THE UNIVERSITY OF OKLAHOMA

MEMORANDUM

TO: Drug Utilization Review Board Members

FROM: Ron Graham, D.Ph.

SUBJECT: **Packet Contents for Board Meeting – November 12, 2002**

DATE: November 5, 2002

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

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

Call to Order

Public Comment Forum

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

Update on DUR/MCAU Program - **See Appendix B.**

Action Item – Review and Vote on Moving ADHD Therapies to Product Based Prior Authorization – **See Appendix C.**

Review and Discuss Prospective Drug Utilization Update for New Fiscal Agent (EDS) – **See Appendix D.**

Review and Discuss Utilization of Actiq™ – **See Appendix E.**

Review and Discuss Utilization of Plavix™ – **See Appendix F.**

Review and Discuss Utilization of Atypical Antipsychotics – **See Appendix G.**

SoonerCare Formulary Change Requests for January 2003 – **See Appendix H.**

FDA Information Updates – **See Appendix I.**

Future Business

Adjournment

DEFENDANT EXHIBIT

J 794

OUCOP-00039954

J794.0001

Drug Utilization Review Board

(DUR Board)

Meeting – November 12, 2002 @ 6:00p.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. Whitsett, Chairman:

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

Items to be presented by Dr. Whitsett, Chairman:

2. **Public Comment Forum**
   A. Acknowledgment of Speakers and Agenda Item

Items to be presented by Dr. Whitsett, Chairman:

3. **Action Item - Approval of DUR Board Meeting Minutes – See Appendix A.**
   A. October 8, 2002 DUR Minutes
   B. DUR Board Memorandum

Items to be presented by Dr. Flannigan, Dr. Browning, Dr. Graham, Ms. Puckett, Dr. Whitsett, Chairman:

4. **Update on DUR/MCAU Program - See Appendix B.**
   A. Retrospective DUR Report for August 2002
   B. Medication Coverage Activity Audit for October 2002
   C. Help Desk Activity Audit for October 2002
   D. Secure Provider Website Demonstration

Items to be presented by Dr. Nesser, Dr. Whitsett, Chairman:

5. **Action Item - Review and Vote On Moving ADHD Therapies to Product Based Prior Authorization- See Appendix C.**
   A. Explanation Sheet

Items to be presented by Dr. Gorman, Dr. Whitsett, Chairman:

6. **Review and Discuss Prospective Drug Utilization Update for New Fiscal Agent (EDS) – Part V – See Appendix D.**
   A. Drug Age Precaution Modules
   B. New Recommended Criteria
   C. Table 1 – Geriatric Precautions Criteria

Items to be presented by Dr. McIlvain, Dr. Whitsett, Chairman:

7. **Review and Discuss Utilization of Actiq™ – See Appendix E.**
   A. Drug Information
   B. Oklahoma Medicaid Utilization

Items to be presented by Dr. Flannigan, Dr. Whitsett, Chairman:

8. Review and Discuss Utilization of Plavix™ – See Appendix F.

A. Drug Information
B. Oklahoma Medicaid Utilization

Items to be presented by Dr. Park, Dr. Whitsett, Chairman:

9. Review and Discuss Utilization of Atypical Antipsychotics– See Appendix G.

A. Oklahoma Medicaid Utilization

Items to be presented by Dr. Egesdal, Dr. Whitsett, Chairman:

10. SoonerCare Formulary Change Requests for January 2003 – See Appendix H.

A. CommunityCare HMO
B. Heartland Health Plan
C. UniCare

11. FDA Information Updates – See Appendix I.

A. FDA Updates

12. Future Business

A. Utilization Review of Prozac™ Weekly
B. Quantity Limitations on Inhalers
C. Utilization Review of SSRI's
D. Utilization Review of Factor Products
E. Utilization Review of Lamictal™
F. Utilization Review of Non-Sedating Antihistamines
G. Prior Authorization Class Reviews

13. Adjournment

APPENDIX A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES of MEETING of OCTOBER 8, 2002

BOARD MEMBERS:	PRESENT	ABSENT
William Banner, M.D.	X	
Rick G. Crenshaw, D.O.	X	
Francoise DuToit, M.D.		X
Dorothy Gourley, D.Ph.	X	
Cathy Hollen, D.Ph.	X	
Dan McNeill, Ph.D., PA-C	X	
Cliff Meece, D.Ph.	X	
Dick Robinson, D.Ph., Vice-Chair	X	
James M. Swaim, D.Ph.	X	
Thomas Whitsett, M.D., Chair		X

COLLEGE of PHARMACY STAFF:	PRESENT	ABSENT
Carl Buckner, Ph.D./Dean , College of Pharmacy	X	
Jack Coffey, Assistant Dean, College of Pharmacy		X
Leslie Browning, D.Ph./Clinical Pharmacist	X	
Karen Egesdal, D.Ph./Clinical Pharmacist/OHCA Liaison	X	
Kelly Flannigan, D.Ph./Clinical Pharmacist	X	
Shellie Gorman, Pharm.D./Clinical Pharmacist	X	
Ronald Graham, D.Ph., Manager, Operations/DUR	X	
Elgene Jacobs, Ph.D.; Manager, Research	X	
Ann McIlvain, Pharm.D.; Clinical Pharmacist	X	
Alex Park, Pharm.D.; Clinical Pharmacist	X	
Visiting Pharmacy Student – n/a		

OKLAHOMA HEALTH CARE AUTHORITY STAFF:	PRESENT	ABSENT
Mike Fogarty, C.E.O		X
Lynn Mitchell, M.D., M.P.H, Medical Director		X
Nancy Nesser, D.Ph., J.D.; Pharmacy Director	X	
Howard Pallotta, J.D.		X
Lynn Rambo-Jones, J.D.	X	
Kristall Bright, Pharmacy Claims Specialist	X	

OTHERS PRESENT:

Jim Goddard, Shire	John Crumly, PPOK
Chris Bryant, Shire	Carla McGee, GSK
JA Mays, GSK	Becky Alderson, BMS
Cindy Flesher, BMS	Tara Linuke, Sepracor
Traci Tarwater, Sepracor	Toby Thompson, Pfizer
Laura Stwint, Merck	Mila Maxwell, CCHMO
Doug McCann, Wellpoint	Johnna Shinn, Unicare
Holly Jacques, Merck	

PRESENT FOR PUBLIC COMMENT:

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

1A: Roll Call

Dick Robinson called the meeting to order. Roll call established the presence of a quorum.

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 2: PUBLIC COMMENT FORUM

2A: Acknowledgement of Speakers and Agenda Item

There were no speakers for public comment.

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 3: APPROVAL OF DUR BOARD MINUTES

3A: August 13, 2002 DUR Minutes

Dr. Meece moved to approve minutes as submitted; second by Dr. Gourley.

ACTION: MOTION CARRIED.

3C: September 10, 2002 DUR Minutes

Dr. McNeill moved to approve minutes as submitted; second by Dr. Swaim.

ACTION: MOTION CARRIED.

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

4A: Prospective DUR Quarterly Report: 1st Quarter SFY03

Report was submitted to the Board in the agenda packet for this meeting. Material presented by Dr. Gorman.

4B: Retrospective DUR Report: July 2002

Antidepressants, Parkinson's, and Alzheimer's medications were selected for retrospective review for July 2002. There were 1,167,249 claims screened, with follow-up on 43 cases. Pharmacy and physician response was 50% and 62% respectively. Potential annualized savings related to this DUR run are $37,243; total YTD is $423,101. Material presented by Dr. Flannigan.

4C: Medication Coverage Activity Report: September 2002

The September 2002 activity audit noted total number of petitions submitted was 9793 including super-PA's and special circumstance PA's. Approval/denial/duplicate percentages were indicated on the reports included in the agenda packet for this meeting. Material presented by Dr. Browning, including 1st Quarter SFY03 reports.

4D: Help Desk Activity Report: September 2002

Total calls for September numbered 8664. Call Volume and Call Log reports were submitted to the Board in the agenda packet for this meeting. Material presented by Dr. Graham, including 1st Quarter SFY03 reports.

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 5: REVIEW & VOTE ON SOONERCARE FORMULARY CHANGE REQUESTS FOR OCTOBER / 2002

5A: Heartland Response to Board Member Questions

Submitted in agenda packet for this meeting. Board members looked over the responses with approval.

5B: Vote – CommunityCare HMO Formulary Request for October / 2002

Dr. McNeill moved to approve as submitted; second by Dr. Meece.

ACTION: MOTION CARRIED.

5C: Vote – Prime Advantage Formulary Request for October / 2002

Dr. McNeill moved to approve as submitted; second by Dr. Gourley. Dr. Hollen requested that specific answers to her questions be provided at the next meeting.

ACTION: MOTION CARRIED.

5D: Vote – UniCare Formulary Request for October / 2002

Dr. Meece moved to approve as submitted; second by Dr. McNeill.

ACTION: MOTION CARRIED.

AGENDA ITEM NO. 6: REVIEW & VOTE ON TIER CHANGE AND BID DOSING WITHOUT PA FOR AXID & PEPCID

6A: PBPA Medication Tiers

6B: Recommendations by College of Pharmacy

Materials included in agenda packet; presented by Dr. Graham. The PBPA table will be revised to include both generic and brand name consistently.

Dr. Meece moved to approve as submitted; second by Dr. McNeill.

ACTION: MOTION CARRIED.

AGENDA ITEM No. 7: **REVIEW & DISCUSS PROSPECTIVE DRUG UTILIZATION UPDATE FOR NEW FISCAL AGENT (EDS) – PART IV**

7A: High Dose Alert
7B: Therapeutic Duplication
7C: Ingredient Duplication
7D: Under Use and Low Dose

Material included in agenda packet, presented by Dr. Gorman. Dr. McNeill asked about low dose alerts becoming a problem. Some low doses may need to be adjusted if they become problematic. Dr. Crenshaw asked about ACE Inhibitors and ARB's being prescribed together and if that would cause a problem with duplication therapy? All of these alerts will be watched very closely after start up of EDS and can be changed if necessary.

ACTION: NONE REQUIRED.

AGENDA ITEM No. 8: **REVIEW & DISCUSS UTILIZATION OF GABAPENTIN**

8A: Drug Information
8B: Oklahoma Medicaid Utilization

Material included in agenda packet, presented by Dr. McIlvain.

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 9: **REVIEW & DISCUSS UTILIZATION OF STADOL ®**

9A: Drug Information
9B: Oklahoma Medicaid Utilization

Material included in agenda packet, presented by Dr. Gorman.

ACTION: NONE REQUIRED.

AGENDA ITEM No. 10: **30-DAY NOTICE TO VOTE ON MOVING ADHD THERAPIES TO PRODUCT BASED PRIOR AUTHORIZATION**

Material included in agenda packet, presented by Dr. Nesser.

ACTION: NONE REQUIRED.

AGENDA ITEM No. 11: **FDA INFORMATION UPDATES**

11A: FDA Updates

Updates were included in agenda packet. Material presented by Dr. Graham.

ACTION: NONE REQUIRED.

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

12A: Utilization Review of Plavix™
12B: Utilization Review of Prozac™ Weekly
12C: Adding ADHD Therapies to PBPA
12D: Demo for New Secure Provider Website
12E: Quantity Limitations on Inhalers

ACTION: NONE REQUIRED.

Dr. Hollen requested a list of dates of reviews for SoonerCare Plus Formulary Changes in the next packet.

AGENDA ITEM No. 13: **ADJOURNMENT**

The meeting was declared adjourned.

The University of Oklahoma
College of Pharmacy

Pharmacy Management Consultants
ORI W-4403; PO Box 26901
Oklahoma City, OK 73190
(405)-271-9039

Memorandum

October 14, 2002

To: Nancy Nesser, DPh, JD
Pharmacy Director
Oklahoma Health Care Authority

Ron Graham, DPh
Operations Coordinator / DUR Manager
Pharmacy Management Consultants

Subject: DUR Board Recommendations from Meeting of **October 8, 2002**

Recommendation 1: Discussion and Vote on SoonerCare Plus Formulary Changes

- **Community Care HMO** – The Board voted approval on formulary change request as presented.
- **Prime Advantage** – The Board voted approval on formulary change request as presented.
- **UniCare** – The Board voted approval on formulary change request as presented.

Recommendation 2: Discussion and Vote on Tier Change and BID Dosing Without Prior Authorization for Axid™ and Pepcid™.

- The Board voted approval on the recommendation of the College of Pharmacy to move Axid from Tier 2 status to Tier 1 status. The Board also voted to approve twice daily dosing without prior authorization for nizatidine (Axid) and famotidine (Pepcid) as per attached.

Recommendations in Red

The College of Pharmacy recommends the following additions/**changes** to the current anti-ulcer guidelines:

Tier 1	Tier 2
Cimetidine (Tagamet)	Lansoprazole (Prevacid)
Ranitidine (Zantac)	Omeprazole (Prilosec)
Famotidine (Pepcid)	Rabeprazole (Aciphex)
Nizatidine (Axid)	Pantoprazole (Protonix)
	Esomeprazole (Nexium)

Dosages Currently Available Without Prior Authorization

Tier One	Tier Two
Ranitidine (Zantac) 150mg BID	
Cimetidine (Tagamet) 400mg BID	
Famotidine (Pepcid) 20mg QD	
Recommendations in Red	
Famotidine (Pepcid) 20mg BID	
Nizatidine (Axid) 150mg BID	

October 7, 2002

Dear DUR board members,

I am writing to express concern about current difficulties prescribing long acting stimulants to my patients. Prior authorization serves as a roadblock to efficient care of kids with ADHD. I have witnessed many cases of kids not getting medication because of these arbitrary restrictions (which of all psychotropic meds are imposed only on stimulant medications for some reason).

This makes no sense from a practical viewpoint. If a child misses second or third doses of medicine, they are likely to need more intensive services--sometimes even in-patient care. Also, extended release forms of these meds are usually cheaper than multiple doses of regular release forms. And extended release stimulants are probably less abusable than short acting ones. There are so many advantages to the once-a-day stimulants that the old ones are virtually obsolete.

I note the purpose of the DUR is to "improve patient outcomes by encouraging optimal drug use". If true, please eliminate this obstacle to that goal.

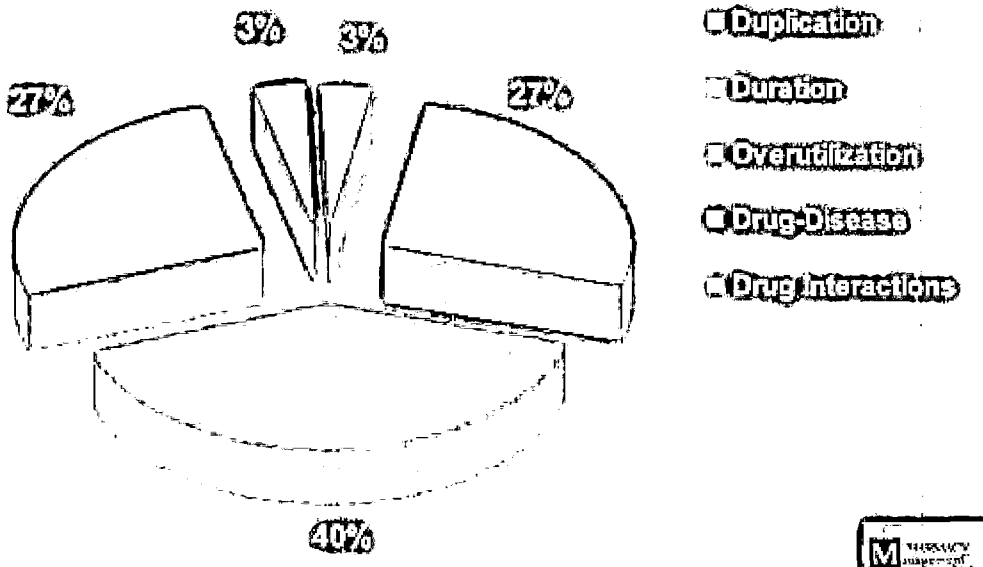
Sincerely,

Dean Martin MD
Tulsa, Oklahoma

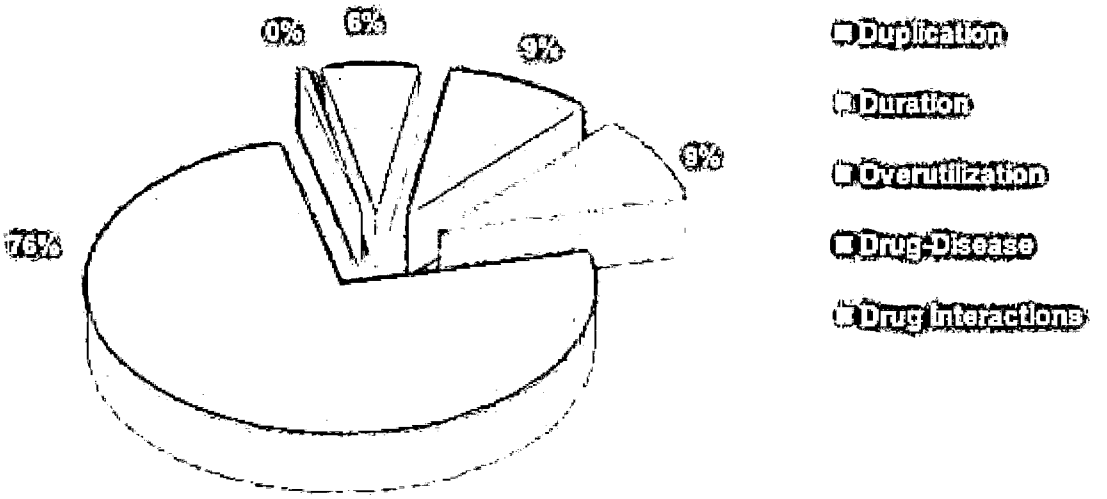
cc: Oklahoma Psychiatric Association
Oklahoma Child and Adolescent Psychiatry Council
Tulsa Psychiatric Association
Oklahoma Medical Association

APPENDIX B

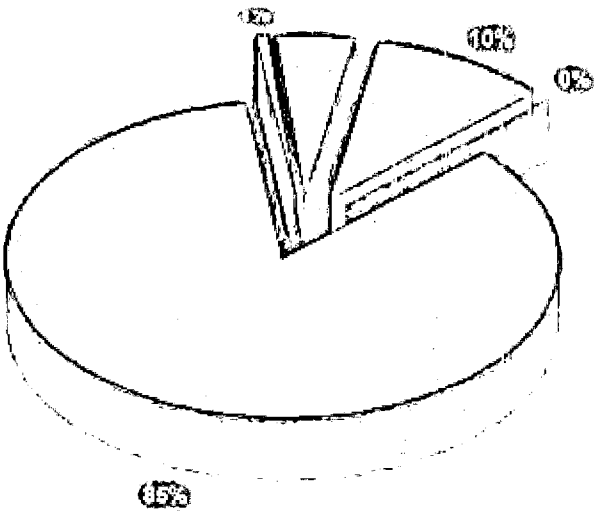
Oklahoma Medicaid RetroDUR Report
August 2002
Criteria: Asthma & COPD



Oklahoma Medicaid RetroDUR
Activity Report - Reviewed
August 2002



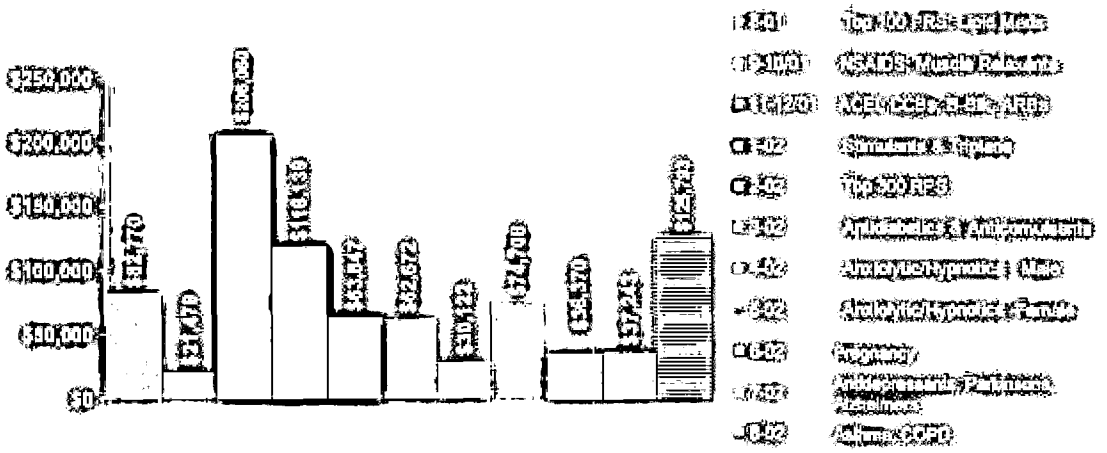
Oklahoma Medicaid RetroDUR Activity Report - Follow Up August 2002



Total Responses

Pharmacy 59/128 (46%)
Physician 60/116 (52%)

Oklahoma Medicaid RetroDUR Savings Report August 2001 - August 2002



Calendar YTD Savings
1-02/8-02 $548,895

Activity Audit for

October 01 2002 Through October 31 2002

Date	Antiulcers		Anxiolytic/ Hypnotics		Antihistamine		Growth Hormones		Stimulant		Smoking Cess.		Nsaids		ACE Inhibitors		HTN Combos		Calcium Channel Blockers		NPA		Misc		Daily Total
	approved	denied	approved	denied	approved	denied	approved	denied	approved	denied	approved	denied	approved	denied	approved	denied	approved	denied	approved	denied	approved	denied	approved	denied	
1	90	36	173	27	34	9	0	0	40	16	0	1	36	29	6	6	5	0	9	8	5	0	0	2	532
2	104	39	159	30	27	11	1	0	41	16	3	0	52	31	13	6	6	4	9	8	5	0	0	3	568
3	77	44	130	42	31	6	4	0	33	19	0	0	40	17	10	16	2	6	14	7	11	0	0	3	512
4	105	42	162	33	36	16	0	0	49	20	0	0	44	32	7	10	4	2	8	16	8	0	0	4	598
5	16	10	48	17	4	5	0	0	9	3	0	0	8	8	3	2	2	1	3	1	0	0	0	2	142
6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7	47	18	62	24	16	8	1	0	18	13	0	0	17	15	3	6	2	1	5	7	5	0	0	0	268
8	83	41	109	33	23	16	0	0	27	22	1	0	34	30	8	13	3	3	9	11	4	0	0	3	473
9	45	24	114	29	25	8	0	0	26	16	1	0	31	18	6	5	1	0	10	5	9	0	0	1	374
10	61	30	98	29	20	6	0	0	43	14	0	0	37	19	8	5	3	5	13	11	5	0	0	2	409
11	65	39	98	25	27	13	1	0	29	11	0	0	27	24	7	15	1	2	5	5	3	0	0	1	398
12	16	8	45	14	5	4	0	0	15	7	0	0	7	9	5	5	0	0	1	6	1	0	0	0	148
13	3	1	3	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	8
14	19	8	79	13	5	4	0	0	6	6	0	0	7	7	3	4	1	1	1	3	1	0	0	2	170
15	77	37	124	34	26	10		0	42	19	1	0	19	25	8	11	3	0	10	15	16	0	0	5	483
16	62	34	122	22	23	10	0	0	37	17	2	0	29	26	7	10		3	11	17	5	0	0	2	440
17	57	33	132	23	23	15	3	0	44	8	1	0	29	31	4	13	4	5	5	8	4	0	0	2	444
18	40	24	97	32	16	8	0	0	41	14	0	0	11	15	3	6	1	4	6	4	5	0	0	4	331
19	16	7	29	9	7	5	0	0	12	2	0	0	5	6	0	5	1	0	4	1	1	0	0	1	111
20	6	0	5	0	3	0	0	0	3	0	0	0	1	0	0	0	0	0	2	1	0	0	0	0	21
21	31	14	60	16	13	4	0	0	22	7	0	0	16	10	1	5	1	2	4	4	9	0	0	1	220
22	45	32	96	19	24	7	0	0	32	16	0	0	28	26	5	1	2	3	8	6	7	0	0	0	357
23	51	27	117	34	12	5	1	0	30	14	0	0	35	20	8	6	3	2	6	6	5	0	0	6	388
24	52	23	134	24	13	7	0	0	30	11	0	0	21	13	6	10	4	2	11	11	5	0	0	3	380
25	25	29	80	12	15	5	2	0	28	9	0	0	8	15	3	6	3	1	5	2	3	0	0	2	253
26	17	12	42	10	10	3	0	0	16	5	0	0	14	6	1	2	1	0	3	2	0	0	0		145
27	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
28	25	19	51	16	9	5	0	0	21	5	0	0	10	5	3	4	2	2	7	4	3	0	0	0	191
29	40	31	95	28	25	8	0	0	40	10	0	0	16	18	3	6	6	2		4	7	0	0	0	343
30	36	27	94	20	24	8	0	0	30	10	0	0	19	28	4	8	4	1		5	2	0	0	2	326
31	41	30	123	22	18	10	2	0	23	22	2	0	29	19	2	10	2				11	0	0	3	387

Activity Audit for

October 01 2002 Through October 31 2002

Date	Antiulcers approved	Antiulcers denied	Anxiolytic/ Hypnotics approved	Anxiolytic/ Hypnotics denied	Antihistamine approved	Antihistamine denied	Growth Hormones approved	Growth Hormones denied	Stimulant approved	Stimulant denied	Smoking Cess. approved	Smoking Cess. denied	Nsaids approved	Nsaids denied	ACE Inhibitors approved	ACE Inhibitors denied	HTN Combos approved	HTN Combos denied	Calcium Channel Blockers approved	Calcium Channel Blockers denied	NPA approved	NPA denied	Misc approved	Misc denied	Daily Total
Approved	1352		2681		514		16		787		11		631		137		68		183		140		0		
Denied		719		637		216		0		332		1		502		196		53		189		0		55	
Average Length of Approvals in Days	138		122		120		164		351		92		349		340		339		343		0		0		

Smoking Cessation		
	4 PA's for Zyban	11 Total PA's Approved
	7 PA's for Nicotine Patch	11 Unique RID's

Changes to existing PA's	496
Total (Previous Year)	7957

Monthly Totals

	Number	Percent of Total
Approved	6536	57.91%
Additional PA's	3	0.03%
SUPER PA's	246	2.18%
Emergency PA's	4	0.04%
Duplicates	33	0.29%
Incompletes	1535	13.60%
Denied *	2929	25.95%
Total	11286	100.00%

Daily Average of 403.07 for 31 Days

*** Denial Codes**

762 = Lack of clinical informatio	36.87%
763 = Medication not eligible	1.78%
764 = Existing PA	38.07%
772 = Not qualified for requested Tier	12.94%

SUPER PA's

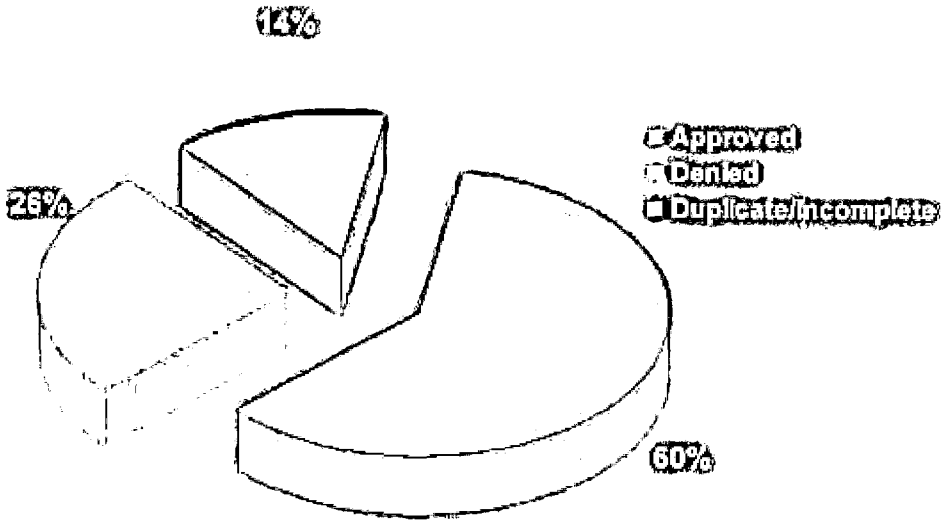
Early Refill Attempts	21200
Dosing Change	177
lost/stolen/broke	20
Other	29
wrong DS	20

Changes to existing PA's: Backdates, changing units, end dates, etc.

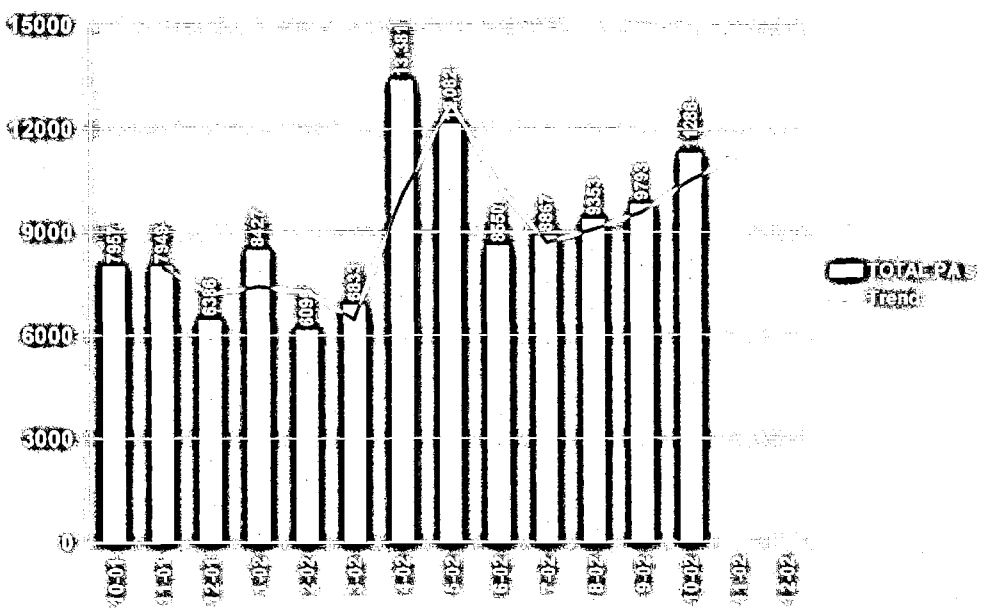
Additional PA's: Done by the help desk (doctor letter responses, PA ran for the wrong person)

Incompletes: Missing necessary information (NDC, SIG, Diagnosis, etc.)

PRIOR AUTHORIZATION ACTIVITY REPORT
October 2002



PRIOR AUTHORIZATION REPORT
October 2001 - October 2002

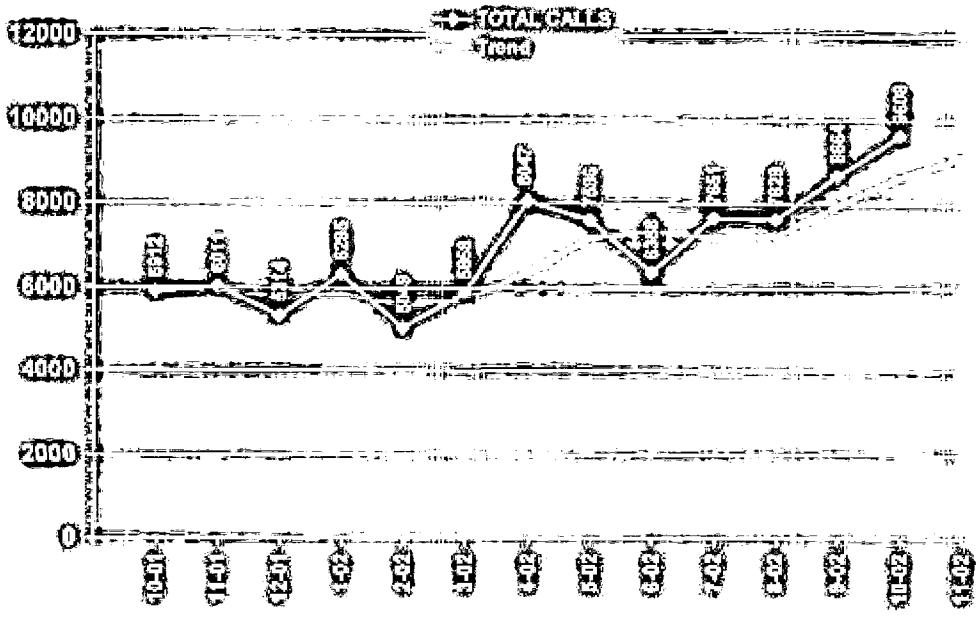


CALL VOLUME - OCTOBER 2002

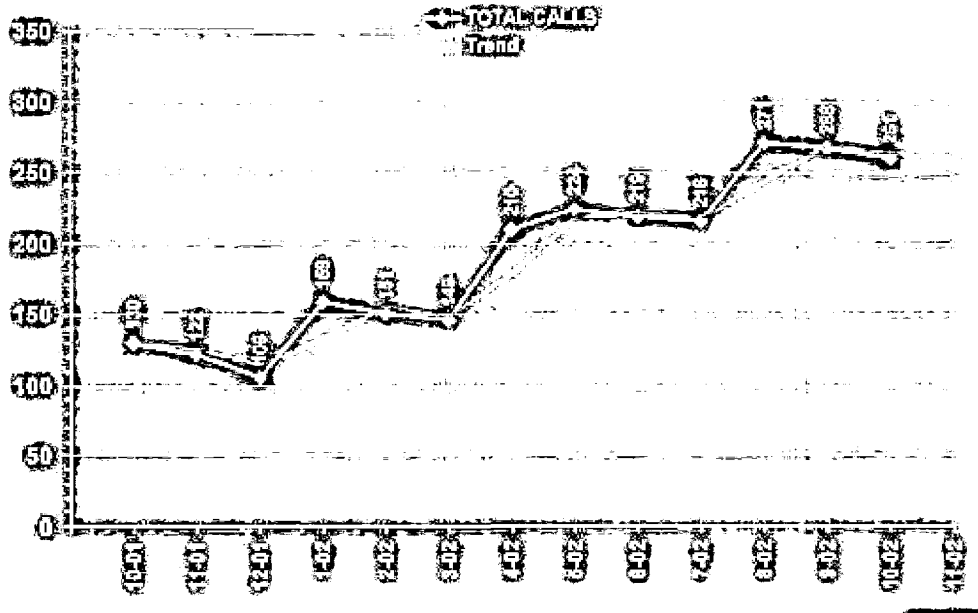
	CALLER					ISSUE					TYPE OF CALL								RE[illegible]OT		
Oct-02	Call Volume	Physician	Pharmacies	Clients	Other	Eligibility	Claims	PA Issue	SMAC	Other	Regular	Callback	Trans-RPh	Trans-Sup	Proactive	ProDUR	Other	Resolved	H.D. PA	PA unit	Other
1	477	10	407	32	28	136	233	90	8	18	450	10	0	0	5	10	2	471	6	0	0
2	447	11	353	28	55	103	178	147	0	22	388	36	0	2	5	13	3	443	4	0	0
3	389	10	334	28	17	71	197	96	1	24	368	8	0	0	1	7	5	386	3	0	0
4	428	16	330	35	45	93	172	141	0	20	380	28	1	0	7	6	4	421	5	0	0
5	50	1	47	2	0	12	17	19	0	2	49	0	0	0	0	1	0	50	0	0	0
6	9	0	9	0	0	4	4	1	0	0	9	0	0	0	0	0	0	9	0	0	0
7	387	9	324	36	18	88	173	97	0	29	369	5	2	0	0	8	3	385	2	0	0
8	367	10	287	20	48	87	152	107	0	21	332	21	0	0	8	3	3	367	0	0	0
9	364	13	298	34	21	53	153	128	0	30	345	9	0	0	2	6	2	359	5	0	0
10	374	8	289	21	42	94	163	139	0	28	320	31	0	1	9	9	4	371	3	0	0
11	365	14	298	12	31	66	183	87	0	19	328	19	1	3	0	2	2	350	5	0	0
12	55	0	49	1	5	5	46	3	0	1	50	1	0	0	1	3	0	54	1	0	0
13	5	0	5	0	0	0	5	0	0	0	3	2	0	0	0	0	0	5	0	0	0
14	359	10	277	25	35	73	125	129	0	35	313	27	0	0	10	6	3	357	2	0	0
15	402	15	334	25	28	92	155	133	0	22	371	21	0	0	1	7	2	401	1	0	0
16	370	17	296	24	33	61	164	117	0	28	327	31	0	0	2	7	3	369	1	0	0
17	370	8	314	21	27	70	167	102	0	25	342	14	0	1	3	6	4	367	3	0	0
18	301	12	239	21	29	67	127	85	0	22	264	18	1	1	0	12	5	299	2	0	0
19	112	1	108	2	1	78	29	4	0	1	107	5	0	0	0	0	0	110	2	0	0
20	198	0	5	0	193	2	2	14	0	180	4	3	0	0	190	0	4	198	0	0	0
21	369	15	308	19	27	91	122	126	0	30	337	24	0	1	1	4	2	369	0	0	0
22	436	11	305	53	52	73	160	115	0	79	342	32	0	0	52	4	6	435	1	0	0
23	415	10	279	22	95	75	186	77	0	97	311	6	1	0	82	12	3	411	4	0	0
24	363	9	256	40	58	68	146	82	0	67	301	4	1	0	47	6	4	362	1	0	0
25	365	9	237	32	87	84	125	64	4	88	283	10	0	0	64	5	5	362	3	0	0
26	40	0	39	1	0	21	13	6	0	0	40	0	0	0	0	0	0	40	0	0	0
27	279	0	6	2	271	2	2	1	0	274	5	0	0	0	274	0	0	279	0	0	0
28	328	7	243	22	56	72	138	88	0	30	274	35	2	0	2	8	7	327	1	0	0
29	392	8	255	27	91	82	145	82	0	83	296	26	0	0	59	5	3	389	3	0	0
30	318	9	261	32	16	83	141	93	0	21	303	6	0	0	1	6	2	314	4	0	0
31	486	7	231	26	219	76	119	84	0	205	264	23	1	0	190	5	3	483	3	0	0
	8608	261	7031	647	1627	1930	3718	2454	5	1501	7878	455	10	9	1015	159	84		65	0	0
	100.00%	2.72%	73.18%	6.73%	16.93%	20.09%	38.70%	25.54%	0.05%	15.62%	81.99%	4.74%	0.10%	0.09%	10.57%	1.65%	0.87%		0.68%	0.00%	0.00%

Survey dates: 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 31

CALL VOLUME MONTHLY REPORT
October 2001 - October 2002

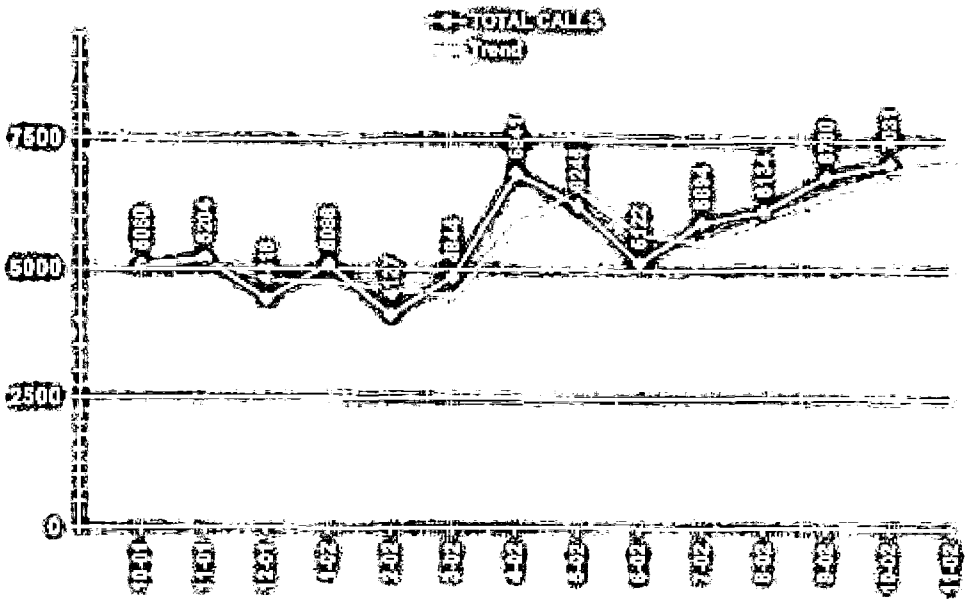


PHYSICIAN CALL VOLUME MONTHLY REPORT
October 2001 - October 2002

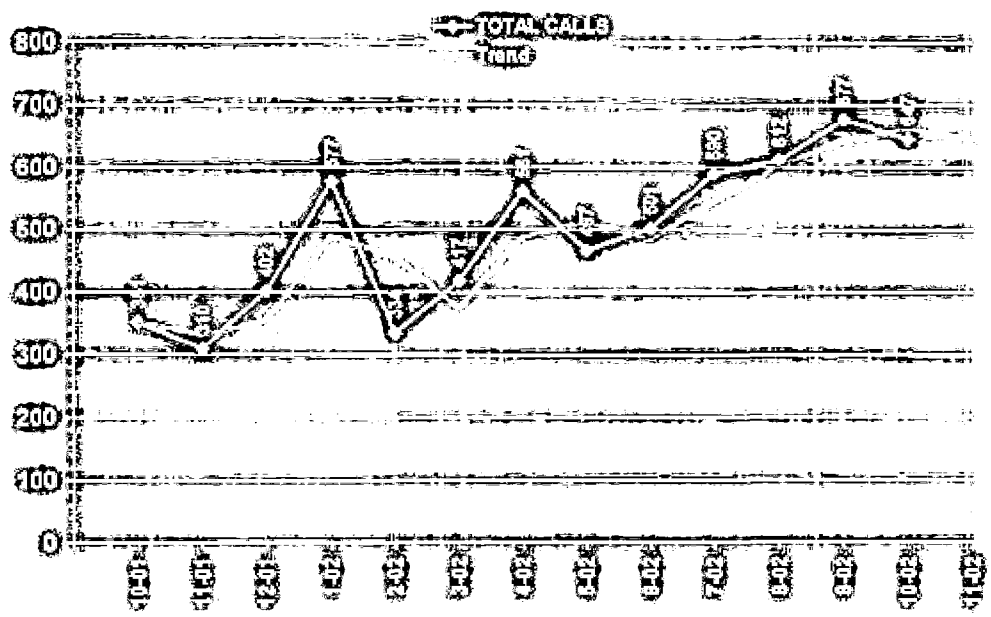


OUCOP-00039971

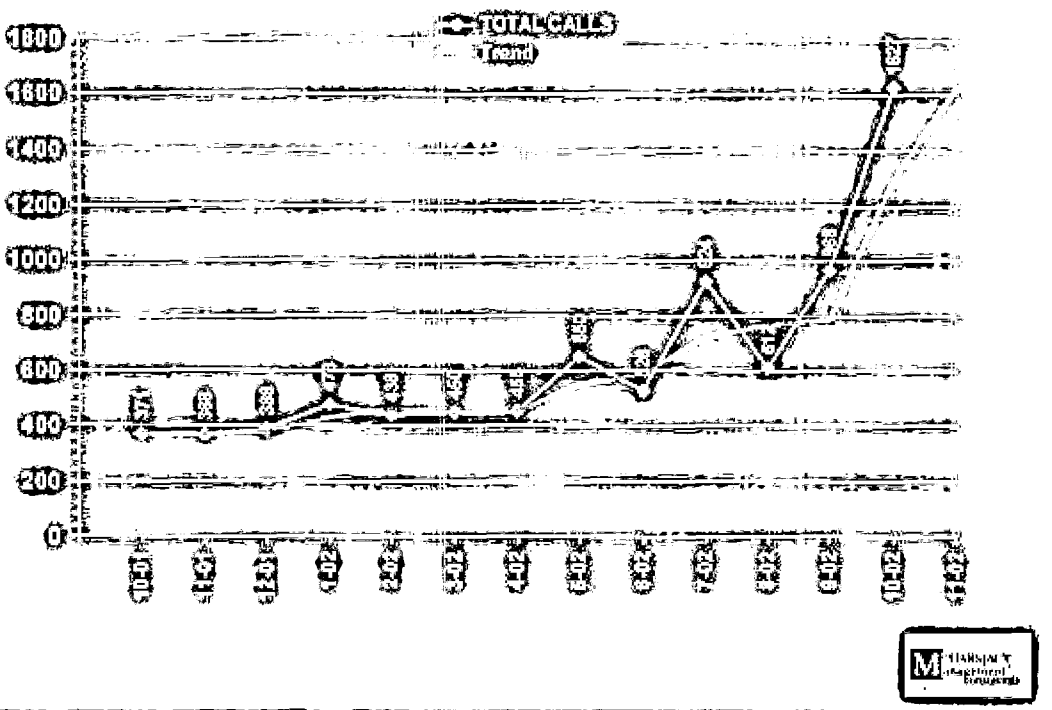
PHARMACY CALL VOLUME MONTHLY REPORT
October 2001 - October 2002



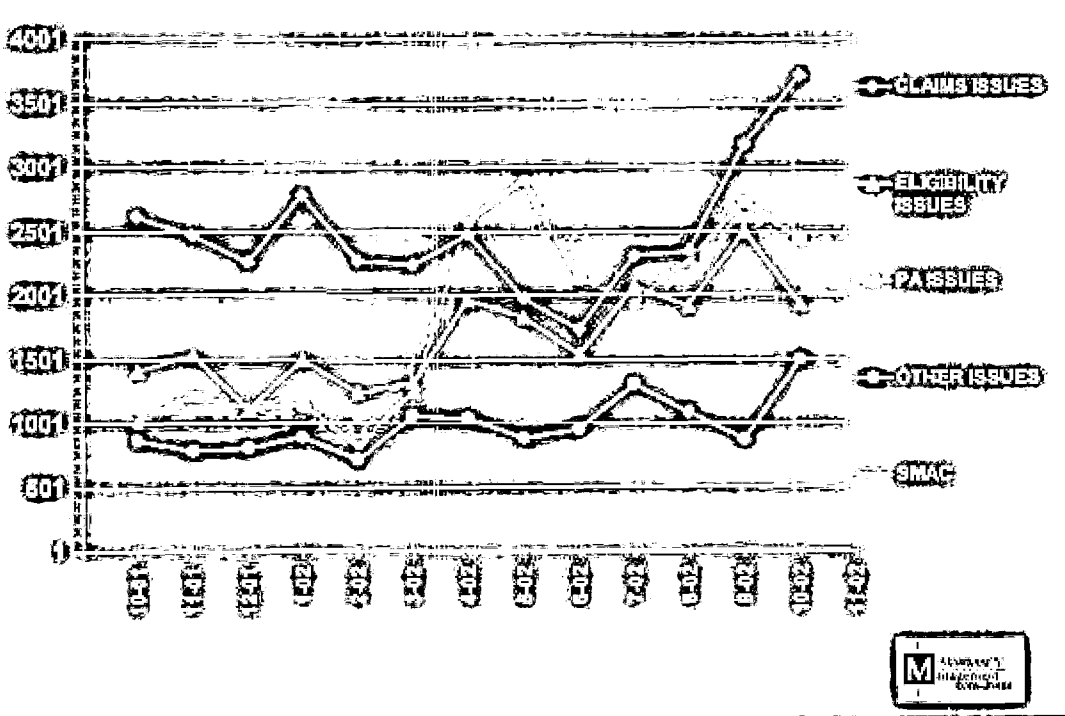
CLIENT CALL VOLUME MONTHLY REPORT
October 2001 - October 2002



OTHER CALL VOLUME MONTHLY REPORT
October 2001 - October 2002



CALL VOLUME ISSUES
October 2001 - October 2002



APPENDIX C

Adding ADHD Treatments to the Product Based Prior Authorization Program

Treatments for ADHD are typically classified as stimulant or anorexiant medications. For this reason, OHCA has considered these drugs to be in the optional coverage category of the Medicaid pharmacy benefit.

Because these drugs require prior authorization, the name of each drug has been listed in the Oklahoma Administrative Code with the requirements for obtaining prior authorization. In the past 18 months, at least five new products in this class have been brought to market. Each new product has required the engagement of the rule-change process which starts with the Drug Utilization Review Board and ends with legislative and gubernatorial approval.

This lengthy process has the potential to delay the availability of treatment for Medicaid clients and creates confusion among providers. By moving the medications used to treat ADHD into the Product Based Prior Authorization program, the process of adding new products into the program would be taken out of the rule-making arena.

No new restrictions are being sought. The products would continue to be available under the current guidelines. Currently, the medications used to treat ADHD are sorted into three tiers. The first tier includes brand and generic versions of immediate and sustained release formulations of methylphenidate and dextroamphetamine as well as the immediate release Adderall products. The second tier of products includes the once daily dosing products such as Concerta, Metadate CD, Ritalin LA and Adderall XR. Additionally, Focalin, the dextrorotary isomer of methylphenidate is also available in this tier. The third tier includes Desoxyn (methamphetamine) and Cylert (pemoline). These drugs are known to have more adverse affects than those medications in the other two tiers.

Drugs in the second and third tiers require prior authorization for all ages and require a diagnosis of ADHD or narcolepsy. First tier drugs are available to clients under the age of 21 without a prior authorization. First tier drugs require prior authorization for adults. Second tier drugs require a trial of a first tier drug and third tier drugs require trials with two first tier products.

Financial Impact/Savings Estimate Statement

In compliance with 63 O.S. § 5030.5(E), OHCA is required to prepare and release an estimated savings statement. OHCA does not expect savings to accrue from this administrative action. The products which are currently available will continue to be available under identical guidelines.

APPENDIX D

Prospective Drug Utilization Review Update

Oklahoma Medicaid
November 2002

Drug Age Precaution Modules
Current Recommended Criteria

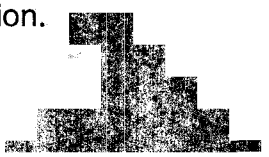
Based on current programming capabilities, the recommended criteria for the Drug Age – Geriatric Precautions will not be feasible. The following lists the previously proposed criteria for both Drug Age Precaution modules.

Drug Age – Pediatric Precautions (PD)

1. Proposed claims review for recipients less than 12 years of age.
2. FDB assigned severity levels for this module.

Severity Level	Description
1	an absolute contraindication
2	a relative contraindication
3	no studies have been done but warnings exist

3. State Severity Rankings.
   - Level 1 – Suspend with pharmacist override option.
   - Level 2 – Pay and Educate.
   - Level 3 – Pay and Report.
4. Expected implementation date: April 9, 2003.



Drug Age – Geriatric Precautions (GR)

1. Proposed claims review for recipients greater than 65 years of age.
2. FDB assigned severity levels for this module.

Severity Level	Description
1	contraindication
2	precaution

3. State Severity Rankings.
   - Level 1 – Pay and Educate.
   - Level 2 – Pay and Report.
4. Expected implementation date: April 9, 2003.

Problem with current criteria due to inability to have separate State Severity Rankings for each module.

Options

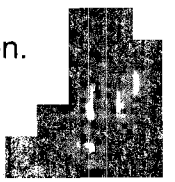
1. Set both modules to same State Severity Ranking.
2. Turn off one of the modules.
3. Set Geriatric to higher age for review.
4. Only activate certain medications within module.

New Recommended Criteria

Based on the previous options, the following recommendations are made (changes in red):

Drug Age – Pediatric Precautions (PD)

1. Proposed claims review for recipients less than 12 years of age.
2. FDB assigned severity levels for this module.
3. State Severity Rankings.
   - Level 1 – Suspend with pharmacist override option.
   - Level 2 – Pay and Educate.
   - Level 3 – Pay and Report.
4. Expected implementation date: April 9, 2003.



Drug Age – Geriatric Precautions (GR)

1. Proposed claims review for recipients greater than 75 years of age.
2. See table 1 for list of active medications.
3. FDB assigned severity levels for this module.
4. State Severity Rankings.
   - Level 1 – Suspend with pharmacist override option.
   - Level 2 – Pay and Educate.
5. Expected implementation date: April 9, 2003.

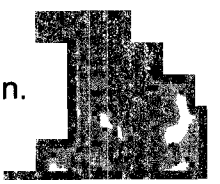


Table 1

Drug Age – Geriatric Precautions Criteria

Severity Level 1 – All Active

Amobarbital and combinations
Butabarbital and combinations
Danazol
Ergotamine combination (Ergocaff)
Methocarbamol injection
Naratriptan HCl
Pentobarbital and combinations
Secobarbital and combinations

Severity Level 2

Alprazolam
Amitriptyline and combinations
Belladonna alkaloids/Phenobarbital
Butalbital
Carisoprodol and combinations
Chlordiazepoxide and combinations
Chlorpropamide
Chlorzoxazone
Clonidine
Cyclobenzaprine
Diazepam
Dicyclomine
Digoxin
Diphenhydramine
Dipyridamole
Disopyramide
Doxepin
Ergot Mesyloids and combinations
Flurazepam
Hydroxyzine
Hyoscyamine
Indomethacin
Lorazepam
Meperidine
Mephobarbital
Meprobamate
Metaxalone
Methocarbamol Oral
Methyldopa and combinations
Oxazepam
Oxybutynin
Pentazocine

Phenylbutazone
Promethazine
Propantheline and combinations
Propoxyphene and combinations
Reserpine and combinations
Temazepam
Triazolam

APPENDIX E

Oral Transmucosal Fentanyl Citrate (Actiq®)

Use in the Oklahoma Medicaid Population

General Information

- Fentanyl lozenge on a stick
- Indication: the management of breakthrough cancer pain in patients who are already tolerant to opioid therapy
- Rapid onset, short duration of action
- Metabolized in the liver
- Precautions: chronic pulmonary disease, head injury & increased intracranial pressure, bradyarrhythmia, hepatic or renal disease; pregnancy category C
- Drug interactions: metabolized by cytochrome P450 3A4; may need to reduce Actiq® dose if given to patients receiving macrolide antibiotics, azole antifungals, or protease inhibitors; may need to increase Actiq® dose if given to patients receiving phenytoin, carbamazepine, rifabutin, or rifampin; risk of serotonin syndrome if given with Meridia® (sibutramine); not recommended for use in patients who have received MAO inhibitors within 14 days.

Special Considerations

- "Black box" warning in package labeling:

PHYSICIANS AND OTHER HEALTHCARE PROVIDERS MUST BECOME FAMILIAR WITH THE IMPORTANT WARNINGS IN THIS LABEL.

***Actiq* is indicated only for the management of breakthrough cancer pain in patients with malignancies who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain.** Patients considered opioid tolerant are those who are taking at least 60 mg morphine/day, 50 mcg transdermal fentanyl/hour, or an equianalgesic dose of another opioid for a week or longer.

Because life-threatening hypoventilation could occur at any dose in patients not taking chronic opiates, *Actiq* is contraindicated in the management of acute or postoperative pain. This product **must not** be used in opioid non-tolerant patients.

Actiq is intended to be used only in the care of cancer patients and only by oncologists and pain specialists who are knowledgeable of and skilled in the use of Schedule II opioids to treat cancer pain.

Patients and their caregivers must be instructed that Actiq contains a medicine in an amount which can be fatal to a child. Patients and their caregivers must be instructed to keep all units out of the reach of children and to discard open units properly. (See Information for Patients and Their Caregivers for disposal instructions).

Dosing should always start at the lowest dose, 200 mcg, and then titrate up

Pediatric use: dosing and safety have not been established below the age of 16 years

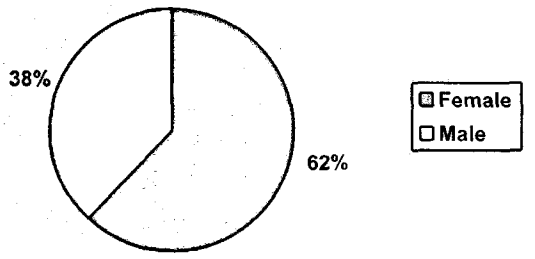
Actiq® Use in Oklahoma Medicaid Population
July 2001 – June 2002

General Usage

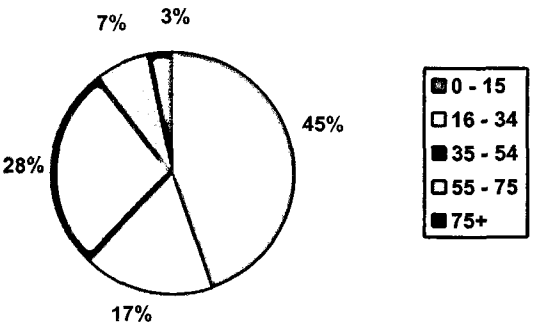
- Total paid **$56,173.56**
- Total number of clients using Actiq® ..... **29 clients**
- Total number of Actiq® claims ..... **79 claims**
- Average dollars spent per client per year **$1,937/client**
- Cost per day of treatment **$55.45/day**
- Average number of Actiq® claims per client ..... **2.72 claims/client**
- Average days per claim ..... **12.82 days/claim**
- Average number of days of treatment per client per year ..... **34.9 days/client**

Demographics

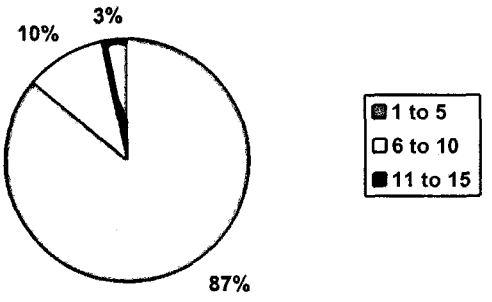
Clients' Gender



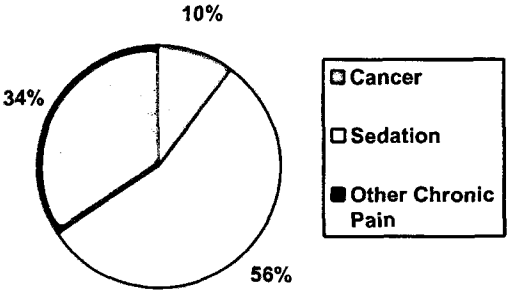
Clients' Age in Years



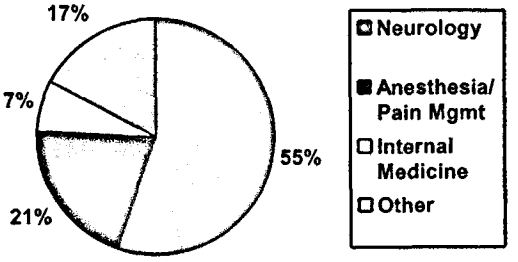
Claims per Client



Actiq Indication



Actiq Prescriber Specialty



Details of Actiq® Usage

Sex	Age	Diagnosis	# Actiq fills	# Actiq units	Days supply	$ Cost	Opioid Tolerant ?	200mcg start dose?	Dr.
F	52	Cancer – breast	9	1630	218	26,645.03	N (?)	N (?)	Pain Management
F	64	Cancer – bladder	1	24	15	301.74	Y	N	Radiologic Oncology
M	38	Cancer – lung, bladder	1	24	4	299.74	Y	N	Radiologic Oncology
F	51	Chronic pain - back?	12	2310	257	18,110.72	Y	Y	Anesthesiology
F	36	Chronic pain - back?	9	246	131	3,464.59	Y	N	Anesthesiology
F	76	Chronic pain - arthritis?	9	288	72	1,951.72	N (?)	Y	Family Practice
F	47	Chronic pain - painful skin ulcers?	3	156	62	1,251.84	Y	Y	Psychiatry/ Pain Management
F	33	Chronic pain - back?	4	84	66	964.72	Y	N	Anesthesiology
M	33	Chronic pain - HIV?	5	120	22	839.36	Y	Y	Infectious Disease
F	43	Chronic pain - ?	1	60	30	831.50	Y	Y	Physical Medicine
F	37	Chronic pain - Trigeminal Neuralgia?	2	96	24	735.07	N	Y	Pain Management
F	42	Chronic pain - ?	2	48	10	335.18	Y	Y	Internal Medicine
F	75	Chronic pain - back pain?	1	24	24	216.23	Y	N	Anesthesiology
F	12	Sedation	2	2	2	22.08	N	Y	Neurology
M	3	Sedation	1	1	1	11.04	N	Y	Neurology
M	3	Sedation	1	2	1	?	N	Y	Neurology
M	5	Sedation	1	1	1	10.69	N	Y	Neurology
F	9	Sedation	1	2	1	17.94	N	Y	Neurology
M	9	Sedation	1	2	1	17.94	N	Y	Neurology
M	1	Sedation	1	2	1	17.44	N	Y	Neurology
F	16	Sedation	1	3	1	24.83	N	Y	Neurology
F	5	Sedation	1	1	1	?	N	Y	Neurology

Sex	Age	Diagnosis	# Actiq fills	# Actiq units	Days supply	$ Cost	Opioid Tolerant ?	200mcg start dose?	Dr
M	10	Sedation	1	2	1	17.22	N	Y	Neurology
M	6	Sedation	2	2	2	22.08	N	Y	Neurology
F	4	Sedation	1	2	1	17.94	N	Y	Neurol
M	2	Sedation	1	2	1	17.94	N	Y	
M	2	Sedation	2	2	2	11.04 (?)	N	Y	
F	20	Sedation	1	2	30	17.94	N	Y	

	Yes = # (%) of Clients	= # (%) of Clients
Was Actiq® prescribed for an FDA approved indication?	3 (10.3%)	26 (89.7%)
Was the patient already opioid tolerant when he/she started using Actiq®?	10 (34.5%)	19 (65.5%)
Was the patient's age ≥ 16 years?	16 (55.2%)	13 (44.8%)
Was the first Actiq® dose 200 mcg?	23 (79.3%)	6 (20.7%)
Was the patient averaging 4 or fewer Actiq® units per day?	24 (82.8%)	5 (17.2%)

Actiq® Prescribing Problems: Use for Pre-Procedural Sedation

- 2 prescribers in the same practice prescribed Actiq® in combination with oral midazolam to 16 opioid-naïve patients, all but 3 of whom were under the age of 16
- Used Actiq® to replace fentanyl Oralets, which are no longer on the market
- Oral transmucosal fentanyl citrate lozenges-on-a-stick were developed by Anesta (now Cephalon), the same company that makes Actiq®, but they were originally called Fentanyl Oralets
- Oralets were developed as a pre-procedural sedative/anesthetic specifically for pediatric patients
- The lollipop format made the medication more acceptable to children and, it was hoped, avoided the necessity of giving injections.
- Oralets came in weaker strengths than Actiq®, with smaller dose increments:

Available Actiq®doses:	Oralet doses:
200 mcg	100 mcg
400 mcg	200 mcg
600 mcg	300 mcg
800 mcg	400 mcg
1200 mcg	
1600 mcg	

- Problems with the Oralets:
  - Nausea/vomiting: rates approached 50%; danger of aspiration if patient vomited while under anesthesia
  - Respiratory depression: required dedicated observer to watch patients constantly
  - Oralets are no longer available, although it does not appear that the FDA required their removal from the market

Actiq® Prescribing Problems: Use for Chronic Pain

- Problems seen with prescribing for off-label uses, to opioid-naïve patients, starting at higher doses than recommended, and using more units per day than recommended.

Conclusion & Recommendations:

- Letters with questionnaires will be sent to all Actiq® prescribers
- Letter will contain entire boxed warning, and will review safety information and recommendations from package labeling
- Questionnaires will inquire about patient's diagnosis, reason patient needed Actiq® rather than opioid tablet or capsule, prescriber's specialty, and whether patient was opioid tolerant when started Actiq®

APPENDIX F

Plavix® (clopidogrel) Utilization

November 2002

Mechanism of Action

Clopidogrel is a platelet aggregation inhibitor. Clopidogrel selectively inhibits adenosine diphosphate (ADP) from binding to its platelet receptor and the subsequent ADP-mediated activation of the glycoprotein GPIIb/IIIa complex. Clopidogrel irreverisably modifies the ADP receptor; therefore, the platelets are affected for their lifespan.

Indications and Usage

Clopidogrel is indicated for the reduction of atherosclerotic events as follows:

1. Recent MI, recent stroke or established peripheral arterial disease.
2. Acute Coronary Syndrome (unstable angina/non-Q-wave MI).

Off label Use

1. Adjunct to aspirin after coronary stent implantation.
2. Use with or without dalteparin to promote healing of refractory stasis ulcers.
3. To reduce the risk of recurrent stroke or other vascular events in patients that have experienced a Transient Ischemic Attack.

Adverse Reactions

The major adverse reactions seen with clopidogrel use are bleeding, abdominal pain, vomiting, dyspepsia, gastritis, upper respiratory infections, flu-like syndromes, and chest pain. Thrombotic thrombocytopenic purpura (TTP) has been reported even after a short exposure of less than 2 weeks. This particular reaction however has been rare.

Contraindications

The use of clopidogrel is contraindicated in those patients that are hypersensitive to the drug, or have active pathological bleeding such as peptic ulcer or intracranial hemorrhage.

Drug Interactions

Clopidogrel in high concentrations inhibits the P450 (2C9) enzyme. The metabolism of drugs such as phenytoin, tamoxifen, warfarin, torsemide, fluvastatin, and many NSAIDs could be affected.

Dosing

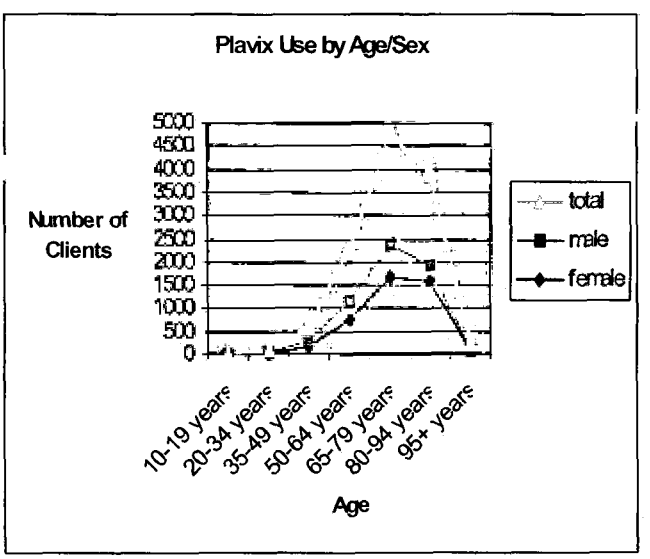
For patients with recent MI, stroke or peripheral vascular disease the approved dosing is 75mg daily. For Acute Coronary Syndrome, patients should receive a 300mg loading dose, then 75mg daily.

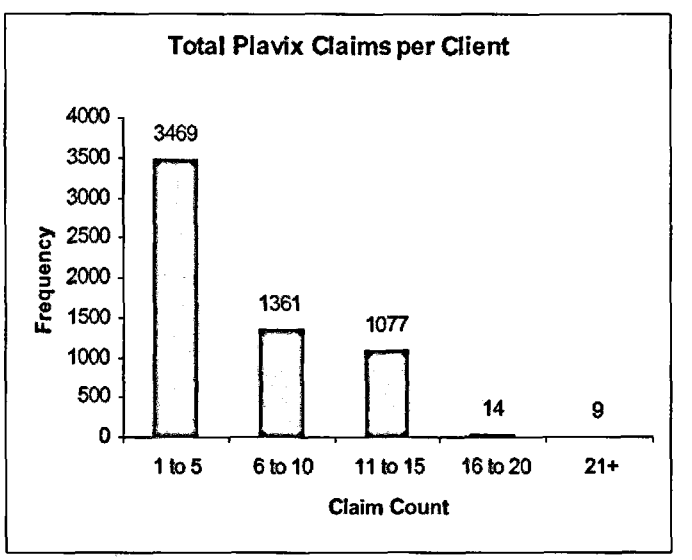
Utilization

Medicaid fee for service pharmacy claims were reviewed from July 2001 to June 2002.

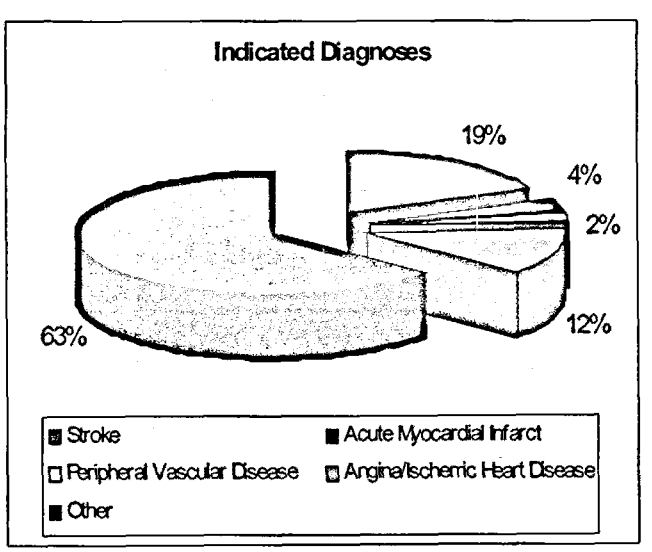
# of Claims	Total Units	Total Days	Units/ Day	Total $	Per Diem	Client Total	$/Client	$/Claim
32,430	1,090,063	32,430	1.01	$3,507,945.26	$3.29	5930	$591.56	$108.17

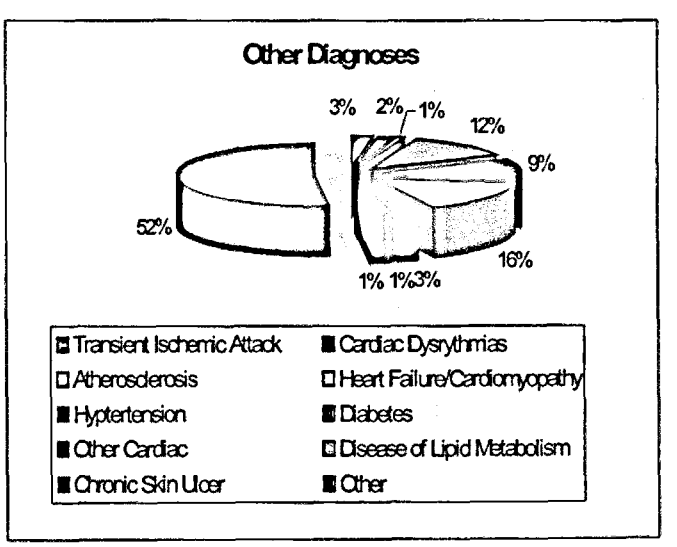
The pharmacy claims were reviewed to look at utilization by client age and sex as well as the number of claims per client. The peak age for both male and female clients is from 65 to 94 years of age. The majority of clients received 10 fills of clopidogrel or less for the year.





Medical claims for these clients were reviewed to investigate how the diagnoses compared with the approved indications. Of the 5930 clients identified, 2450 clients had diagnoses listed in the medical claims database.





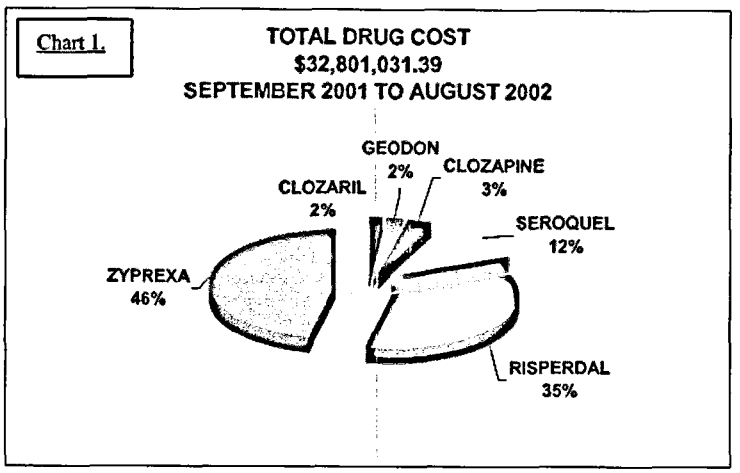
Conclusion

If the diagnosis information is to be accepted, the usage of clopidogrel that falls within FDA approved indications is approximately thirty-six percent. If off label uses are included, then the appropriate usage increases to approximately forty-one percent. There is not enough clear data in the medical claims database to ascertain if the remaining fifty-nine percent of the populace is receiving clopidogrel without indication. A large number of these patients have diagnoses of hypertension, heart failure, lipid disorders, and diabetes. All of these diagnoses are risk factors for acute myocardial infarction, stroke, and peripheral artery disease. At this point, no action to restrict the use of clopidogrel is recommended; however, utilization should be reviewed in the future.

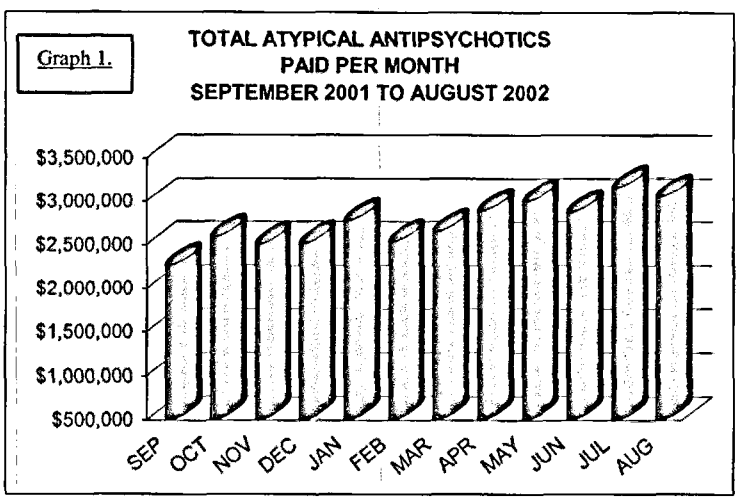
APPENDIX G

Atypical Antipsychotic Utilization in Oklahoma Medicaid

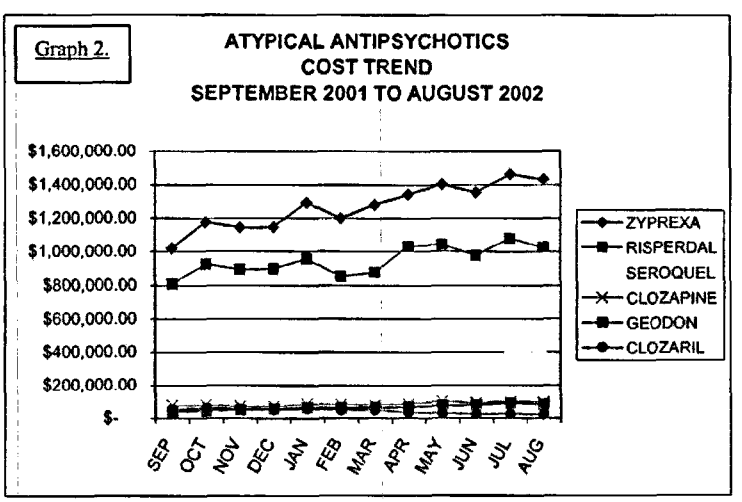
Chart 1.



Graph 1.

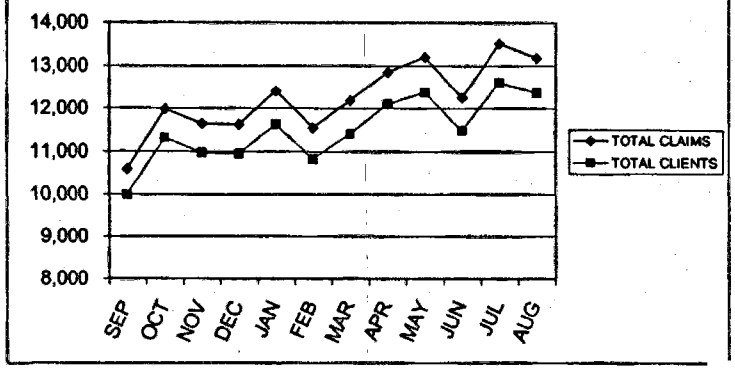


Graph 2.



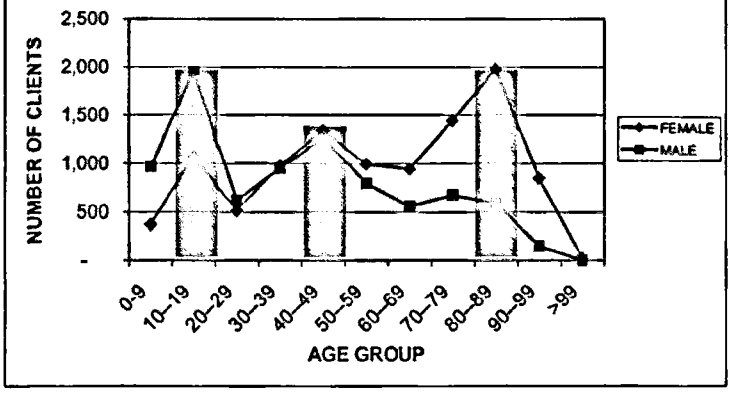
Graph 3.

NUMBER OF ATYPICAL ANTIPSYCHOTIC CLAIMS AND CLIENTS PER MONTH SEPTEMBER 2001 TO AUGUST 2002



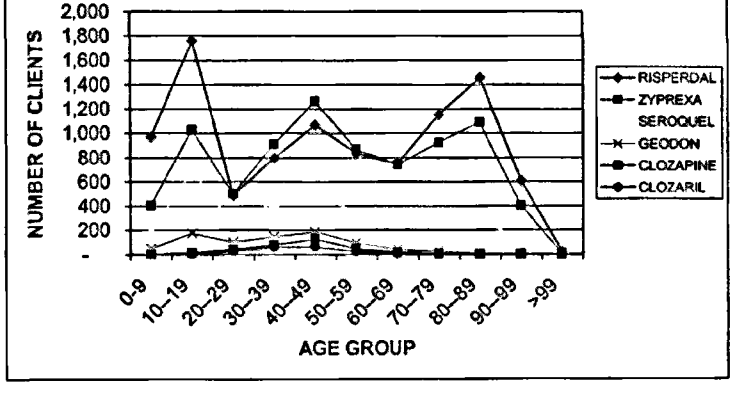
Graph 4.

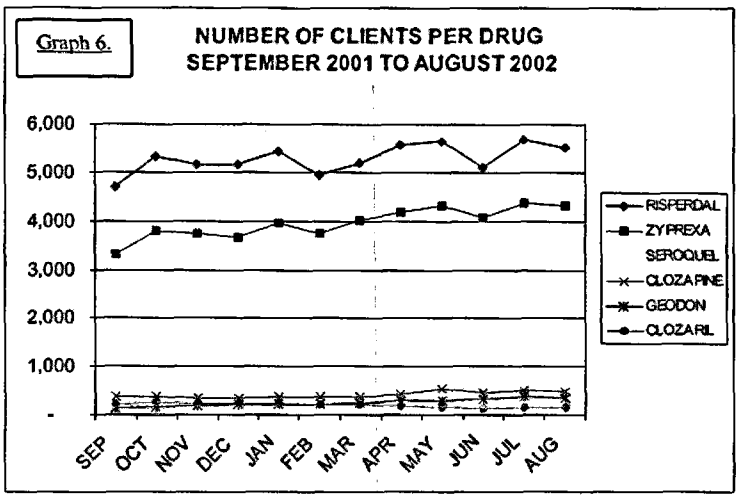
AGE DISTRIBUTION OF TOTAL CLIENTS SEPTEMBER 2001 TO AUGUST 2002

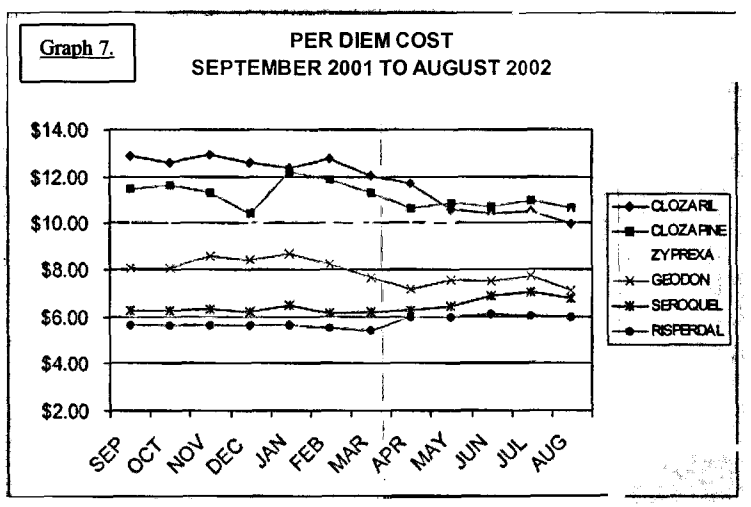


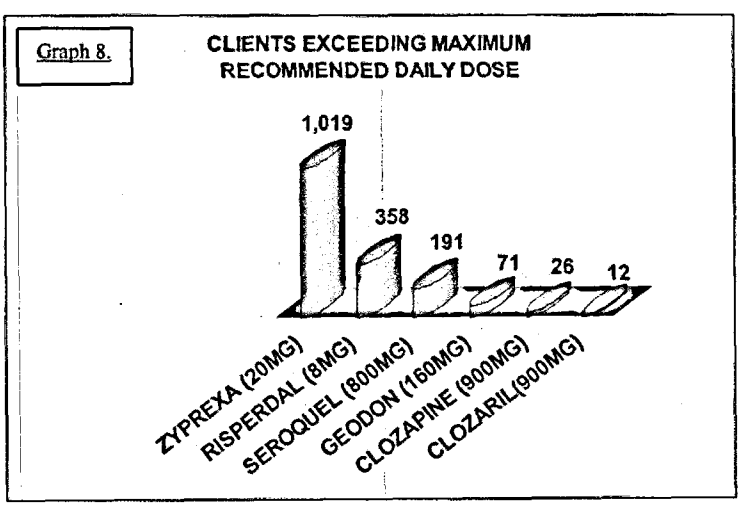
Graph 5.

AGE DISTRIUBUTION PER DRUG SEPTEMBER 2001 TO AUGUST 2002









The currently available atypical antipsychotics are clozapine (Clozaril®), ziprasidone (Geodon®), risperidone (Risperdal®), quetiapine (Seroquel®), and olanzapine (Zyprexa®).

Between September 1, 2001 and August 30, 2002 there were 147,027 atypical antipsychotic paid prescription claims at a cost of $32,801,031.39. Of this total, $15,264,117.07 was for Zyprexa®, $11,356,331.79 for Risperdal®, $3,917,319.31 for Seroquel®, $1,002,423.44 for clozapine, $755,864.84 for Geodon®, and $504,974.94 for Clozaril®. [See Chart 1.]

The majority of clients were in three age groups, 10-19, 40-49, and 80-89. [See Graph 4.] Furthermore, there are differences in utilization of atypical antipsychotics between the sexes. For male clients, the utilization is highest among the age group 10 to 19 years and inversely proportional to the increase in age. Conversely, the utilization increases with age for female clients and the age group 80 to 89 years has the highest utilization. [See Graph 4.]

The top 3 drugs based on the number of clients using each are risperidone, olanzapine, and quetiapine. [See Graph 5 & Graph 6.] These same three drugs also rank highest when considering the total amount paid for each. [See Chart 1 & Graph 2.] Additionally, risperidone has the lowest per diem cost and olanzapine has the highest per diem cost based on day supply indicated on paid claims. [See Graph 7.]

When the daily dose exceeds the recommended maximum dose, the development of EPS is more likely. A review of the data suggest there are many clients whose dose exceeds the recommended maximum as calculated by dividing total milligrams per prescription by day supply reported on prescription claims. [See Graph 8.]

In the past 12 month period, the monthly atypical antipsychotic expenditure has grown steadily from approximately $2.26 million to over $3 million. [See Graph 1.] The data suggests that the main reason for the continual increase in spending is most closely related to the number of clients utilizing atypical antipsychotics. [See Graph 3.]

APPENDIX H

October 30, 2002

Ms. Nancy Nesser, JD., D.Ph.
Pharmacy Director
Oklahoma Health Care Authority
4545 N. Lincoln Blvd, Suite 124
Oklahoma City, OK 73105

RE: CommunityCare SoonerCare Formulary Changes

Dear Ms. Nesser,

The following are proposed changes for the January 1, 2003 CommunityCare SoonerCare Formulary:

Add to existing language:

NARCOTIC ANALGESICS

Prior-Authorization required for amounts beyond quantities specified:

Oxycontin – Limited to 60 tablets per 30 days.

NON-NARCOTIC ANALGESICS

Prior-Authorization required for:	**Recommended Therapy:**
Ultracet	Tramadol

SELECTIVE SEROTONIN REUPTAKE INHIBITORS

Prior-Authorization required for:	**Recommended Therapy:**
Sarafem	fluoxetine

Please let me know if additional information is required to process this request for formulary change.

Sincerely,

Melanie Maxwell
Ancillary Services

Hand Delivered and Electronically

October 31, 2002

Oklahoma Health Care Authority
Drug Utilization Committee
Attn: Nancy Nesser, Pharmacy Program Director
4545 Lincoln Avenue, Suite 124
Oklahoma City, OK 73105

Dear Ms. Nesser:

Heartland Health Plan of Oklahoma (HHPO) respectfully requests the committee's approval of the enclosed recommended changes. If approved, Heartland Health Plan providers will be notified of the changes at least 30 days prior to the effective date.

1. Request prior authorization for Geodon.
   a. All members presently utilizing Geodon will be grandfathered indefinitely.
   b. Prior Authorization will be granted for any of the following:
      (1) Members who have a documented prior history of good response to Geodon.
      (2) Members who have a clinical issue or risk factor which necessitates use of Geodon.
      (3) Failure of an adequate trial of the maximum tolerable dosage of Risperdal or Seroquel. See Addendum.
      (4) Patients with a long history of treatment, resistant to standard treatment approaches; upon submission of appropriate clinical documentation.
2. Request prior authorization for Zyprexa.
   a. All members presently utilizing Zyprexa will be grandfathered indefinitely.
   b. Prior Authorization will be granted for any of the following:
      (1) Members who have a prior history of good response to Zyprexa.
      (2) Members who have a clinical issue or risk factor which necessitates use of Zyprexa.
      (3) Failure of an adequate trial of the maximum tolerable dosage of Risperdal or Seroquel. See Addendum.
      (4) Patients with a long history of treatment, resistant to standard treatment approaches; upon submission of appropriate clinical documentation.
3. Request removal of Augmentin XR 1000-62.5 tab; numerous other forms of Augmentin remain on formulary.
4. Request removal of Vfend: Sporonox, Lamasil, and Diflucan remain on the formulary.
5. Request prior authorization of Hepsera.
6. Request removal of Eligard Syringe; Lurpon remains on the formulary.
7. Request removal of Lofibra 67mg Capsule; gemfibrozil remains on the formulary.
8. Request removal of Altocor; Lovastatin remains on formulary.
9. Request removal of Avinza Capsule SA; other long and short acting morphine agents remain on the formulary.
10. Request removal of Axocet; other acetominophen/butalbital medications remain on the formulary.
11. Request removal of Lexapro; Celexa remains on the formulary. Present Lexapro users will be grandfathered indefinitely.
12. Request removal of Wellbutrin SR 200mg Tab SA; other forms of Wellbutrin remain on the formulary.
13. Request removal of Ritalin LA Capsule; other forms of short and long acting methylphenidate remain on the formulary.
14. Request removal of IB-Stat Oral Spray; generic anticholinergic medications remain on the formulary.
15. Request prior authorization of Zelnorm Tablet.

Should you have any questions or require additional information prior to the formal presentation of this to the November Drug Utilization Review Committee meeting, please contact Kenneth E. Joslyn, MD, MPH by e-mail at KenJ@schalleranderson.com or by telephone at (405) 552-6508.

Sincerely,

Kenneth E. Joslyn, MD, MPH
Associate Medical Director

Cc: Ron Graham

Heartland Health Plan of Oklahoma
Addendum to Request for Prior Authorization
For Geodon and Zyprexa.

Clarification of "adequate trial" and "maximum tolerated doses" mentioned in section 1-b-(3) and 2-b-(3)

Recommended adequate trial on a single atypical antipsychotic is 16 weeks. Clinical circumstances may dictate the need to add a second atypical antipsychotic or change to another atypical antipsychotic earlier than 16 weeks. Such changes will be approved upon submission of appropriate clinical justification for the change.

Maximum tolerable dosage is that maximum dose for which there is an absence of unwanted adverse effects that make the drug unacceptable *in the prescribing physician's opinion.* Unacceptable side effects warrant a change in therapy. Such changes will be approved upon submission of appropriate clinical justification for the change.

Heartland Health Plan of Oklahoma assembled a group of local academic and community based psychiatrists to develop a clinical decision process and a "Clinical Issue/Risk Factor Table" for use of atypical antipsychotics. These tools will be used as a basis of educational outreach to prescribing physicians and as guidelines for use in Prior Authorizing atypical antipsychotics.

UNICARE.

UNICARE Health Plan of Oklahoma
Outpatient Prescription Drug Formulary Amendment
Submission Date: 11/01/02

The following changes have been approved by the UNICARE Pharmacy and Therapeutics Committee

Brand and Generic Medications Added to Formulary	
Brand Name	**Generic Name**
Generic Augmentin	amoxicillin/clavulanate
Generic Ceftin	cefuroxime axetil
Concerta	methylphenidate ER
Cozaar	losartan
Generic Triphasil, generic Tri-Levlen	Enpresse
Generic Tricor	fenofibrate – micronized
	losartan/HCTZ
Generic Zestril, generic Prinivil	
Lotrel 10/20mg	amlodipine/benazepril
Generic Axid	nizatidine
Generic Nordette	Portia
Rebif	interferon β-1a
Generic Zanaflex	tizanidine hydrochloride
Zithromax TriPak	azithromycin

Brand Medications Removed from Formulary		
Brand Name	**Generic Name**	**Formulary Alternatives**
Accupril (brand only)**	quinapril	quinapril (generic)
Avapro	irbesartan	Cozaar (losartan), Hyzaar (losartan/HCTZ), diovan/HCT (valsartan/HCTZ)
Lotensin (brand only)**		benazepril (generic)
Metadate CD	methylphenidate CD	methylphenidate (generic)
Ritalin/SR	methylphenidate	methylphenidate (generic)
Zestril (brand only)	lisinopril/HCTZ	lisinopril (generic)
Zestoretic (brand only)	lisinopril	lisinopril/HCTZ (generic)
Multi source brand ADHD* stimulants with generic equivalents		Dextroamphetamine (generic), methylphenidate (generic)

*ADHD = Attention Deficit and Hyperactivity Disorder
**Upon availability of the generic equivalent

UNICARE.

Prior Authorization of Benefits Programs Added:

The purpose of these prior authorization of benefits programs is to ensure appropriate prescribing and member safety.

Lotronex

APPROVAL CRITERIA:

- Patient is female, AND
- Patient has a diagnosis of Irritable Bowel Syndrome (IBS) including diarrhea as the predominant symptom, AND
- Patient has SEVERE symptoms of IBS, AND
- Symptoms have persisted for > 6 months

Zelnorm

APPROVAL CRITERIA:

- Patient is female, AND
- Patient has a diagnosis of IBS including constipation as the predominant symptom, AND
- Patient has moderate to severe symptoms of IBS

10/10/02

APPENDIX I

Footnotes for
Recommended Adult Immunization Schedule, United States, 2002-2003

1. **Tetanus and diphtheria (Td)**—A primary series for adults is 3 doses: the first 2 doses given at least 4 weeks apart and the 3rd dose, 6-12 months after the second. Administer 1 dose if the person had received the primary series and the last vaccination was 10 years ago or longer. *MMWR* 1991; 40 (RR-10): 1-21. The ACP Task Force on Adult Immunization supports a second option: a single Td booster at age 50 years for persons who have completed the full pediatric series, including the teenage/young adult booster. *Guide for Adult Immunization*. 3rd ed. ACP 1994: 20.

2. **Influenza vaccination**—Medical indications: chronic disorders of the cardiovascular or pulmonary systems including asthma; chronic metabolic diseases including diabetes mellitus, renal dysfunction, hemoglobinopathies, immunosuppression (including immunosuppression caused by medications or by human immunodeficiency virus [HIV]), requiring regular medical follow-up or hospitalization during the preceding year; women who will be in the second or third trimester of pregnancy during the influenza season. Occupational indications: health-care workers. Other indications: residents of nursing homes and other long-term care facilities; persons likely to transmit influenza to persons at high-risk (in-home care givers to persons with medical indications, household contacts and out-of-home caregivers of children birth to 23 months of age, or children with asthma or other indicator conditions for influenza vaccination, household members and care givers of elderly and adults with high-risk conditions); and anyone who wishes to be vaccinated. *MMWR* 2002; 51 (RR-3): 1-31.

3. **Pneumococcal polysaccharide vaccination**—Medical indications: chronic disorders of the pulmonary system (excluding asthma), cardiovascular diseases, diabetes mellitus, chronic liver diseases including liver disease as a result of alcohol abuse (e.g., cirrhosis), chronic renal failure or nephrotic syndrome, functional or anatomic asplenia (e.g., sickle cell disease or splenectomy), immunosuppressive conditions (e.g., congenital immunodeficiency, HIV infection, leukemia, lymphoma, multiple myeloma, Hodgkins disease, generalized malignancy, organ or bone marrow transplantation), chemotherapy with alkylating agents, anti-metabolites, or long-term systemic corticosteroids. Geographic/other indications: Alaskan Natives and certain American Indian populations. Other indications: residents of nursing homes and other long-term care facilities. *MMWR* 1997; 47 (RR-8): 1-24.

4. **Revaccination with pneumococcal polysaccharide vaccine**—One time revaccination after 5 years for persons with chronic renal failure or nephrotic syndrome, functional or anatomic asplenia (e.g., sickle cell disease or splenectomy), immunosuppressive conditions (e.g., congenital immunodeficiency, HIV infection, leukemia, lymphoma, multiple myeloma, Hodgkins disease, generalized malignancy, organ or bone marrow transplantation), chemotherapy with alkylating agents, anti-metabolites, or long-term systemic corticosteroids. For persons 65 and older, one-time revaccination if they were vaccinated 5 or more years previously and were aged less than 65 years at the time of primary vaccination. *MMWR* 1997; 47 (RR-8): 1-24.

5. **Hepatitis B vaccination**—Medical indications: hemodialysis patients, patients who receive clotting-factor concentrates. Occupational indications: health-care workers and public-safety workers who have exposure to blood in the workplace, persons in training in schools of medicine, dentistry, nursing, laboratory technology, and other allied health professions. Behavioral indications: injecting drug users, persons with more than one sex partner in the previous 6 months, persons with a recently acquired sexually-transmitted disease (STD), all clients in STD clinics, men who have sex with men. Other indications: household contacts and sex partners of persons with chronic HBV infection, clients and staff of institutions for the developmentally disabled, international travelers who will be in countries with high or intermediate prevalence of chronic HBV infection for more than 6 months, inmates of correctional facilities. *MMWR* 1991; 40 (RR-13): 1-25. (www.cdc.gov/travel/diseases/hbv.htm)

6. **Hepatitis A vaccination**—For the combined HepA-HepB vaccine use 3 doses at 0, 1, 6 months). Medical indications: persons with clotting-factor disorders or chronic liver disease. Behavioral indications: men who have sex with men, users of injecting and noninjecting illegal drugs. Occupational indications: persons working with HAV-infected primates or with HAV in a research laboratory setting. Other indications: persons traveling to or working in countries that have high or intermediate endemicity of hepatitis A. *MMWR* 1999; 48 (RR-12): 1-37. (www.cdc.gov/travel/diseases/hav.htm)

7. **Measles, Mumps, Rubella vaccination (MMR)**—Measles component: Adults born prior to 1957 may be considered to be immune to measles. Give 2 doses of MMR for adults with one or more of the following conditions and without vaccination history:
   - adults born after 1956
   - persons vaccinated with killed measles virus vaccine 1963-1969
   - students in post-secondary education institutions
   - health care workers
   - susceptible international travelers to measles endemic countries.

   Mumps component: 1 dose of MMR should be adequate for protection. Rubella component: Give 1 dose of MMR to women whose rubella vaccination history is unreliable and counsel women to avoid becoming pregnant for 4 weeks after vaccination. For women of child-bearing age, regardless of birth year, routinely determine rubella immunity and counsel women regarding congenital rubella syndrome. Do not vaccinate pregnant women or those planning to become pregnant in the next 4 weeks. If pregnant and susceptible, vaccinate as early in postpartum period as possible. *MMWR* 1998; 47 (RR-8): 1-57.

8. **Varicella vaccination**—Recommended for all persons who do not have reliable clinical history of varicella infection, or serological evidence of varicella zoster virus (VZV) infection; health-care workers and family contacts of immunocompromised persons, those who live or work in environments where transmission is likely (e.g., teachers of young children, day care employees, and residents and staff members in institutional settings), persons who live or work in environments where VZV transmission can occur (e.g., college students, inmates and staff members of correctional institutions, and military personnel), adolescents and adults living in households with children, women who are not pregnant but who may become pregnant in the future, international travelers who are not immune to infection. Note: Greater than 90% of U.S. born adults are immune to VZV. Do not vaccinate pregnant women or those planning to become pregnant in the next 4 weeks. If pregnant and susceptible, vaccinate as early in postpartum period as possible. *MMWR* 1996; 45 (RR-11): 1-36, *MMWR* 1999; 48 (RR-6): 1-5.

9. **Meningococcal vaccine (quadrivalent polysaccharide for serogroups A, C, Y, and W-135)**—Consider vaccination for persons with medical indications: adults with terminal complement component deficiencies, with anatomic or functional asplenia. Other indications: travelers to countries in which disease is hyperendemic or epidemic ("meningitis belt" of sub-Saharan Africa, Mecca, Saudi Arabia for Hajj). Revaccination at 3-5 years may be indicated for persons at high risk for infection (e.g., persons residing in areas in which disease is epidemic). Counsel college freshmen, especially those who live in dormitories, regarding meningococcal disease and the vaccine so that they can make an educated decision about receiving the vaccination. *MMWR* 2000; 49 (RR-7): 1-20. Note: The AAFP recommends that colleges should take the lead on providing education on meningococcal infection and vaccination and offer it to those who are interested. Physicians need not initiate discussion of the meningococcal quadravalent polysaccharide vaccine as part of routine medical care.

Recommended Adult Immunization Schedule United States, 2002-2003

and

Recommended Immunizations for Adults with Medical Conditions United States, 2002-2003

Summary of Recommendations Published by

The Advisory Committee on Immunization Practices

Department of Health and Human Services
Centers for Disease Control and Prevention

Recommended Adult Immunization Schedule, United States, 2002-2003

For all persons in this group | Catch-up on childhood vaccinations | For persons with medical / exposure indications

Vaccine ▼ / Age Group ▶	19–49 Years	50–64 Years	65 Years and Older
Tetanus, Diphtheria (Td)*	1 dose booster every 10 years [1]		
Influenza	1 dose annually for persons with medical or occupational indications, or household contacts of persons with indications [2]	1 annual dose	
Pneumococcal (polysaccharide)	1 dose for persons with medical or other indications.	1 dose for unvaccinated persons [3]	1 dose revaccination [4]
Hepatitis B*	3 doses (0, 1–2, 4–6 months) for persons with medical, behavioral, occupational, or other indications [5]		
Hepatitis A	2 doses (0, 6–12 months) for persons with medical, behavioral, occupational, or other indications [6]		
Measles, Mumps, Rubella (MMR)*	1 dose if measles, mumps, or rubella vaccination history is unreliable; 2 doses for persons with occupational or other indications [7]		
Varicella*	2 doses (0, 4–8 weeks) for persons who are susceptible [8]		
Meningococcal (polysaccharide)	1 dose for persons with medical or other indications [9]		

See Footnotes for Recommended Adult Immunization Schedule, United States, 2002-2003 on back cover.

*Covered by the Vaccine Injury Compensation Program. For information on how to file a claim call 800-338-2382. Please also visit www.hrsa.gov/vicp To file a claim for vaccine injury write: U.S. Court of Federal Claims, 717 Madison Place, N.W., Washington D.C. 20005. 202 219-9657.

This schedule indicates the recommended age groups for routine administration of currently licensed vaccines for persons 19 years of age and older. Licensed combination vaccines may be used whenever any components of the combination are indicated and the vaccine's other components are not contraindicated. Providers should consult the manufacturers' package inserts for detailed recommendations.

Report all clinically significant post-vaccination reactions to the Vaccine Adverse Event Reporting System (VAERS). Reporting forms and instructions on filing a VAERS report are available by calling 800-822-7967 or from the VAERS website at www.vaers.org.

For additional information about the vaccines listed above and contraindications for immunization, visit the National Immunization Program Website at www.cdc.gov/nip/ or call the National Immunization Hotline at 800-232-2522 (English) or 800-232-0233 (Spanish).

Approved by the Advisory Committee on Immunization Practices (ACIP), and accepted by the American College of Obstetricians and Gynecologists (ACOG) and the American Academy of Family Physicians (AAFP)

Recommended Immunizations for Adults with Medical Conditions, United States, 2002-2003

For all persons in this group | Catch-up on childhood vaccinations | For persons with medical / exposure indications | Contraindicated

Medical Conditions ▼ / Vaccine ▶	Tetanus-Diphtheria (Td)*	Influenza	Pneumococcal (polysaccharide)	Hepatitis B*	Hepatitis A	Measles, Mumps, Rubella (MMR)*	Varicella*
Pregnancy		A					
Diabetes, heart disease, chronic pulmonary disease, chronic liver disease, including chronic alcoholism		B	C		D		
Congenital immunodeficiency, leukemia, lymphoma, generalized malignancy, therapy with alkylating agents, antimetabolites, radiation or large amounts of corticosteroids			E				F
Renal failure / end stage renal disease, recipients of hemodialysis or clotting factor concentrates			E	G			
Asplenia including elective splenectomy and terminal complement component deficiencies			E, H, I				
HIV infection			E, J			K	

A. If pregnancy is at 2nd or 3rd trimester during influenza season.

B. Although chronic liver disease and alcoholism are not indicator conditions for influenza vaccination, give 1 dose annually if the patient is ≥ 50 years, has other indications for influenza vaccine, or if the patient requests vaccination.

C. Asthma is an indicator condition for influenza but not for pneumococcal vaccination.

D. For all persons with chronic liver disease.

E. Revaccinate once after 5 years or more have elapsed since initial vaccination.

F. Persons with impaired humoral but not cellular immunity may be vaccinated. *MMWR* 1999; 48 (RR-06): 1-5.

G. Hemodialysis patients: Use special formulation of vaccine (40 ug/mL) or two 1.0 mL 20 ug doses given at one site. Vaccinate early in the course of renal disease. Assess antibody titers to hep B surface antigen (anti-HBs) levels annually. Administer additional doses if anti-HBs levels decline to <10 milliinternational units (mIU)/ mL.

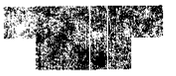
H. Also administer meningococcal vaccine.

I. Elective splenectomy: vaccinate at least 2 weeks before surgery.

J. Vaccinate as close to diagnosis as possible when CD4 cell counts are highest.

K. Withhold MMR or other measles containing vaccines from HIV-infected persons with evidence of severe immunosuppression. *MMWR* 1996; 45: 603-606, *MMWR* 1992; 41 (RR-17): 1-19.

FDA Updates
11/04/02



Smallpox Vaccine Clears FDA Hurdles

Newsbytes via NewsEdge Corporation : Ceci Connolly 11/02/2002

The Food and Drug Administration has granted a license for the federal government's 30-year-old stockpile of smallpox vaccine, easing the way for millions of Americans to be inoculated eventually against the deadly virus.

Jerome M. Hauer, head of bioterrorism at the Department of Health and Human Services, said the bulk of the first batch of 1.7 million doses had been promised to the Pentagon, which is preparing for potential war with Iraq. The remaining 13.7 million doses could be used to respond to a smallpox attack or to vaccinate emergency responders prior to any attack.

The Bethesda-based FDA approved the license on Oct. 25 but did not announce its decision. In response to inquiries, officials confirmed yesterday that the vaccine had cleared all regulatory hurdles.

Securing the FDA license makes future use of the vaccine, known as Dryvax, significantly easier for federal health officials, said Dartmouth University's John F. Modlin, who chairs the government's advisory panel on vaccines.

"The only legal way to administer an unlicensed vaccine would be under Investigational New Drug regulations," which involve cumbersome informed consent and patient monitoring, he said. "The license will allow the vaccine to be distributed and administered in a more efficient manner."

Last summer, the nation's top bioterrorism experts recommended a three-step smallpox immunization plan. Under the proposal, presented to President Bush by HHS Secretary Tommy G. Thompson, about 500,000 health care workers would be inoculated immediately and serve as the early investigators into any possible outbreak. Later, as many as 10 million police, fire and emergency responders would be offered the vaccine. Eventually, all 280 million Americans would have the option of being vaccinated, though that would likely not occur until a new batch of vaccine is licensed sometime in 2004.

Several sources have indicated that Vice President Cheney has advocated broad vaccination in part to deter an attack. But Bush has voiced concerns over the vaccine's dangerous, sometimes fatal, side effects and has not yet decided who should be offered it.

In addition to the 15.4 million doses of Dryvax, the government has 75 million doses of vaccine made by Aventis Pasteur Inc. and has ordered 209 million doses from partners Acambis PLC and Baxter International Inc. It could take as long as a year before the latter two vaccines are licensed.

Technically, the Dryvax was licensed when it was made in the 1970s, but manufacturer Wyeth needed supplemental approval for new bifurcated needles and diluent, the liquid material used to reconstitute freeze-dried vaccine, said Karen Midthun, the FDA's director of the Office of Vaccines Research and Review.

10/28/02

FDA Takes Action on Long-acting Guaifenesin Products

Chemical Business NewsBase - FDA Release via NewsEdge Corporation : 10/21/2002
Adams Laboratories Inc commented on recent regulatory action by the US Food and Drug Administration (FDA) that has resulted in Mucinex becoming the only long-acting, single ingredient, guaifenesin product available in the US. Specifically, the FDA has sent warning letters to all manufacturers and distributors of long-acting, single ingredient, guaifenesin, stating that their products must be withdrawn immediately from the market until they submit a new drug application (NDA) or abbreviated new drug application (ANDA) and receive approval by the FDA for marketing. This regulatory action came as a result of three separate regulatory requirements. First, only Adams Laboratories has an approved NDA for a long-acting, single ingredient, guaifenesin drug, and all others are therefore illegal under a 1984 FDA Compliance Policy Guide. Second, an FDA regulation requires an NDA for any long-acting drug product. Third, the Durham-Humphrey Amendment of 1951 to the Federal Food, Drug, and Cosmetic Act stipulates that a drug product cannot be marketed simultaneously both as a prescription and as a nonprescription product at the same strength and same dosage. Because the Adams Laboratories' NDA for Mucinex was approved in Jul 2002, all current long-acting, single ingredient, guaifenesin products are classified as misbranded and therefore illegal and are subject to this FDA regulatory action. The company has a significant opportunity to gain a sizeable portion of the cough, cold and flu market, which is about $2.4 bn in the US sales each year, with guaifenesin product sales alone making up nearly 50% of that total. Mucinex provides the maximum therapeutic daily dosage of guaifenesin for adults by taking two 600 mg tablets every 12 hours. It is indicated to help loosen phlegm and thin bronchial secretions to rid the bronchial passageways of bothersome mucus and make coughs more productive. Based in Fort Worth, TX, Adams Laboratories Inc develops, markets and sells prescription and non-prescription pharmaceuticals for the treatment of respiratory disorders and diseases.

Drug Trials and Comparisons

10/25/02

ADHD Patch Demonstrates Efficacy in Trial

MIAMI--(BUSINESS WIRE) via NewsEdge Corporation -- Noven Pharmaceuticals, Inc. (Nasdaq:NOVN) today announced positive Phase III clinical study results for its once-daily transdermal methylphenidate system. The double-blind, placebo-controlled, multi-center Phase III study was conducted to assess the efficacy and safety of Noven's developmental methylphenidate patch for Attention-Deficit Hyperactivity Disorder (ADHD), which Noven intends to market under the trade name MethyPatch(R).

The four-week study involved 212 patients (ages 6 to 12 years) meeting the DSM-IV criteria for ADHD. Patients were randomized to apply MethyPatch or a placebo transdermal patch once-daily to the hip area. Six MethyPatch dosage strengths were available for titration. The primary efficacy measure was improvement in patient behavior and attention as rated by community school teachers using the Inattention/Overactivity with Aggression (IOWA) Conners behavioral rating scale. Secondary efficacy measures included improvement in patient behavior as rated by parents and clinicians.

The study results indicated that MethyPatch was significantly superior to placebo on all primary and secondary efficacy measures. Compared with placebo, MethyPatch, worn for approximately 12 hours per day, resulted in significantly improved scores in teacher, parent and clinician ratings of patient behavior and attention. The p-value for each measure was less than 0.0001, reflecting high statistical significance.

At week four of the study, patient mean Inattention/Overactivity scores (scores range from 0 to 15) as rated by teachers showed highly significant improvement (p-value less than 0.0001) from baseline as compared to placebo (MethyPatch group improved 6.1 points; placebo group improved 2.0 points).

No serious adverse events occurred in patients receiving MethyPatch. The most common adverse events were reduced appetite, insomnia, abdominal pain and headache. Four patients (3.8%) in the MethyPatch group and three patients (2.9%) in the placebo group withdrew from treatment due to adverse events.

As part of the study, parents were asked to complete a MethyPatch satisfaction survey. 98.5% of responding parents agreed that being able to remove the patch and discontinue treatment at any time provided them with a sense of control, and 64.2% indicated that they had no difficulty in properly applying MethyPatch.

MethyPatch combines methylphenidate - an established ADHD therapy - with Noven's patented DOT Matrix(TM) patch technology. DOT Matrix permits Noven to deliver predictable therapeutic doses of a range of prescription therapies through discreet, comfortable and adherent patches that are well suited to active lifestyles. In addition to DOT Matrix patents, Noven holds patents on the transdermal delivery of methylphenidate via a patch system.

The Phase III study was part of a MethyPatch clinical trial program sponsored by Noven that spanned several years and included over 700 subjects in centers across the U.S. In June 2002, Noven submitted a New Drug Application to the U.S. Food & Drug Administration seeking approval to market MethyPatch for the treatment of ADHD, and the application is currently under review.

ADHD is characterized by developmentally inappropriate impulsivity, inattention and hyperactivity. ADHD affects 3% to 5% of school-aged children, and an estimated 1.5 million children are currently on medication to treat this disorder. All presently approved ADHD medications are delivered orally.

FDA Updates
10/23/02

Repaglinide Approved for Combination Therapy in Diabetes

PR Newswire Leased Line via NewsEdge Corporation : With Insulin Sensitizers Studies Show Greater Glycemic Improvements With Prandin and Sensitizers Compared to Monotherapy in Treating Type 2 Diabetes

PRINCETON, N.J., Oct. 22 /PRNewswire/ -- Novo Nordisk announced today that the U.S. Food and Drug Administration (FDA) approved a new indication for use of the oral antidiabetic drug (OAD) Prandin(r) (repaglinide): combination therapy with rosiglitazone or pioglitazone, members of another class of OADs called insulin sensitizers, for the treatment of type 2 diabetes. Prandin, an "insulin secretagogue" because it stimulates insulin secretion, was previously approved for use as monotherapy or in combination with metformin, another type of insulin sensitizer.

The new indication for Prandin is important because combination therapy may improve control of blood glucose levels for many people with type 2 diabetes whose condition has progressed and oral monotherapy together with diet and exercise cannot maintain adequate glycemic control. At that point, combination therapy with an additional OAD with a different mechanism of action may be appropriate.

"Prandin is a highly effective agent to use with insulin sensitizers because of its ability to augment mealtime insulin secretion and proven efficacy in attaining glycemic control," said Alan J. Garber, M.D., Ph.D., professor of medicine, biochemistry and cell biology at Baylor College of Medicine in Houston. He explained that Prandin, which is taken with meals, in part to control postprandial glycemia, rapidly stimulates insulin secretion, whereas insulin sensitizers primarily improve the body's response to the hormone. He said that two recent studies support this combination approach, showing that, among patients previously poorly controlled with monotherapy with either a sulfonylurea or metformin, "the combination of Prandin with a sensitizer resulted in better blood glucose control than monotherapy with either of these agents alone."

Supportive findings

The FDA approval was based in large part on findings from two studies of Prandin in combination with either rosiglitazone (1, 2) or pioglitazone (3, 4) (preliminary data was presented at the American Diabetes Association annual meeting, 2001). Each study was a multicenter, open-label, randomized, 24-week trial in approximately 250 participants with type 2 diabetes inadequately controlled by previous oral therapy with sulfonylureas or metformin. The trials consisted of 12 weeks of dose-adjustment and 12 weeks of maintenance therapy.

"Both studies showed significant improvement in glycemic control with Prandin in combination with the insulin sensitizer compared to monotherapy with these agents," said Dr. Garber. He added that, because the benefits were shown in patients who previously had unsatisfactory glycemic control with sulfonylurea or metformin monotherapy, the findings "are important for many people with type 2 diabetes who need to improve glycemic control, and provide new approaches to attaining control for patients as well as the physicians who treat them."

In the Prandin-rosiglitazone trial, levels of glycated hemoglobin (A1c) -- the percent hemoglobin with glucose attached to it and an indicator of long-term blood glucose control -- decreased by 1.43% (from 9.1% at baseline to 7.7% at the end of the trial) for the Prandin/rosiglitazone group, but only by 0.17% and 0.56% for the Prandin-only and rosiglitazone-only groups, respectively. Fasting plasma glucose levels decreased by 94 mg/dL, 54 mg/dL, and 67 mg/dL in the Prandin/rosiglitazone, Prandin-only and rosiglitazone-only groups, respectively. Declines in A1c and fasting plasma glucose in the Prandin/rosiglitazone group were significantly greater than in the two monotherapy groups (p 0.001).

The results in the Prandin-pioglitazone trial were very similar. A1c levels decreased by 1.76% (from 9.3% to 7.5%) in the combination group, compared to changes of -0.18% and +0.32% in the Prandin-only and pioglitazone-only groups, respectively. Fasting plasma glucose levels decreased by 82 mg/dL, 34 mg/dL, and 19 mg/dL in the three groups, respectively. Declines in A1c and fasting plasma glucose in the Prandin/pioglitazone group were significantly greater than in the two monotherapy groups (p 0.001).

In these studies, hypogycemia occurred in 7% of combination therapy patients in comparison to 7% for Prandin monotherapy and 2% for sensitizer monotherapy patients. Peripheral edema was reported in 12 out of 250 patients who received combination therapy and 3 out of 124 who received only sensitizers, with no cases reported for those who received Prandin. There were reports in 2 patients, both of whom had a prior history of coronary artery disease, of episodes of edema with congestive heart failure. Both recovered after diuretic treatment. No such cases were reported in the monotherapy groups. Mean weight change was +4.9 kg for the combination therapy groups from the 2 studies.

About Prandin(r) (Repaglinide) Tablets

Prandin(r) (repaglinide), the first product of a unique class (the meglitinides), rapidly stimulates insulin secretion,

and its action profile coincides with mealtime dosing to control postprandial glycemia (5). Prandin is indicated as monotherapy or in combination with metformin, rosiglitazone or pioglitazone for individuals with type 2 diabetes whose hyperglycemia (abnormally high blood glucose) cannot be controlled by diet and exercise alone plus monotherapy with metformin, sulfonylureas, repaglinide or thiazolidinediones (rosiglitazone / pioglitazone). While it improves overall glycemic control, including fasting blood glucose levels, (6) Prandin was developed specifically for dosing at mealtime, to control postprandial hyperglycemia as well. In addition, Prandin may allow greater flexibility in eating patterns.

In one-year clinical trials, the most common adverse events leading to discontinuation of Prandin therapy were hyperglycemia, hypoglycemia and related symptoms. The most common other side effects reported were cold- and flu-like symptoms, headache, diarrhea, joint ache and back pain.

About Diabetes

The prevalence of diabetes is skyrocketing in many countries around the world. According to the World Health Organization (WHO), the number of people worldwide with the condition was estimated at 30 million in 1985, 135 million in 1995, and 177 million in 2000, and is expected to increase to at least 300 million by 2025. Overall, direct health care costs of diabetes range from 2.5% to 15% of annual national health care budgets, depending on diabetes prevalence and the sophistication of the treatment available (7).

Full prescribing information for Prandin(r) is available by contacting Novo Nordisk Pharmaceuticals, Inc.

FDA Update
10/17/02

ANDA Filed for Generic Norvasc

PITTSBURGH--(BUSINESS WIRE) via NewsEdge Corporation -- Robert J. Coury, Vice Chairman and CEO of Mylan Laboratories Inc. (NYSE: MYL) today acknowledged that Mylan has filed an Abbreviated New Drug Application (ANDA) seeking U.S. Food and Drug Administration (FDA) approval to sell amlodipine besylate tablets (Norvasc(R)) prior to the expiration of patents owned by Pfizer Inc.

Pfizer filed suit against Mylan, but not before the expiration of the 45 day statutory period, meaning the FDA can approve Mylan's ANDA as soon as the Agency determines that all regulatory requirements have been satisfied.

Mr. Coury believes that Mylan is the first-to-file an amlodipine ANDA containing a "paragraph IV" certification. However, FDA policy prohibits the Agency from confirming first-to-file status until an application receives final approval.

Mr. Coury took exception to comments made by Pfizer regarding the merits of Mylan's amlodipine patent challenge. "Contrary to Pfizer's comments, Mylan has been very selective in choosing which patents to challenge in these cases." He further stated that "it has been eighteen years since the Hatch Waxman amendments became law and during this period Mylan has been very successful in challenging patents and bringing high quality generic products to market sooner than would have otherwise been possible. You don't enjoy that kind of success unless your legal positions are consistently meritorious. Consumers have enjoyed tens of billions of dollars in savings as a result of the success of Mylan and other generic companies and they will continue to reap these savings as we go forward."

"Mylan, which has its own line of branded products and an expanding patent portfolio respects the valid intellectual property rights of others and appreciates the importance of rewarding and protecting truly novel discoveries which advance medical science" stated Coury. He concluded his remarks by stating, "Mylan looks forward to the opportunity to present in court the merits of the Company's defenses to Pfizer's allegations of infringements and that a positive outcome for Mylan in this litigation would obviously represent a tremendous opportunity for the Company and its shareholders."

FDA Updates
10/08/02
Terazosin Receives Final Approval
Drug Week via NewsEdge Corporation : Ranbaxy Pharmaceuticals, Inc., (RPI), a wholly owned subsidiary of Ranbaxy Laboratories, Ltd., (RLL), announced that RLL has received final approval from the U.S. Food and Drug Administration to manufacture and market Terazosin Hydrochloride Capsules, 1 mg, 2 mg, 5 mg, and 10 mg. Based on bioequivalent studies, the Ranbaxy formulation has been deemed to be bioequivalent and therapeutically equivalent to the listed drug Hytrin capsules by Abbott Laboratories.
Terazosin hydrochloride capsules are indicated for the treatment of symptomatic benign prostatic hyperplasia (BPH).
It is also indicated for the treatment of hypertension and can be used alone or in combination with other antihypertensive agents such as diuretics or beta-adrenergic blocking agents. It is anticipated that product will be made available for sales, marketing, and distribution through the RPI commercial teams later this year. This article was prepared by Drug Week editors from staff and other reports.

FDA Updates
10/09/02
Opiate Dependence Treatment Now Available
PR Newswire Leased Line via NewsEdge Corporation : RICHMOND, Va., and LONDON, Oct. 8 /PRNewswire-FirstCall/ -- Reckitt Benckiser plc announced today that its new treatments for opiate dependence, Suboxone(r) (buprenorphine/naloxone) and Subutex(r) (buprenorphine) 2mg and 8mg tablets have been approved by the US Food and Drug Administration for the treatment of opiate dependence. These products were developed under a Cooperative Research and Development Agreement between Reckitt Benckiser and the National Institutes of Health's National Institute on Drug Abuse in the USA over the past ten years.
Subutex and Suboxone will become useful additions to the available range of pharmacotherapies that can help opiate-dependent patients overcome their addiction. The major benefit of Subutex/Suboxone is that qualified physicians in the US will now be able to treat patients with these products in the privacy of the Doctor's office rather than only from the limited number of existing drug treatment programs.
Subutex first received marketing approval in France and was launched in February 1996 by Schering-Plough under licence from Reckitt Benckiser. Since then the product has been launched in 24 countries. Licence income from these sales forms a modest but growing contribution to Reckitt Benckiser's core Health & Personal Care category.

FDA Updates
10/23/02
OTC Version of Mevacor Under Consideration
Chemical Business NewsBase - Chemical Market Reporter via NewsEdge Corporation : 10/14/2002
Johnson & Johnson/Merck Consumer Pharmaceuticals are in talks with the FDA over a non-prescription OTC version of Merck's cholesterol-lowering drug Mevacor (lovastatin). The joint venture would sell the drug.