63
Zetia (Ezetimibe)	340	14	0	4	18
Emergency PAs		2	0	0	2
Regular PAs Total		**6,142**	**1,015**	**3,248**	**10,405**

Overrides					
Brand	205	68	6	19	93
Dosage Change	12	423	10	22	455
High Dose	29	2	0	0	2
IHS - Brand	74	41	1	4	46
Ingredient Duplication	17	8	1	2	11
Lost/Broken Rx	10	76	2	5	83
Nursing Home Issue	6	68	0	3	71
Other	10	16	4	2	22
Quantity vs. Days Supply	225	286	57	111	454
Stolen	8	5	0	1	6
Wrong D.S. on Previous Rx	0	0	0	1	1
Overrides Total		**993**	**81**	**170**	**1,244**
Grand Total (Regular PAs + Overrides)		**7,135**	**1,096**	**3,418**	**11,649**

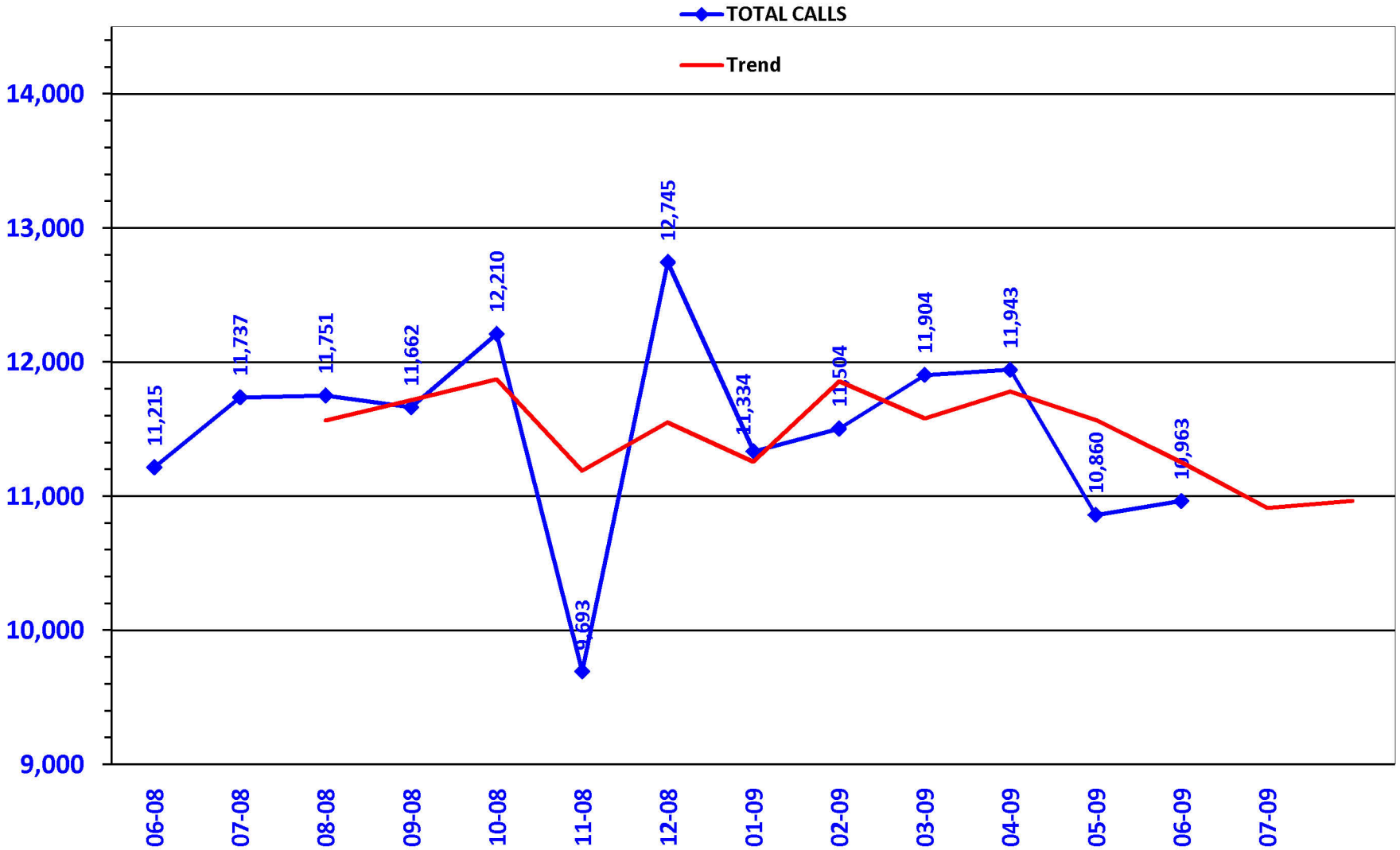
Denial Reasons

Lack required information to process request.	1,928
Unable to verify required trials.	1,830
Does not meet established criteria.	287
Not an FDA approved indication/diagnosis.	142
Member has active PA for requested medication.	125
Requested dose exceeds maximum recommended FDA dose.	67
Considered duplicate therapy. Member has a prior authorization for similar medication.	63
Medication not covered as pharmacy benefit.	30
Drug Not Deemed Medically Necessary	7

Duplicate Requests: 861

Changes to existing PAs: 1,021

CALL VOLUME MONTHLY REPORT: June 2008 – June 2009



Appendix C

Vote to Prior Authorize Anti-Migraine Medications

Oklahoma HealthCare Authority, July 2009

This category was introduced for possible inclusion in the Product Based Prior Authorization program in March 2009. See the March, April, and June DUR packets for a more complete discussion of the category. These notices and statement of potential economic impact are presented to meet the statutory requirements of 63 O.S. Sec. 5030.5.

Recommendations

The College of Pharmacy recommends the addition of the Anti-Migraine class to the Product Based Prior Authorization program once a reasonable SMAC has been placed on the generic sumatriptan. The following Tier 1 drug list has been reviewed and determined to be acceptable for use as initial therapy for the majority of members. The College of Pharmacy recommends this list to the Drug Utilization Review Board based on cost and clinical effectiveness for approval before referral to the Oklahoma Healthcare Authority.

Approval Criteria

To qualify for a Tier 2 product the member must meet one of the following criteria:

- Trial of all available Tier 1 products with inadequate response, or
- Documented adverse effect to all the Tier 1 products, or
- Previous success with a Tier 2 product within the last 60 days.

To qualify for a Tier 3 product the member must meet one of the following criteria:

- Trial of all available Tier 2 products with inadequate response, or
- Documented adverse effect to all available Tier 2 products, or
- Previous success with a Tier 3 medication within the last 60 days.

Approvals will be granted for one year.

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

*Mandatory generic plan

Appendix D

30 DAY NOTICE TO APPLY QUANTITY RESTRICTIONS TO HYDROCODONE COMBINATION PRODUCTS

OKLAHOMA HEALTHCARE AUTHORITY

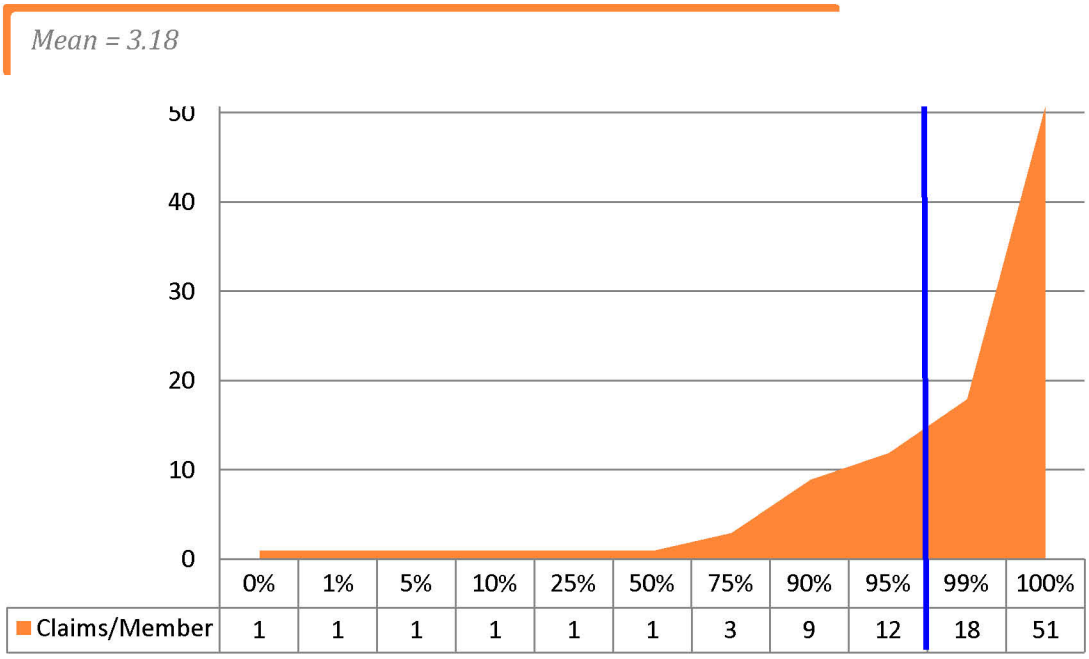
JULY 2009

UTILIZATION REVIEW

CLAIMS JANUARY 2008 THROUGH DECEMBER 2008

RANK CLAIMS	RANK COST	BRAND NAME	CLAIMS	UNITS	DAYS	MEMBERS	UNITS/ DAY	CLAIMS/ MEMBER	PERCENT COST
1	2	HYDROCO/APAP TAB 7.5-500	93,358	4,187,635	1,055,319	36,767	3.97	2.54	28.98%
2	1	HYDROCO/APAP TAB 10-500MG	52,813	4,485,753	1,115,902	11,220	4.02	4.71	33.29%
3	3	HYDROCO/APAP TAB 5-500MG	52,308	1,506,706	351,833	31,425	4.28	1.66	9.73%
4	5	HYDROCODONE/ SOL APAP	13,410	3,141,760	90,542	10,055	34.7	1.33	5.23%
5	4	HYDROCO/APAP TAB 10-325MG	11,001	1,059,745	226,281	2,684	4.68	4.10	9.01%
6	6	HYDROCO/APAP TAB 10-650MG	8,023	655,438	166,326	2,029	3.94	3.95	4.05%
7	7	HYDROCO/APAP TAB 7.5-325	5,524	282,103	59,758	2,846	4.72	1.94	2.98%
8	9	HYDROCO/APAP TAB 5-325MG	4,385	164,827	33,353	2,833	4.94	1.55	1.78%
9	8	HYDROCOD/IBU TAB 7.5-200	2,958	164,884	41,828	1,288	3.94	2.30	2.42%
10	10	HYDROCO/APAP TAB 7.5-650	2,840	132,759	34,223	1,127	3.88	2.52	0.89%
11	11	HYDROCO/APAP TAB 7.5-750	1,479	68,077	18,996	807	3.58	1.83	0.45%
12	12	HYDROCO/APAP TAB 2.5-500	982	32,619	8,122	715	4.02	1.37	0.32%
13	13	HYCET SOL 7.5-325	167	36,258	1,007	119	36.01	1.40	0.27%
14	14	ZAMICET SOL 10-325MG	94	22,374	722	68	30.99	1.38	0.21%
15	20	LORTAB 5 TAB	80	1,973	404	72	4.88	1.11	0.01%
16	17	HYDROCO/APAP TAB 10-750MG	59	2,447	551	40	4.44	1.48	0.05%
17	19	HYDROCO/APAP TAB 10-660MG	46	2,504	634	26	3.95	1.77	0.02%
18	15	XODOL TAB 10-300MG	33	2,880	864	7	3.33	4.71	0.15%
19	26	STAGESIC CAP 500-5MG	14	486	86	9	5.65	1.56	0.00%
20	18	LORTAB 7.5 TAB	13	1,170	390	1	3	13.00	0.04%
21	21	XODOL TAB 5-300MG	11	322	37	8	8.7	1.38	0.01%
22	23	REPREXAIN TAB 7.5-200	10	620	146	4	4.25	2.50	0.01%
23	22	XODOL TAB 7.5-300	9	295	67	7	4.4	1.29	0.01%
24	16	LORTAB 10 TAB	7	1,440	197	2	7.31	3.50	0.05%
25	28	REPREXAIN TAB 5-200MG	2	120	20	1	6	2.00	0.00%
26	29	IBUDONE TAB 10-200MG	2	80	16	1	5	2.00	0.00%
27	30	ZYDONE TAB 10-400MG	2	60	14	1	4.29	2.00	0.00%
28	31	HYDROCO/APAP TAB 10/660MG	2	80	22	2	3.64	1.00	0.00%
29	34	HY-PHEN TAB 500-5MG	2	36	9	2	4	1.00	0.00%
30	32	LORTAB 2.5 TAB	1	30	10	1	3	1.00	0.00%
31	33	HYDROCO/APAP CAP 5-500MG	1	30	5	1	6	1.00	0.00%
32	24	HYDROCO/APAP SOL 10-325MG	1	120	6	1	20	1.00	0.01%
33	25	LORCET TAB 10/650	1	100	16	1	6.25	1.00	0.01%
34	27	IBUDONE TAB 5-200MG	1	150	30	1	5	1.00	0.00%
			249,639	**15,955,881**	**3,207,736**		**4.97**	**3.18**	

DISTRIBUTION OF CLAIMS PER MEMBER

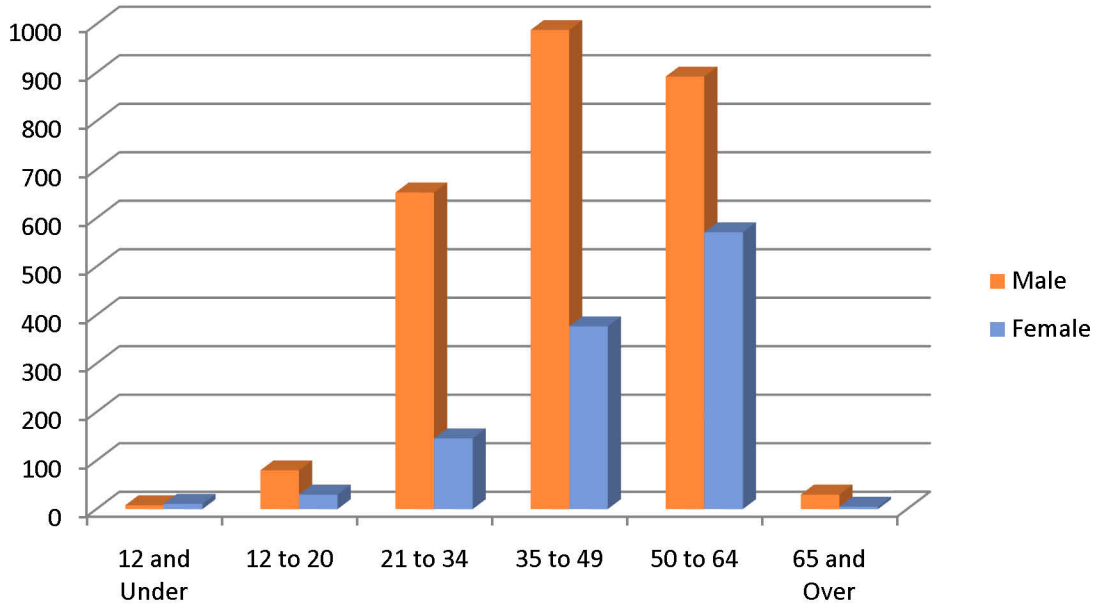


UTILIZATION FOR MEMBERS WITH 13 OR MORE CLAIMS

Product	Total Claims	Total Units	Total Days	Total Members	Percent Cost
STAGESIC CAP 500-5MG	2	32	8	2	0.00%
HYDROCO/APAP TAB 10-325MG	4,995	503,244	100,149	716	13.34%
HYDROCO/APAP TAB 2.5-500MG	62	3,212	820	32	0.09%
XODOL TAB 5-300MG	2	80	8	1	0.01%
HYDROCO/APAP TAB 5-500MG	6,357	264,070	63,127	1,514	4.29%
XODOL TAB 7.5-300	5	170	29	4	0.02%
HYDROCO/APAP TAB 7.5-500MG	21,805	1,264,463	314,562	2,518	24.97%
HYDROCO/APAP TAB 10-500MG	21,319	1,849,845	439,717	2,268	42.70%
HYDROCO/APAP TAB 7.5-650	751	44,613	10,924	126	0.85%
HYDROCO/APAP TAB 10-650MG	2,909	264,865	64,001	403	4.96%
HYDROCO/APAP TAB 10-660MG	6	273	73	6	0.01%
HYDROCO/APAP TAB 7.5-750MG	365	23,564	7,014	90	0.44%
HYDROCO/APAP TAB 10-750MG	16	1,350	337	1	0.07%
HYDROCO/APAP TAB 5-325MG	776	44,420	8,383	255	1.34%
HYDROCO/APAP TAB 7.5-325MG	1,560	100,288	20,802	375	3.12%
XODOL TAB 10-300MG	1	10	1	1	0.00%
HYDROCODONE/ SOL APAP	471	252,236	3,959	78	1.01%
REPREXAIN TAB 5-200MG	2	120	20	1	0.01%
REPREXAIN TAB 7.5-200	875	61,509	15,456	159	2.76%
	62,279	**4,678,364**	**1,049,390**	**3,794***	

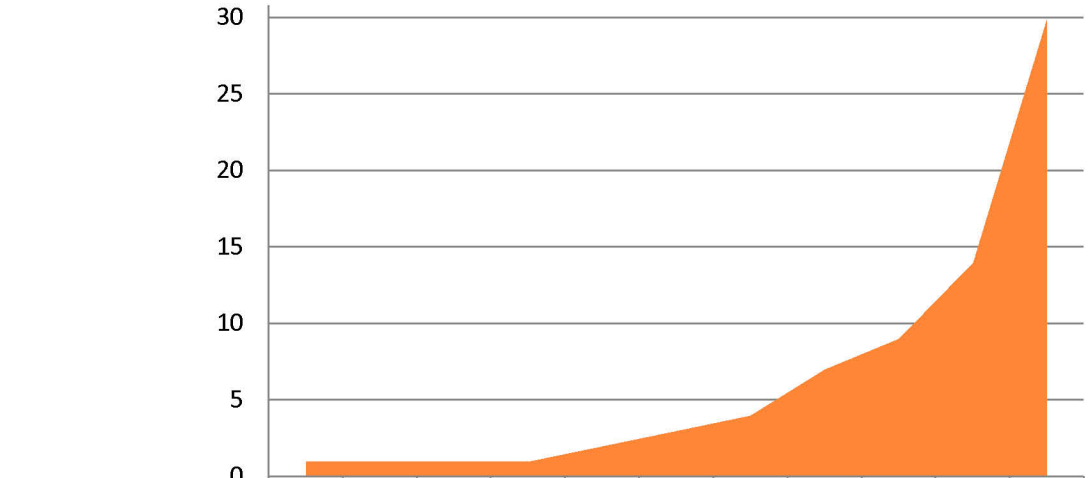
*Unduplicated Members

AGE AND GENDER FOR MEMBERS WITH 13 OR MORE CLAIMS



NUMBER OF UNIQUE PRESCRIBERS FOR MEMBERS WITH 13 OR MORE CLAIMS

Mean = 3.44



	0%	1%	5%	10%	25%	50%	75%	90%	95%	99%	100%
Prescribers/Member	1	1	1	1	2	3	4	7	9	14	30

TOP 10 DIAGNOSES FOR MEMBERS WITH 13 OR MORE CLAIMS

Diagnosis	Number of Unique Members
Lumbago	1,140
Unspecified Chest Pain	962
Abdominal Pain at Unspecified Site	833
Hypertension Unspecified	796
Diabetes Uncomplicated Type II	790
Pain in Limb	758
Urinary Tract Infection Unspecified	695
Shortness of Breath	568
Chronic Airway Obstruction	535
Lumbar/Sacral disc Degeneration	529

MEAN VALUES FOR SELECTED VARIABLES FOR MEMBERS WITH 13 CLAIMS OR OVER

Variable	Mean
Number of Claims	16.42
Total Day Supply	276.59
Total Units	1,233.10
Units per Claim	70.79
Day Supply per Claim	15.87

CURRENT RESTRICTIONS

INGREDIENT DUPLICATION MODULE

Claims for additional hydrocodone combination products are denied if less than 90 percent of a previous claim's day supply has not been exhausted. Claims from the same prescriber are exempt.

HIGH DOSE MODULE

All hydrocodone/acetaminophen combination products are set to deny if acetaminophen is twice the maximum dose of 4,000 mg daily. (This module is active for multiple products and changes apply to all products.)

RECOMMENDATIONS

1. Retain Ingredient Duplication Module.
2. Establish a new quantity limit for a maximum of 6 units per day for all strengths.
3. Establish an annual claim limit of 12 per 365 days.

The combination of these restrictions would provide a maximum of 2,448 units annually. A review of total units for members with greater than 13 claims indicated that only 5 % of members had greater than 2,448 units, and between 50 and 75% had less than 365 days of therapy.

Members requiring chronic pain control should be on long-acting pain therapy. This restriction would provide adequate coverage to members requiring chronic use of this medication for breakthrough pain coverage.

Appendix E

30 Day Notice to Prior Authorize Gelnique™ (oxybutynin) and Update of Bladder Control Product Based Prior Authorization Criteria

Oklahoma Health Care Authority
July 2009

Manufacturer	Watson Pharmaceuticals, Inc.
Classification	Antispasmodic, Anticholinergic Agent
Status	Prescription Only

Gelnique™ Summary

Gelnique™ (oxybutynin) received FDA approval in January 2009. Gelnique is oxybutynin formulated in a 10% topical gel and is approved for the treatment of overactive bladder with symptoms of urge urinary incontinence, urgency, and frequency. Oxybutynin is an antispasmodic, anticholinergic agent also available as oral tablets (Ditropan®), syrup (Ditropan® Syrup), and transdermal patch (Oxytrol®).

Gelnique is indicated to be applied topically once daily on the abdomen, upper arms/shoulder, or thigh. After topical application, oxybutynin is slowly delivered through the skin to the bloodstream for 24 hours.

Recommendations

The College of Pharmacy recommends immediate placement of Gelnique into Tier 2 of the Bladder Control PBPA Category. The College of Pharmacy also recommends a 3 tiered system for this category to be effective January of 2010. The College recommends product placement in Tier 1 and Tier 3 as shown below, with the following prior authorization criteria:

Tier 2 Authorization Criteria:

1. Trial of one tier 1 medication that yielded inadequate clinical response or adverse effects, or
2. Previous stabilization on the tier 2 drug, or
3. A unique indication which the tier 1 drugs lack.

Tier 3 Authorization Criteria:

1. Trial of all tier 2 medications that yielded inadequate clinical response or adverse effects, or
2. Previous stabilization on the tier 3 drug, or
3. A unique indication which the tier 2 drugs lack.

Bladder Control Medications		
Tier 1	*Tier 2*	*Tier 3*
Flavoxate **(Urispas®)**	**Supplemental Rebated Tier 3**	Trospium **(Sanctura™, Sanctura XR™)**
Oxybutynin **(Ditropan®)**		Oxybutynin ER Tabs **(Ditropan XL®)**
Tolterodine **(Detrol®)**		Oxybutynin Patch **(Oxytrol®)**
		Oxybutynin Gel **(Gelnique™)**
		Tolterodine ER Tabs **(Detrol LA®)**
		Darifenacin **(Enablex®)**
		Solifenacin **(VESIcare®)**
		Fesoterodine **(Toviaz™)**

*Hyoscyamine can be used as adjuvant therapy only. By itself, it will not count as a Tier 1 trial.

Gelnique™ Product Details

Indication and Administration

- Gelnique™ is indicated for the treatment of overactive bladder.
- Apply contents of 1 sachet (100 mg/g) once daily.

Dosage Form

10% topical gel

Contraindications

Gelnique™ is contraindicated in patients with Hypersensitivity to oxybutynin or any component of the formulation, uncontrolled narrow-angle glaucoma, urinary retention, gastric retention or conditions with severely decreased GI motility.

Pregnancy Risk Factor B

Precautions

- **Anticholinergic effects**: May cause anticholinergic effects which may require dose reduction or discontinuation of therapy.
- **CNS depression**: May cause CNS depression, which may impair physical or mental abilities; patients must be cautioned about performing tasks which require mental alertness.
- **Heat prostration**: May increase the risk of heat prostration.
- **Autonomic neuropathy**: Use with caution in patients with autonomic neuropathy; may exacerbate condition.
- **Cardiovascular disease**: Use with caution in patients with CAD, heart failure, hypertension, and/or cardiac arrhythmias; may exacerbate condition.
- **Dementia:** Use with caution in patients with dementia; may aggravate symptoms of disease.
- **Gastrointestinal disorders**: Use with caution in patients with ulcerative colitis, intestinal atony, gastroesophageal reflux or with medications that may exacerbate esophagitis
- **Glaucoma**: Use with caution in patients with treated angle-closure glaucoma; may exacerbate condition; use is contraindicated with uncontrolled narrow-angle glaucoma.
- **Hepatic impairment**: Use with caution in patients with hepatic impairment; due to limited experience.
- **Hiatal hernia**: Use with caution in patients with hiatal hernia.
- **Hyperthyroidism**: Use with caution in patients with hyperthyroidism; may exacerbate condition.
- **Myasthenia gravis**: Use with caution in patients with myasthenia gravis; may exacerbate condition.
- **Prostatic hyperplasia/urinary stricture**: Use with caution in patients with prostatic hyperplasia and/or urinary stricture; may cause urinary retention.
- **Renal impairment**: Use with caution in patients with renal impairment; due to limited experience. Use caution with bladder outflow obstruction; may increase risk of urinary retention.

- **Elderly**: Use with caution in the elderly due to anticholinergic activity (eg, confusion, constipation, blurred vision, and tachycardia).
- **Pediatrics**: Safety and efficacy of the gel and transdermal patch have not been established in children.

Common Adverse Effect

- Dizziness
- Constipation
- Headache
- Application site reaction
- Pruritus
- UTI
- Xerostomia

Drug Interactions

- Caution is advised with concurrent use of CYP3A4, CYP2C8, CYP2D6 inhibitors.
- Gelnique™ should not be used with potassium chloride, pramlintide and secretin.

Patient Information

- Use ethanol with caution as it may increase CNS depression and toxicity. Watch for sedation.
- Do not apply Gelnique™ to areas of the skin that have been treated with oils, lotions, or powders as that could affect the absorption of the medicine.
- Gelnique™ contains alcohol; avoid fire, flame, or smoking until the gel has dried.

REFERENCE

Gelnique Product Information. Watson Pharamaceuticals, Inc. January 2009. Accessed at: http://pi.watson.com/data_stream.asp?product_group=1634&p=pi&language=E

Appendix F

Review of Fibromyalgia Medications

Oklahoma Health Care Authority, July 2009

Introduction[1]

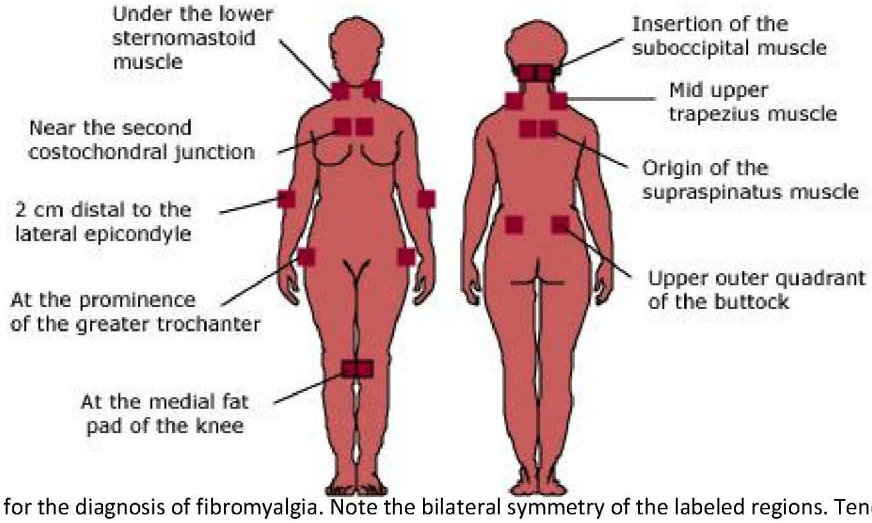
Fibromyalgia is a clinical syndrome defined by chronic widespread muscular pain, fatigue and tenderness. Many people with fibromyalgia also experience additional symptoms such as fatigue, headaches, irritable bowel syndrome, irritable bladder, cognitive and memory problems, temporomandibular joint disorder, pelvic pain, restless leg syndrome, sensitivity to noise and temperature, and anxiety and depression. These symptoms can vary in intensity and, like the pain of fibromyalgia, wax and wane over time.

Fibromyalgia affects 2 to 4 percent of the population, predominantly women. There is no laboratory or other diagnostic test for fibromyalgia so it must be diagnosed based on patient symptoms and physical examination. Medication, while important, is not the only treatment. Patient education, exercise, self management skills and alternative therapies help treat fibromyalgia symptoms.

Before a diagnosis of fibromyalgia can be made, according to the American College of Rheumatology, patients must meet both of the following criteria:

1. History of widespread pain for at least 3 months.
   Definition: Pain is considered widespread when all of the following are present: pain in the left side of the body, pain in the right side of the body, pain above the waist, and pain below the waist. In addition, axial skeletal pain (cervical spine or anterior chest or thoracic spine or low back) must be present. In this definition, shoulder and buttock pain is considered as pain for each involved side. "Low back" pain is considered lower segment pain.
2. Pain in 11 of 18 tender point sites on digital palpation.
   Definition: Pain, on digital palpation, must be present in at least 11 of the following 18 sites shown by this diagram:

Tender points in fibromyalgia [2]



The 18 "tender points" important for the diagnosis of fibromyalgia. Note the bilateral symmetry of the labeled regions. Tenderness on palpation of at least 11 of these sites in a patient with at least a three month history of diffuse musculoskeletal pain is recommended as a diagnostic standard for fibromyalgia. Adapted from Goldenberg, DL, Hosp Pract (Off Ed) 1989; 24:39.

1. Management of Fibromyalgia Syndrome. JAMA 2004[3]

Strong Evidence for Efficacy

Amitriptyline: often helps sleep and overall well-being; dose, 25-50 mg at bedtime
Cyclobenzaprine: similar efficacy to amitriptyline; similar adverse effects; dose, 10-30mg at bedtime

Modest Evidence for Efficacy

Tramadol: administered with or without acetaminophen; dose, 200-300 mg/day

Serotonin reuptake inhibitors (SSRIs):

Fluoxetine (only one carefully evaluated at this time): dose, 20-80 mg/day; may be used with tricyclic given at bedtime

Dual-reuptake inhibitors (SNRIs):

Venlafaxine: found ineffective in single Randomized Controlled Trial (RCT), but 2 case reports found higher dose effective
Milnacipran: found effective in single RCT
Duloxetine: found effective in single RCT
Pregabalin: found effective in single RCT

Weak Evidence for Efficacy

Growth hormone: modest improvement in subset of patients with FMS with low growth hormone levels at baseline
5-Hydroxytryptamine (serotonin): methodological problems
Tropisetron: not commercially available
S-adenosyl-methionine: mixed results

No Evidence for Efficacy

Opioids, corticosteroids, nonsteroidal anti-inflammatory drugs, benzodiazepene and nonbenzodiazepene hypnotics, melatonin, calcitonin, thyroid hormone, guaifenesin, dehydroepiandrosterone, magnesium.

2. European League against Rheumatism (EULAR) Evidence-Based Recommendations for the Management of Fibromyalgia Syndrome. Ann Rheum Dis 2007[4]

Table 3 Effect size calculated using modified Cohen's d method for recommended treatments where data available

	Effect size (95% confidence interval)		
Intervention	**Pain**	**Function**	**NNH**
Pharmacological			
Amitriptyline	1.033 (−0.393, 2.458)[20–23]	0.51 (−12.847, 13.868)[22 24]	45.56 (−36.06, 127.17)
Dual re-uptake	0.341 (−0.644, 1.323)[25 26]	0.438 (−2.77, 3.647)[25 27]	9.91 (6.87, 12.96)
MAOI	0.822 (−0.024, 1.669)[22 23]	Cannot calculate	24.29 (2.93, 37.14)
SSRI	0.824 (−0.417, 2.064)[22 28 29]	0.536 (−7.323, 8.395)[22 28 29]	8.25 (5.8, 10.7)
Tramadol	0.657 (−0.276, 1.589)[30 31]	0.189 (−6.312, 6.689)[30 31]	35 (only one study)
Tropisetron	0.799 (−0.884, 2.482)[32]	Cannot calculate	27.47 (only one study)
Pramipexole	0.736 (−0.556, 2.028)[33]	0.606 (−7.073, 8.285)[33]	−21 (only one study)
Non-pharmacolcgical			
Pool-based exercise	0.437 (−0.659, 1.532)[34 35]	0.495 (−1.68, 2.67)[34]	−8 (one study)
Balneotherapy	1.408 (0.684, 2.133)[36–38]	2.085 (−5.334, 9.979)[36 38]	Cannot calculate
Aerobic exercise	0.377 (−0.794, 1.549)[39–43]	0.062 (−5.174, 5.297)[39–42]	−13.5 (one study)
Strength training	2.225 (1.159, 3.292)[44 45]	1.031 (−29.197, 31.259)[44 46]	16.15 (one study)

MAOI, monoamine oxidase inhibitor; NNH, number needed to harm; SSRI, selective serotonin reuptake inhibitor.

Conclusions of the EULAR:

- Tramadol is recommended for the management of pain in Fibromyalgia. (Ib A)
- Simple analgesics such as Acetaminophen and other weak opioids can also be considered in the treatment of fibromyalgia. Corticosteroids and strong opioids are not recommended. (IV D)
- Antidepressants: amitriptyline, fluoxetine, duloxetine, and milnacipran reduce pain and often improve function, therefore they are recommended for the treatment of fibromyalgia. (Ib A)
- Pramipexole and pregabalin reduce pain and are recommended for the treatment of fibromyalgia. (Ib A)

3. Treatment of Fibromyalgia Syndrome with Antidepressants. JAMA 2009[5]

This is a meta-analysis of randomized controlled clinical trials to determine the efficacy of antidepressants in the treatment of FMS. The following table shows the results:

Table 1. Effect Sizes of the Different Classes of Antidepressants on Selected Outcome Variables

Outcome	No. of Studies	Patients Taking Antidepressants, No.	Statistical Method	Effect Size (95% CI)	Test for Overall Effect *P* Value
Tricyclic Antidepressants					
Pain	6	128	SMD (random)	–1.64 (–2.57 to –0.71)	<.001
Fatigue	4	95	SMD (random)	–1.12 (–1.87 to –0.38)	.003
Sleep	5	105	WMD (fixed)	–1.84 (–2.62 to –1.06)	<.001
Depressed mood	1	20	WMD (fixed)	–0.60 (–4.53 to 3.33)	.76
HRQOL	3	94	WMD (fixed)	–0.31 (–0.60 to –0.01)	.04
Selective Serotonin Reuptake Inhibitors					
Pain	6	132	SMD (random)	–0.39 (–0.77 to –0.01)	.04
Fatigue	5	94	WMD (fixed)	–0.17 (–0.47 to 0.12)	.25
Sleep	4	75	SMD (random)	–0.23 (–0.56 to 0.10)	.18
Depressed mood	5	94	WMD (fixed)	–0.37 (–0.66 to –0.07)	.02
HRQOL	3	62	WMD (fixed)	–0.41 (–0.78 to –0.05)	.03
Serotonin and Noradrenaline Reuptake Inhibitors					
Pain	3	804	SMD (random)	–0.36 (–0.46 to –0.25)	<.001
Fatigue	1	477	WMD (fixed)	–0.08 (–0.20 to 0.05)	.23
Sleep	2	327	SMD (random)	–0.31 (–0.47 to –0.14)	<.001
Depressed mood	2	309	SMD (random)	–0.26 (–0.42 to –0.10)	.001
HRQOL	2	703	SMD (random)	–0.31 (–0.44 to –0.17)	<.001
Monoamine Oxidase Inhibitors					
Pain	3	89	SMD (random)	–0.54 (–1.02 to –0.07)	.03
Fatigue	1	30	WMD (fixed)	0.30 (–1.04 to 1.64)	.66
Sleep	1	30	WMD (fixed)	1.00 (–0.49 to 2.49)	.19
Depressed mood	1	28	WMD (fixed)	0.18 (–2.16 to 2.52)	.88
HRQOL	NA	NA	NA	NA	NA

Abbreviations: CI, confidence interval; HRQOL, health-related quality of life; NA, not assessed; SMD, standardized mean difference; WMD, weighted mean difference.

Conclusions of the meta-analysis:

- Short-term usage of amitriptyline and duloxetine can be considered for the treatment of pain and sleep disturbances in FMS.
- Before treatment is initiated, concomitant diseases related to potential adverse effects of the drugs and patients' preferences should be considered.
- Goals of pharmacological therapy should be defined (no cure, but possible symptom reduction).

- Since evidence for a long-term effect of antidepressants in FMS is still lacking, their effects should be re-evaluated at regular intervals to determine whether benefits outweigh adverse effects.

Utilization

Currently there are three agents with the FDA approved indication for treatment of Fibromyalgia:

- Lyrica® (Pregabalin)- Approved June 2007
- Cymbalta® (Duloxetine HCl)- Approved June 2008
- Savella® (Milnacipran)- Approved January, 2009

For the 2008 calendar year, a total of 6,001 members received Cymbalta or Lyrica (regardless of diagnosis) through the *SoonerCare* program.

BRAND NAME	CLAIMS	UNITS	DAYS	MEMBERS	PERCENT COST	UNITS/ DAY	CLAIMS/ MEMBER
CYMBALTA CAP 60MG	9,228	348,025	317,693	2,026	31.91%	1.1	4.55
LYRICA CAP 75MG	5,974	407,888	180,341	1,901	19.57%	2.26	3.14
LYRICA CAP 150MG	3,304	227,607	102,105	832	10.96%	2.23	3.97
CYMBALTA CAP 30MG	3,018	123,308	100,534	973	11.29%	1.23	3.1
LYRICA CAP 50MG	2,833	214,569	84,921	1,030	10.35%	2.53	2.75
LYRICA CAP 100MG	2,279	184,856	69,201	662	8.88%	2.67	3.44
CYMBALTA CAP 20MG	631	29,053	19,273	190	2.39%	1.51	3.32
LYRICA CAP 300MG	579	39,048	17,880	122	1.87%	2.18	4.75
LYRICA CAP 200MG	444	32,310	13,766	106	1.57%	2.35	4.19
LYRICA CAP 25MG	220	14,641	6,480	89	0.66%	2.26	2.47
LYRICA CAP 225MG	196	11,666	5,973	47	0.56%	1.95	4.17
TOTALS	**28,706**	**1,632,971**	**918,167**			**1.78**	**4.78**

Total Claims: Cymbalta®- 12,877, Lyrica®- 15,829, Savella®-not marketed until 2009

Recommendations

The College of Pharmacy recommends prior authorization of the Fibromyalgia medications with the following criteria:

Tier 1	Tier 2
Amitriptyline Cyclobenzaprine Fluoxetine Tramadol	Lyrica® (Pregabalin) Cymbalta® (Duloxetine HCl) Savella® (Milnacipran)

1. Trials of two tier-1 medications within the last 90 days that did not provide adequate response, or
2. Contraindication(s) to all available tier-1 medications;
3. Clinical Exceptions include:
    a. Diagnosis of seizures, diabetic neuropathy, or neuropathy for Lyrica®(Pregabalin)
    b. Diagnosis of diabetic neuropathy for Cymbalta® (Duloxetine HCl)

Appendix

Lyrica Summary[6]

Clinical Studies

The efficacy of Lyrica® for management of fibromyalgia was established in one 14-week, double-blind, placebo-controlled, multicenter study (F1) and one six-month, randomized withdrawal study (F2). The studies showed a reduction in pain by visual analog scale. In addition, improvement was demonstrated based on a patient global assessment (PGIC), and on the Fibromyalgia Impact Questionnaire (FIQ).

Study F1: This 14-week study compared Lyrica® total daily doses of 300 mg, 450 mg and 600 mg with placebo. Patients were enrolled with a minimum mean baseline pain score of greater than or equal to 4 on an 11-point numeric pain rating scale and a score of greater than or equal to 40 mm on the 100 mm pain visual analog scale (VAS). The baseline mean pain score in this trial was 6.7. Responders to placebo in an initial one-week run-in phase were not randomized into subsequent phases of the study. A total of 64% of patients randomized to Lyrica® completed the study. There was no evidence of a greater effect on pain scores of the 600 mg daily dose than the 450 mg daily dose, but there was evidence of dose-dependent adverse reactions. Some patients experienced a decrease in pain as early as Week 1, which persisted throughout the study.

Study F2: This randomized withdrawal study compared Lyrica® with placebo. Patients were titrated during a 6-week open-label dose optimization phase to a total daily dose of 300 mg, 450 mg, or 600 mg. Patients were considered to be responders if they had both: 1) at least a 50% reduction in pain (VAS) and, 2) rated their overall improvement on the PGIC as "much improved" or "very much improved." Those who responded to treatment were then randomized in the double-blind treatment phase to either the dose achieved in the open-label phase or to placebo. Patients were treated for up to 6 months following randomization. Efficacy was assessed by time to loss of therapeutic response, defined as 1) less than 30% reduction in pain (VAS) from open-label baseline during two consecutive visits of the double-blind phase, or 2) worsening of FM symptoms necessitating an alternative treatment. Fifty-four percent of patients were able to titrate to an effective and tolerable dose of Lyrica® during the 6-week open-label phase. Of the patients entering the randomized treatment phase assigned to remain on Lyrica®, 38% of patients completed 26 weeks of treatment versus 19% of placebo-treated patients. When considering return of pain or withdrawal due to adverse events as loss of response (LTR), treatment with Lyrica® resulted in a longer time to loss of therapeutic response than treatment with placebo. Fifty-three percent of the pregabalin-treated subjects compared to 33% of placebo patients remained on study drug and maintained a therapeutic response to Week 26 of the study. Treatment with Lyrica® also resulted in a longer time to loss of response based on the FIQ1, and longer time to loss of overall assessment of patient status, as measured by the PGIC2.

Manufacturer	Pfizer
Classification	Anticonvulsant, Neuropathic Pain Agent
Status	Prescription Only

Indication and Administration

Lyrica® is indicated for:

- management of pain associated with diabetic peripheral neuropathy
- management of pain associated with neuralgia
- adjunctive therapy for partial-onset seizure disorder in adults
- management of fibromyalgia

Lyrica® may be administered orally, twice daily or three times daily.

Dosage Forms: 25, 50, 75, 100, 150, 200, 225, 300 mg capsules

Contraindications
Lyrica® is contraindicated in patients with known pregabalin hypersensitivity or with product specific ingredient hypersensitivity.

Pregnancy Risk Factor C

Precautions
- **do no abruptly discontinue**; increased risk of adverse events and seizure frequency
- **angioedema,** history of; increased risk of potentially life-threatening angioedema
- **concomitant use of thiazolidinedione antidiabetic agents**; increased risk for weight gain and peripheral edema
- **concomitant use of drugs associated with angioedema**, such as ACE inhibitors; increased risk of developing angioedema
- **heart failure**, New York Heart Association Class III and IV; increased risk of peripheral edema
- **may impair ability to drive or operate heavy machinery**; dizziness and somnolence have been commonly reported
- **ocular conditions**; pregabalin associated with vision changes
- **renal function** reduced, including hemodialysis
- **risk of myopathy**; creatine kinase elevations have been reported
- **suicidality, increased risk of**; based on data analysis of 199 placebo-controlled studies of 11 antiepileptic drugs, small elevated risk occurred as early as 1 week after starting therapy and continued to at least 24 weeks

Common Adverse Effect
- Peripheral edema
- Dizziness
- Somnolence
- Ataxia
- Headache
- Weight gain
- Xerostomia
- Neuromuscular and skeletal tremor
- Blurred vision
- Infection
- Accidental injury

Drug Interactions
- **alcohol:** CNS depressants may enhance depressant effect of alcohol
- **thiazolidinedione:** pregablin may enhance the fluid-retaining effect of antidiabetic agents
- **CNS Depressants:** may enhance the adverse/toxic effect of other CNS Depressants
- **ketorolac:** may diminish the therapeutic effect of anticonvulsants
- **mefloquine:** May diminish the therapeutic effect of Anticonvulsants

Patient Information

- Use ethanol with caution as it may increase CNS depression and toxicity. Watch for sedation.
- Stop using this medicine and call your doctor right away if you have swelling of the face, eyes, lips, gums, or tongue, or problems with swallowing or breathing.
- If you miss a dose or forget to use your medicine, use it as soon as you can. If it is almost time for your next dose, wait until then to use the medicine and skip the missed dose. Do not use extra medicine to make up for a missed dose.

Cymbalta Summary[7]

Clinical Studies

The efficacy of Cymbalta® for the management of fibromyalgia was established in two randomized, double-blind, placebo-controlled, fixed-dose studies in adult patients meeting the American College of Rheumatology criteria for fibromyalgia (a history of widespread pain for 3 months, and pain present at 11 or more of the 18 specific tender point sites). Study 1 was three months in duration and enrolled female patients only. Study 2 was six months in duration and enrolled male and female patients.

Approximately 25% of participants had a comorbid diagnosis of major depressive disorder (MDD). Study 1 and 2 enrolled a total of 874 patients of whom 541 (62%) completed the studies. The patients had a baseline pain score of 6.5 on an 11-point scale ranging from 0 (no pain) to 10 (worse possible pain).

Both studies compared Cymbalta® 60 mg once daily or 120 mg daily (given in divided doses in Study 1 and as a single daily dose in Study 2) with placebo. Study 2 additionally compared Cymbalta® 20 mg with placebo during the initial three months of a six-month study. A total of 354 patients (234 Cymbalta®, 120 placebo) were enrolled in Study 1 and a total of 520 patients (376 Cymbalta®, 144 placebo) were enrolled in Study 2 (5% male, 95% female). Treatment with Cymbalta® 60 mg or 120 mg daily significantly improved the mean pain scores from baseline and increased the proportion of patients with at least a 50% reduction in pain score from baseline. Pain reduction was observed in patients both with and without co-morbid MDD. However, the degree of pain reduction may be greater in patients with co-morbid MDD. Patients who did not complete the study were assigned 0% improvement. Some patients experienced a decrease in pain as early as week 1, which persisted throughout the study.

Improvement was also demonstrated on measures of function (Fibromyalgia Impact Questionnaires) and patient global impression of change (PGI). Neither study demon-strated a benefit of the 120 mg dose over the 60 mg dose, and the higher dose was associated with more adverse reactions and premature discontinuation of treatment. Additionally, the benefit of up-titration in non-responders to Cymbalta® at 60 mg/day was evaluated in a separate study. Patients were initially treated with Cymbalta 60 mg once daily for eight weeks in open-label fashion. Subsequently, completers of this phase were randomized to double-blind treatment with Cymbalta® at either 60 mg once daily or 120 mg once daily. Those patients who were considered nonresponders, where response was defined as at least a 30% reduction in pain score from baseline at the end of the 8-week treatment, were no more likely to meet response criteria at the end of 60 weeks of treatment if blindly titrated to Cymbalta® 120 mg as compared to those who were blindly continued on Cymbalta® 60mg.

Manufacturer	Lilly, USA
Classification	Psychotropic Agent, Antidepressants, SNRI
Status	Prescription Only

Indication and Administration

Cymbalta® is indicated for treatment of:

- diabetic peripheral neuropathy pain
- fibromyalgia
- generalized anxiety disorder
- major depressive disorder

Cymbalta® capsules are administered orally twice daily initially and then once daily.

Dosage Forms: 20, 30, 60 mg capsules

Contraindications
Cymbalta® is contraindicated in patients with concomitant use of MAOIs and in narrow-angle glaucoma due to an increased risk of mydriasis.

Pregnancy Risk Factor C

Precautions
- **suicidal ideation and behavior or worsening depression**; increased risk, particularly in children, adolescents, and young adults during the first few months of therapy or following changes in dosage
- **abnormal bleeding** has been reported, including life-threatening hemorrhages
- **abrupt withdrawal**; serious discontinuation symptoms have been reported
- **alcohol**, substantial use; increased risk of liver injury
- **bipolar disorder**; increased risk of precipitation of a mixed/manic episode
- **conditions that slow gastric emptying**, such as diabetes; may affect stability of enteric coating
- **diabetes**; may worsen glycemic control
- **hepatic impairment**; use of duloxetine is not recommended
- **hepatotoxicity**, including hepatitis, jaundice, and elevated transaminase levels, has been reported
- **liver disease**, chronic; may aggravate condition
- **mania**, history; risk of activation of mania/hypomania
- **narrow-angle glaucoma**, controlled; increased risk of mydriasis
- **renal impairment**, severe and end stage renal disease (creatinine clearance less than 30 mL/min); duloxetine use not recommended
- **seizures**, history of
- **use of duloxetine within 14 days of MAOI discontinuation**
- **use of an MAOI within 5 days after duloxetine discontinuation**
- **urinary retention** requiring hospitalization and/or catheterization has been reported
- **volume-depleted, elderly, or concurrent diuretic therapy**; hyponatremia, syndrome of inappropriate antidiuretic hormone secretion (SIADH) has occurred with duloxetine; discontinue if symptoms develop

Common Adverse Effect
- Dizziness
- Constipation
- Diarrhea
- Diaphoresis
- Insomnia
- Somnolence
- Xerostomia

Drug Interactions
- **concomitant use of thioridazine or serotonergic drugs** (serotonin precursors (tryptophan), SSRIs, serotonin-norepinephrine reuptake inhibitors); use is not recommended
- **concomitant use of potent CYP1A2 inhibitors** (fluvoxamine, cimetidine, quinolone antimicrobials (eg, ciprofloxacin, enoxacin)); use should be avoided
- **concomitant use of CNS-acting drugs**, 5-hydroxytryptamine receptor agonist (triptan), drugs that affect coagulation (eg, NSAIDs, aspirin, warfarin), tricyclic antidepressants (nortriptyline, amitriptyline, imipramine), phenothiazines, type 1-C antiarrhythmics (propafenone, and flecainide); use cautiously
- **MAOIs**

Patient Information

- Report worsening depression, suicidal ideation, or unusual changes in behavior, especially at initiation of therapy or with dose changes; Children and adolescents are at higher risk for these effects during the first few months of therapy.
- Patient should not drink alcohol while taking this drug, as concomitant use may lead to liver injury.

Savella Summary[8]

Clinical Studies

The efficacy of Savella® for the management of fibromyalgia was established in two double-blind, placebo-controlled, multicenter studies in adult patients (18-74 years of age). Enrolled patients met the American College of Rheumatology (ACR) criteria for fibromyalgia (a history of widespread pain for 3 months and pain present at 11 or more of the 18 specific tender point sites). Approximately 35% of patients had a history of depression.

Study 1 was six months in duration and Study 2 was three months in duration. A larger proportion of patients treated with Savella® than with placebo experienced a simultaneous reduction in pain from baseline of at least 30% (VAS) and also rated themselves as much improved or very much improved based on the patient global assessment (PGIC). In addition, a larger proportion of patients treated with Savella® met the criteria for treatment response, as measured by the composite endpoint that concurrently evaluated improvement in pain (VAS), physical function (SF-36 PCS), and patient global assessment (PGIC), in fibromyalgia as compared to placebo.

Study 1: This 6-month study compared total daily doses of Savella® 100 mg and 200 mg to placebo. Patients were enrolled with a minimum mean baseline pain score of ≥ 50 mm on a 100 mm visual analog scale (VAS) ranging from 0 ("no pain") to 100 ("worst possible pain"). The mean baseline pain score in this trial was 69. Patients who did not complete the 3-month assessment were assigned 0% improvement. More patients in the Savella® treatment arms experienced at least a 30% reduction in pain from baseline (VAS) and considered themselves globally improved (PGIC) than did patients in the placebo arm. Treatment with Savella® 200 mg/day did not confer greater benefit than treatment with Savella® 100 mg/day.

Study 2: This 3-month study compared total daily doses of Savella® 100 mg and 200 mg to placebo. Patients were enrolled with a minimum mean baseline pain score of ≥ 40 mm on a 100-mm VAS ranging from 0 ("no pain") to 100 ("worst possible pain"). The mean baseline pain score in this trial was 65. Patients who did not complete the 3-month assessment were assigned 0% improvement. More patients in the Savella® treatment arms experienced at least a 30% reduction in pain from baseline (VAS) and considered themselves globally improved (PGIC) than did patients in the placebo arm. Treatment with Savella 200 mg/day did not confer greater benefit than treatment with Savella® 100 mg/day.

In both studies, some patients who rated themselves as globally "much" or "very much" improved experienced a decrease in pain as early as week 1 of treatment with a stable dose of Savella® that persisted throughout these studies.

Manufacturer	Forest Pharmaceuticals, Inc.
Classification	Psychotropic agent, Antidepressant, SSRI
Status	Prescription Only

Indication and Administration
Savella® is indicated for the treatment of fibromyalgia.
Savella® is to be taken orally and not crushed or chewed.

Dosage Forms: 12.5, 25, 50, and 100 mg tablets

Contraindications
Savella® is contraindicated with concomitant use with a MAOI or use of MAOI within the preceding 14 days before milnacipran initiation or within 5 days after milnacipran discontinuation. It is also contraindicated in uncontrolled narrow-angle glaucoma due to increased risk of mydriasis.

Pregnancy Risk Factor C

Precautions
- **suicidal ideation and behavior, worsening depression, and unusual changes in behavior** may occur in adults or pediatric patients; increased risk of suicidal ideation and behavior in children, adolescents, and young adults with major depressive disorder and other psychiatric disorders; monitoring in all patients is recommended, especially during the first few months of therapy or following changes in dosage
- **abnormal bleeding may occur**; increased risk with concomitant use of drugs that affect coagulation
- **abrupt withdrawal should be avoided**; withdrawal symptoms, some severe, have been reported; monitoring recommended; reduce dose gradually if possible
- **alcohol use, substantial**; may exacerbate preexisting liver disease; use not recommended
- **concomitant use with serotonin precursors**, (eg, tryptophan) is not recommended
- **dysuria**, history of, including male patients with prostatic hypertrophy, prostatitis, and other lower urinary tract obstructive disorders; may affect urethral resistance and micturition causing genitourinary adverse effects
- **heart rate increases have been reported**; monitoring recommended; consider a dose reduction or discontinuing therapy for sustained heart rate elevation
- **hepatotoxicity**, including increased liver enzymes and fulminant hepatitis, has been reported; discontinue therapy in patients who develop jaundice or other evidence of liver
- **hypertension** has been reported; use caution in patients with clinically significant hypertension or cardiac disease; consider a dose reduction or discontinuing therapy for sustained blood pressure increases
- **hyponatremia and/or syndrome of inappropriate antidiuretic hormone secretion** (SIADH) has occurred; greater risk in patients who are volume-depleted, elderly, or receiving concurrent diuretic therapy; consider discontinuing therapy if symptomatic hyponatremia occurs
- **liver disease, chronic**; may exacerbate preexisting liver disease; use not recommended
- **mania,** history; risk of activation of mania/hypomania
- **narrow-angle glaucoma**, controlled; increased risk of mydriasis
- **renal impairment**; dosage reduction recommended for severe renal impairment (CrCl, 5 to 29 mL/min); use not recommended in patients with end-stage renal disease
- **seizures**, history of
- **serotonin syndrome may occur**; increased risk with concomitant use of serotonergic drugs (e.g., triptans and tramadol)
- **tartrazine (FD&C Yellow No. 5) allergy**; this product contains tartrazine; may cause allergic-type reactions

Common Adverse Effect
- Dizziness
- Constipation
- Headache
- Nausea
- Hot flashes
- Insomnia

- Palpitation

Drug Interactions

- concomitant use with **IV digoxin** should be avoided
- **CNS Depressants** may enhance the CNS depressant effect of Alcohol
- **serotonin/norepinephrine reuptake inhibitors** may diminish the antihypertensive effect of alpha2-agonists
- may enhance the adverse/toxic effect of other **CNS Depressants**
- **MAOIs** may enhance the serotonergic effect.

Patient Information

- Avoid concomitant use of aspirin and other NSAIDs or warfarin while taking this medication; can cause increased bleeding.
- Avoid use of alcohol.
- Report to your doctor any new or worsening depression, changes in mood, aggressive or violent behavior, panic attacks, or thoughts of suicide.

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Appendix G

Drug Utilization Review of

Otic Anti-Infective Medications

Oklahoma Health Care Authority, July 2009

Diagnosis and Etiology

Otitis Externa ('Swimmer's Ear')

Infection of the external auditory canal (OE) is similar to infection of skin and soft tissue, although, unique problems occur because the canal is narrow. Fluid and foreign objects enter the ear which may result in irritation and damage of the superficial tissues. Otitis externa is an acute infection that frequently causes severe pain. This type of infection is often attributed to recent water exposure or trauma. An antimicrobial agent selected to treat OE must include activity against Gram-negative organisms, particularly P. aeruginosa and Proteus spp. and Gram-positive cocci such as S. aureus as well as organisms that may have caused irritation of the canal after rupture of the tympanic membrane, such as S. pneumoniae and H. influenzae. Otic antibiotics remain in frequent use and are the standard for the treatment of OE.

Acute Otitis Media

Acute otitis media (AOM) with or without tympanostomy tubes is the most common infection for which antibacterial agents are prescribed for children in the United States. It is usually triggered by an upper respiratory tract infection, which causes congestion and swelling of the nasal mucosa, nasopharynx and eustachian tube. Subsequent obstruction and accumulation of middle ear secretions infected with bacterial or viral organism(s) causes acute otitis media. The standard treatment for AOM has been systemic oral antibiotics. However, topical otic anti-infectives are the treatment of choice when there is AOM with perforation and pus in the auditory canal.

Chronic Suppurative Otitis Media

Chronic suppurative otitis media (CSOM) is defined as a chronic infection of the ear and mastoid in which a damaged tympanic membrane is present. CSOM results after an episode of AOM; if damage to the tympanic membrane occurs and remains vulnerable to infection it may result in CSOM and be identified clinically by chronic otorrhea. CSOM can occur in children with ventilating tubes. CSOM includes the same pathogens of AOM, but with a chronic compromised tympanic membrane, organisms from the external canal including S. aureus, P. aeruginosa and Proteus spp. can enter the middle ear, resulting in a secondary infection. Many otic agents have been used for CSOM, however, only ofloxacin is approved for this indication and only for children 12 years of age and older. Treatment may also involve removal of purulent material and debris from the external canal to increase the effectiveness of the otic medication.

Otic Treatment Options: OE, AOM with Tubes, CSOM

Cortisporin otic solution and suspension (neomycin and polymyxin B sulfate, with hydrocortisone) and its newer version, **Cortisporin TC** Otic (with addition of thonzonium bromide), are currently the most popular topical antibiotics for use in the draining ear (otorrhea). **Neomycin**, an aminoglycoside, may be ototoxic and also may cause sensitization in a significant number of patients, resulting in rash and significant pruritis. **Polymyxin B and hydrocortisone** have not been studied in patients with nonintact tympanic membranes; therefore any potential toxicity is unknown. The thonzonium bromide used in Cortisporin TC is a surface-active agent that promotes tissue contact by dispersion and penetration of the cellular debris and exudate. There is a study that compared **tobramycin plus dexamethasone** with tobramycin alone and noted more rapid resolution in the steroid-treated group.

Vosol HC is a hydrocortisone and acetic acid solution. Acetic acid is alleged to be bactericidal to P. aeruginosa, and similar products, e.g. **Hydro** (hydrocortisone, pramoxine, chloroxylenol), claim to eradicate all bacterial and fungal organisms. SoonerCare covers generic versions of these otic agents.

Ophthalmic Treatment Options

Ophthalmic preparations have been used in the ear for years, but there is much concern about the use of aminoglycosides in this fashion because of their record of causing severe hearing impairment when administered systemically. No ophthalmic preparation is approved for use in a draining tympanostomy tube. **Gentamicin, tobramycin** and other ophthalmic solutions are frequently used for otitis externa but are not approved for otic diseases.

Precautions and Recommendations

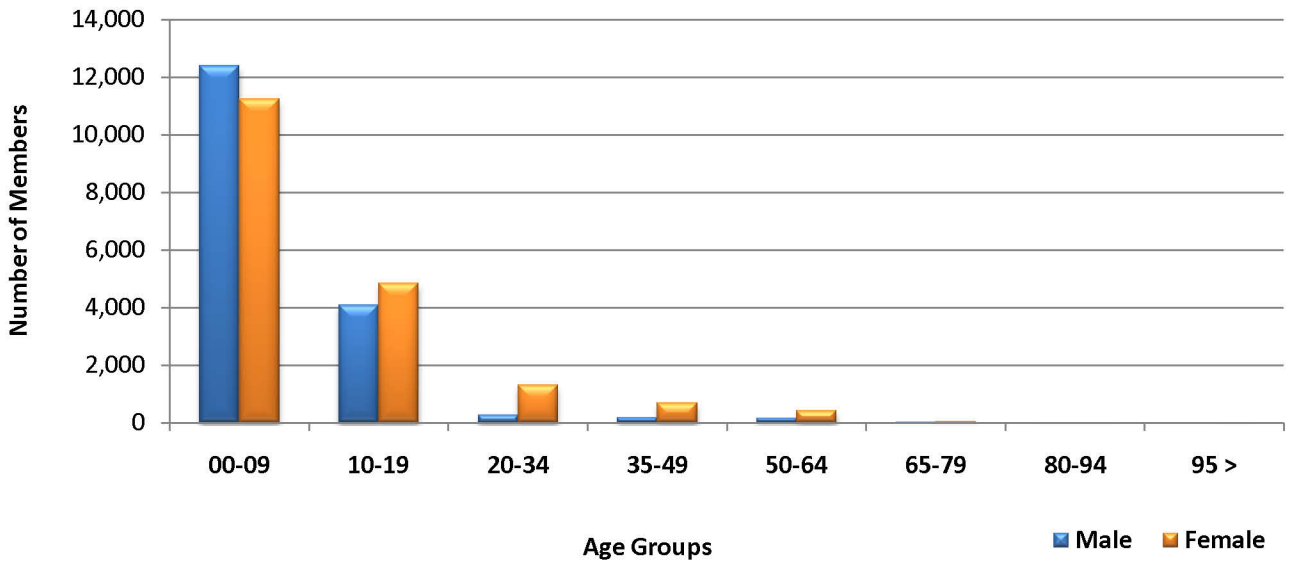
- **Ofloxacin** (Floxin® Otic) is currently the only antibiotic approved for use in patients with perforated tympanic membranes (CSOM).
- Unlike Floxin and Ciprodex, **Cipro HC** is not a sterile product and should not be used in patients with a perforated tympanic membrane.
- Adjunctive therapy with **hydrocortisone and dexamethasone** can help to control inflammation, edema, pruritis and other dermal reactions. American Academy of Pediatrics/American Academy of Family Physician's/American Academy of Otolaryngology Head and Neck Surgery clinical practice guideline recommends against corticosteroid use.

Utilization

Trends in Utilization

Calendar Year	Members	Claims	Claim/Member	Days
2007	29,076	34,826	1.20	353,094
2008	30,626	37,357	1.22	378,694
Percent Change	5.1%	1.0%	1.6%	6.8%
Change	1,550	2,531	0.02	25,600

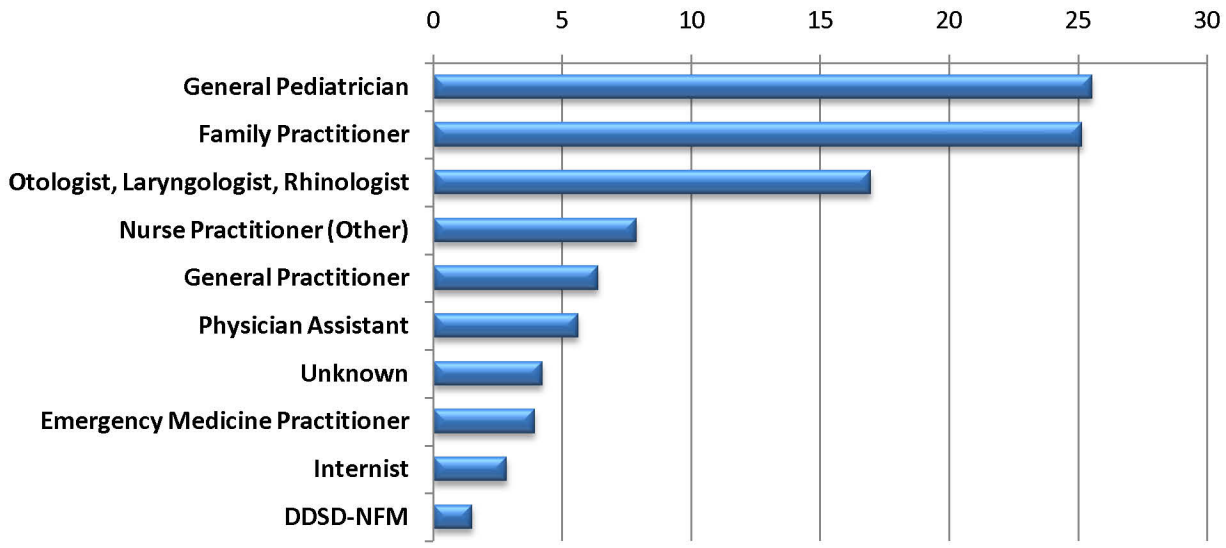
Demographics



Treatment Cost Comparison (Acute Otitis Media)

	Dosing Regimen (FDA Max)	Total Cost (EAC)
Amoxicillin 500mg Capsule	1 capsule Q 8 hours X 14 days	42 Capsules = $13.44
Amoxicillin 250/5ml Susp.	2 tsp Q 8 hours X 14 days.	450 ml's = $18.00
Ofloxacin (Floxin Otic®) *Generic Available	Instill 10 drops (or the contents of 2 single-dose containers) into affected ear BID X 14 days	Two 5ml Bottles = $130.60 SMAC = $23.30
Ciprofloxacin/Dexamethasone (Ciprodex®)	Instill 4 drops into affected ear BID X 7 days.	One 7.5ml bottle = $106.35
Dexamethasone 0.1%	Instill 4 drops into affected ear BID X 7 days.	One 5ml Bottle = $42.45
Ciprofloxacin 0.3%/ Hydrocortisone 1%	Instill 3 drops into affected ear BID X 7 days.	One 10ml Bottle = $106.30

Prescriber Specialty by Percent of Claims



Conclusions

- In regards to the fluroquinolones, ofloxacin (Floxin Otic), Ciprodex (ciprofloxacin and dexamethasone), or Cipro HC (ciprofloxacin and hydrocortisone) provides alternative treatment choices to other topical and oral antibiotics for a variety of ear infections.
- It is recommended that patients with perforated tympanic membrane or with tympanostomy tubes should use non-ototoxic topical antibiotic (i.e. fluroquinolones), however, there is evidence that older anti-infectives, such as Cortisporin, do not cause ototoxicity as suspected.
- Adjunctive therapy with hydrocortisone and dexamethasone can help to control inflammation, edema, pruritis and other dermal reactions. AAP/AAFP/AAOHNS clinical practice guideline recommends against corticosteroid use.

Recommendation

The College of Pharmacy recommends establishing a PBPA category for otic antibiotics to ensure appropriate use in accordance with current treatment guidelines. The establishment of a PBPA category will address safety concerns of otic agents, the potential loss of efficacy due to antibacterial resistance and the growing costs of otic medications. The following are the proposed tiers and prior authorization criteria:

Prior Authorization Criteria:

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

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

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

Calendar Year 2008 Utilization Details:

Chemical Name	Brand Name	Claims	Units	Days	Members	% Cost
Ciprofloxacin-Dexamethasone Otic Susp 0.3-0.1%	CIPRODEX SUS 0.3-0.1%	14,375	108,823	140,735	10,719	58.34
Ofloxacin Otic Soln 0.3%	OFLOXACIN DRO 0.3%OTIC	9,037	63,640	87,901	7,180	22.22
Neomycin-Polymyxin-HC Otic Susp 3.5 MG/ML-10000 Unit/ML-1%	NEO/POLY/HC SUS 1% OTIC	6,714	67,656	66,640	6,202	5.20
Neomycin-Polymyxin-HC Otic Soln 1%	NEO/POLY/HC SOL 1% OTIC	2,685	26,981	28,256	2,512	1.82
Ciprofloxacin-Hydrocortisone Otic Susp 0.2-1%	CIPRO HC SUS OTIC	1,897	18,987	23,506	1,712	7.65
Benzocaine-Antipyrine Otic Soln 1.4-5.4%	AURODEX SOL OTIC	798	11,904	9,043	749	0.20
Chloroxylenol-Pramoxine-Zinc Acetate Otic Liqd 0.1-0.5-0.1%	ZINOTIC DRO	422	6,325	4,270	368	1.02
Ofloxacin Otic Soln 0.3%	FLOXIN OTIC DRO SINGLES	367	6,797	3,118	293	1.06
Hydrocortisone w/ Acetic Acid Otic Soln 1-2%	ACETASOL HC SOL OTIC	286	3,140	3,280	219	0.25
Acetic Acid Otic Soln 2%	ACETIC ACID SOL 2% OTIC	246	3,940	3,635	208	0.33
*Acetic Acid-Antipyrine-Benzocaine-Polycosanol Otic Soln***	AURALGAN SOL	196	2,745	2,002	187	1.24
Neomycin-Colistin-HC-Thonzonium Otic Susp 3.3-3-10-0.5 MG/ML	CORTISPORIN SUS -TC OTIC	173	1,712	1,647	149	0.50
Acetic Acid 2% in Aluminum Acetate Otic Soln	ACE ACD/ALUM SOL 2% OTIC	34	1,995	505	27	0.01
Neomycin-Polymyxin-HC Otic Susp 3.5 MG/ML-10000 Unit/ML-1%	ANTIBIOT EAR SUS 1% OTIC	28	280	234	26	0.02
Neomycin-Colistin-HC Otic Susp	COLY-MYCIN-S SUS OTIC	28	150	259	17	0.05
Hydrocortisone w/ Acetic Acid Otic Soln 1-2%	ACETIC ACID SOL /HC OTIC	26	260	300	24	0.02
Neomycin-Polymyxin-HC Otic Soln 1%	ANTIBIOT EAR SOL 1% OTIC	9	90	81	8	0.01
Neomycin-Polymyxin-HC Otic Susp 3.5 MG/ML-10000 Unit/ML-1%	CORTOMYCIN SUS 1% OTIC	9	95	103	6	0.01
Neomycin-Polymyxin-HC Otic Susp 3.5 MG/ML-10000 Unit/ML-1%	PEDIOTIC SUS 1% OTIC	6	45	51	6	0.02
Neomycin-Colistin-HC Otic Susp	COLY-MYCIN S SUS OTIC	6	40	51	6	0.01
Ofloxacin Otic Soln 0.3%	FLOXIN OTIC DRO 0.3%	2	10	22	2	0.01
Antipyrine-Benzocaine-Zinc Acetate Otic Liquid 5.4-1-1%	NEOTIC LIQ 5.4-1-1%	2	40	16	2	0.00
Acetic Acid Solution 2%	ACETASOL SOL 2% OTIC	2	25	22	2	0.00
Neomycin-Polymyxin-HC Otic Soln 1%	CORTOMYCIN SOL 1% OTIC	1	10	7	1	0.00
Acetic Acid 2% in Aluminum Acetate Otic Soln	BOROFAIR SOL 2% OTIC	1	60	10	1	0.00
Totals		**37,350**	**325,750**	**375,694**	**30,626***	**100.00%**

*Total number of unduplicated members.

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Appendix H

FDA NEWS RELEASE

For Immediate Release: June 16, 2009

Media Inquiries: Siobhan DeLancey, 301-796-4668, siobhan.delancey@fda.hhs.gov
Consumer Inquiries: 888-INFO-FDA

FDA Advises Consumers Not To Use Certain Zicam Cold Remedies

Intranasal Zinc Product Linked to Loss of Sense of Smell

The U.S. Food and Drug Administration today advised consumers to stop using three products marketed over-the-counter as cold remedies because they are associated with the loss of sense of smell (anosmia). Anosmia may be long-lasting or permanent.

The products are:
- --Zicam Cold Remedy Nasal Gel
- --Zicam Cold Remedy Nasal Swabs
- --Zicam Cold Remedy Swabs, Kids Size (a discontinued product)

The FDA has received more than 130 reports of loss of sense of smell associated with the use of these three Zicam products. In these reports, many people who experienced a loss of smell said the condition occurred with the first dose; others reported a loss of the sense of smell after multiple uses of the products.

"Loss of sense of smell is a serious risk for people who use these products for relief from cold symptoms," said Janet Woodcock, M.D., director of the FDA's Center for Drug Evaluation and Research (CDER). "We are concerned that consumers may unknowingly use a product that could cause serious harm, and therefore we are advising them not to use these products for any reason."

People who have experienced a loss of sense of smell or other problems after use of the affected Zicam products should contact their health care professional. The loss of sense of smell can adversely affect a person's quality of life, and can limit the ability to detect the smell of gas or smoke or other signs of danger in the environment.

The FDA has issued Matrixx Initiatives, maker of these Zicam products, a warning letter telling it that these products cannot be marketed without FDA approval.

"Companies have an obligation to the public to demonstrate to the FDA that their products are safe, particularly when there is evidence they may be causing serious adverse events, and they are marketed for minor, self-limiting conditions like the common cold," said Deborah M. Autor, director of CDER's Office of Compliance.

Health care professionals and consumers are encouraged to report adverse events (side effects) that may be related to the use of these products to the FDA's MedWatch Adverse Event Reporting program online, by regular mail, fax or phone.

--Online

--Regular Mail: use FDA postage paid form 3500 and mail to MedWatch, 5600 Fishers Lane, Rockville, MD 20852-9787

--Fax: 800-FDA-0178

--Phone: 800-FDA-1088

For more information:
http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm166834.htm

Communication about an Ongoing Safety Review of Stimulant Medications used in Children with Attention-Deficit/Hyperactivity Disorder (ADHD)

Products involved include: Focalin, Focalin XR (dexmethylphenidate HCl); Dexedrine, Dexedrine Spansules, Dextroamphetamine ER, Dextrostat (dextroamphetamine sulfate); Vyvanse (lisdexamfetamine dimesylate); Desoxyn (methamphetamine); Concerta, Daytrana, Metadate CD, Metadate ER, Methylin, Methylin ER, Ritalin, Ritalin-LA, Ritalin-SR (methylphenidate); Adderall, Adderall XR (mixed salts amphetamine); Cylert (pemoline) and generics

6/23/2009

The U.S. Food and Drug Administration is providing its perspective on data published today in the American Journal of Psychiatry on the potential risks of stimulant medications used to treat Attention-Deficit/Hyperactivity Disorder (ADHD) in children.[1,2]

Given the limitations of this study's methodology, the FDA is unable to conclude that these data affect the overall risk and benefit profile of stimulant medications used to treat ADHD in children.

Therefore, the FDA believes that this study should not serve as a basis for parents to stop a child's stimulant medication. Parents should discuss concerns about the use of these medicines with the prescribing healthcare professional. The FDA's summary of the study and its limitations, and our recommendations for healthcare professionals are provided below.

Study Summary

This study, funded by the FDA and the National Institute of Mental Health (NIMH), compared the use of stimulant medications in 564 healthy children from across the United States who died suddenly to the use of stimulant medications in 564 children who died as passengers in a motor vehicle accident. Use of stimulant medication was determined from parents, medical examiners, and toxicology reports. These two groups of children were compared because the children all died suddenly and the cause of death was not a known health problem.

Findings of the study

- Out of 564 healthy children who died suddenly, 10 were reported to be taking a stimulant medication at the time of death.

- Out of 564 healthy children who died in a motor vehicle accident, 2 were reported to be taking a stimulant medication at the time of death.
- The study authors concluded that there may be an association between the use of stimulant medications and sudden death in healthy children.

Limitations of the study data

- A child's use of a stimulant medication for ADHD was determined many years after each child's death. The deaths occurred between 1985 to1996, but the data on medication usage were collected from March 1997 to January 2008. This time lag may have resulted in reporting errors.
- The differences in cause of death (sudden death versus death from a motor vehicle accident) could have influenced the family or caregiver's recall of information on stimulant medication use at the time of death, creating an elevated rate of stimulant drug use in the group of children who died suddenly, as compared to the children who died in a motor vehicle accidents,
- The sudden unexplained death of a child, in comparison to a death of a child from a motor vehicle accident, may have increased the likelihood of a post-mortem inquiry into medication use.
- The low frequency of stimulant use in both groups, as well as possible differences in the type of post-mortem inquiry, could have a profound biasing effect on the results.

Ongoing FDA Review:

The FDA is continuing its review of the strengths and limitations of this and other epidemiological studies that evaluate the risks of stimulant medications used to treat ADHD in children. The Agency for Healthcare Research and Quality (AHRQ) and the FDA are sponsoring a large epidemiological study that will provide further information about the potential risks associated with stimulant medication use in children. The data collection for this study will be complete later in 2009.

Recommendations for Healthcare Professionals:

Follow all the current prescribing information for use of these medications, including:

- Take a medical history for cardiovascular disease in the child and his or her family.
- Perform a physical exam with special focus on the cardiovascular system (including examination for the signs of Marfan syndrome).
- Consider obtaining further tests such as a screening electrocardiogram and echocardiogram if the history or examination suggests underlying risk for or the presence of heart disease.

The *FDA intends to update this advisory when additional information or analyses*

become available.

Adverse reactions or quality problems experienced with the use of this Product may be reported to the FDA's MedWatch Adverse Event Reporting program either online, by regular mail or by fax, using the contact information at the bottom of this sheet.

Any child who develops cardiovascular symptoms (such as chest pain, shortness of breath or fainting) during stimulant medication treatment should immediately be seen by a doctor.

Prescription stimulant medications are indicated for the treatment of ADHD as part of a comprehensive treatment plan. ADHD is a persistent pattern of inattention and/or hyperactivity-impulsivity that is more severe than expected for a child's developmental age. Although estimates vary, ADHD is diagnosed in about 4% to 10% of children in the United States (more boys than girls). Children with untreated ADHD may have significantly higher rates of behavioral, mood and anxiety disorders, often resulting in problems with family, school and friends. Refer to the Drugs@FDA for further information on, product labeling, and Medication Guides regarding medications for ADHD.

This information reflects FDA's current analysis of available data concerning these drugs. Posting this information does not mean that FDA has concluded there is a causal relationship between the drug products and the emerging safety issue. Nor does it mean that FDA is advising healthcare professionals to discontinue prescribing these products. FDA is considering, but has not reached a conclusion about whether this information warrants any regulatory action. FDA intends to update this document when additional information or analyses become available

[1] Gould MS, Walsh BT, Munfakh JL, Kleinman M, Duan N, Olfson M, Greenhill L, Cooper T: Sudden death and use of stimulant medications in youth. Am J Psychiatry (published online June 15, 2009; doi:10.1176/appi.ajp.2009.09040538)

[2] Study included children and adolescents.

Contact Us

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Updated Information on Leukotriene Inhibitors: Montelukast (marketed as Singulair), Zafirlukast (marketed as Accolate), and Zileuton (marketed as Zyflo and Zyflo CR)

6/12/2009

Updated information

Neuropsychiatric events have been reported in some patients taking montelukast (Singulair), zafirlukast (Accolate), and zileuton (Zyflo and Zyflo CR). FDA has requested that manufacturers include a precaution in the drug prescribing information (drug labeling).

Montelukast is used to treat asthma, and the symptoms of allergic rhinitis (sneezing, stuffy nose, runny nose, itching of the nose), and to prevent exercise-induced asthma. Zafirlukast and zileuton are used to treat asthma.

The reported neuropsychiatric events include postmarket cases of agitation, aggression, anxiousness, dream abnormalities and hallucinations, depression, insomnia, irritability, restlessness, suicidal thinking and behavior (including suicide), and tremor.

This information reflects FDA's current analysis of available data concerning this drug.

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

Advice to patients and healthcare professionals

- Patients and healthcare professionals should be aware of the potential for neuropsychiatric events with these medications.
- Patients should talk with their healthcare providers if these events occur.
- Healthcare professionals should consider discontinuing these medications if patients develop neuropsychiatric symptoms.

Background

In April 2009, FDA completed its review of neuropsychiatric events, (mood and behavioral changes) possibly related to drugs that act through the leukotriene pathway (montelukast, zafirlukast, zileuton). As part of its review, FDA reviewed post-marketing reports and also requested that manufacturers submit all available clinical trial data for these products.

The post-market reports of patients on these medications included cases of neuropsychiatric events. Some reports included clinical details consistent with a drug-induced effect. In the clinical trial data submitted by manufacturers,

neuropsychiatric events were not commonly observed. However, the available data were limited because the trials were not designed to look for neuropsychiatric events. Sleep disorders (primarily insomnia) were reported more frequently with all three products compared to placebo.

Previous Early Communications

- Early Communication About an Ongoing Safety Review of Montelukast (Singulair)
- Follow-up to the March 27, 2008, Communication about the Ongoing Safety Review of Montelukast (Singulair)

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