Drug Utilization Review Board

Oklahoma Health Care Authority

4545 N. Lincoln Suite 124

Oklahoma City, Oklahoma 73105

OHCA Board Room

Wednesday

February 13, 2008

@ 6:00 p.m.

THE UNIVERSITY OF OKLAHOMA

THE UNIVERSITY OF OKLAHOMA

MEMORANDUM

TO: Drug Utilization Review Board Members

FROM: Shellie Gorman, Pharm.D.

SUBJECT: **Packet Contents for Board Meeting – February 13, 2008**

DATE: February 7, 2008

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

Enclosed are the following items related to the February 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.**

60 Day Notice to Prior Authorize Narcotic Analgesics – **See Appendix C.**

30 Day Notice to Prior Authorize Combigan™ – **See Appendix D.**

Beta Blockers Utilization Review – **See Appendix E.**

Erythropoiesis-Stimulating Agents Utilization Review – **See Appendix F.**

Action Item – Annual Review of Insomnia Products – **See Appendix G**

Action Item – Annual Review of Glumetza™ and Fortamet®– **See Appendix H.**

FDA and DEA Updates **– See Appendix I.**

Future Business

Drug Utilization Review Board

(DUR Board)

Meeting – February 13, 2008 @ 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. McNeill, Chairman:

1. Call To Order

A. Roll Call – Dr. Graham

Items to be presented by Dr. McNeill, Chairman:

2. Public Comment Forum

A. Acknowledgment of Speakers and Agenda Item

Items to be presented by Dr. McNeill, Chairman:

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

A. January 9, 2007 DUR Minutes – Vote
B. January 10, 2007 DUR Recommendations Memorandum

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

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

A. Retrospective Drug Utilization Review for October 2007
B. Retrospective Drug Utilization Review Response for July 2007
C. Medication Coverage Activity Audit for January 2008
D. Help Desk Activity Audit for January 2008

Items to be presented by Dr. Gorman, Dr. McNeill, Chairman

5. 60 Day Notice to Prior Authorize Narcotic Analgesics – See Appendix C.

A. Utilization Review
B. COP Recommendations
C. Potential Savings

Items to be presented by Dr. Chonlahan, Dr. McNeill, Chairman:

6. 30 Day Notice to Prior Authorize Combigan™ – See Appendix D.

A. Product Summary
B. COP Recommendations

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

7. Beta Blockers Utilization Review – See Appendix E.

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

Items to be presented by Dr. Flannigan, Dr. McNeill, Chairman

8. Erythropoiesis-Stimulating Agents Utilization Review – See Appendix F.

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

Items to be presented by Dr. Browning, Dr. McNeill, Chairman

9. Action Item: Annual Review of Insomnia Products – See Appendix G.

A. Current PA Criteria
B. Utilization Review
C. COP Recommendations

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

10. Action Item: Annual Review of Glumetza™ and Fortamet® – See Appendix H.

A. Current PA Criteria
B. Utilization Review
C. COP Recommendations

11. FDA and DEA Updates – See Appendix I.

12. Future Business

A. FY07 Annual Review (Presented in March 2008)
B. Osteoporosis Utilization Review
C. Oral Allergy Follow-Up
D. Non-Hypnotic Benzodiazepine Review
E. Nasal Allergy PBPA Review
F. New Product Reviews

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES of MEETING of JANUARY 9, 2008

BOARD MEMBERS:	PRESENT	ABSENT
Brent Bell, D.O., D.Ph.	X	
Jay D. Cunningham, D.O.		X
Mark Feightner, D.Ph.	X	
Dorothy Gourley, D.Ph.	X	
Evelyn Knisely, Pharm.D.	X	
Thomas Kuhls, M.D.	X	
Dan McNeill, Ph.D., PA-C; Chairman	X	
Cliff Meece, D.Ph.; Vice-Chairman	X	
John Muchmore, M.D., Ph.D.	X	
James Rhymer, D.Ph	X	

COLLEGE of PHARMACY STAFF:	PRESENT	ABSENT
Leslie Browning, D.Ph.; PA Coordinator	X	
Metha Chonlahan, D.Ph.; Clinical Pharmacist	X	
Karen Egesdal, D.Ph.; SMAC-ProDUR Coordinator/OHCA Liaison	X	
Kelly Flannigan, Pharm.D.; Operations Manager	X	
Shellie Gorman, Pharm.D., M.S.; DUR Manager	X	
Ronald Graham, D.Ph.; Pharmacy Director	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.; Principal Investigator	X	
Visiting Pharmacy Students: Evelyn Patterson, Shannon Lowe	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 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, Sr. Research Analyst	X	

OTHERS PRESENT:

Sam Smothers, MedImmune	Wade McCreary, Takeda Pharmaceutical	Donna Erwin, Bristol-Myers Squibb
Brian Shank, Astra Zeneca	Tracy Copeland, Daiichi Sankyo	Jim Fowler, Astra Zeneca
Ron Schnare, Shire	Jacque Collier, Abbott	David Williams, Forest
Rachelle Wan, Amgen	Richard Ponder, J&J	Jim Graham, J&J
Mark DeClerk, Lilly	Bruce Christian, Lilly	Joseph Medina, Sepracor
William Dozier, Gilead	Lance Burchan, MedImmune	

PRESENT FOR PUBLIC COMMENT:

n/a

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

1A: Roll Call

Dr. Meece called the meeting to order. Roll call by Dr. Graham noted there was not a quorum. The meeting proceeded with non-voting items. A quorum was established upon late arrival of DUR Board member(s).

ACTION: NONE REQUIRED.

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

There were no speakers for Public Comment.

ACTION: NONE REQUIRED.

Lynn Rambo-Jones spoke regarding the Supplemental Rebate Program. Her interpretation of the law is that the DUR Board Chairman can review decisions after the fact that has been made by the Supplemental Rebate Committee or to participate as a third party. No drug company representatives can be involved.

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

3A: November 14, 2007 DUR Minutes

Dr. Meece moved to approve minutes as submitted; seconded by Dr. Bell.

ACTION: MOTION CARRIED.

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

4A: Retrospective Drug Utilization Review Report: August 2007
4B: Retrospective Drug Utilization Review Report: September 2007
4C: Retrospective Drug Utilization Review Response: May 2007
4D: Retrospective Drug Utilization Review Response: June 2007
4E: Medication Coverage Activity Audit: November 2007
4F: Medication Coverage Activity Audit: December 2007
4G: Help Desk Activity Audit: November & December 2007

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

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 5: **VOTE ON 2008 DUR MEETING DATES**

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

January 9, 2008	July 9, 2008
February 13, 2008	August 13, 2008
March 12, 2008	September 10, 2008
April 9, 2008	October 8, 2008
May 14, 2008	November 12, 2008
June 11, 2008	December 10, 2008

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

ACTION: MOTION CARRIED.

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE TOPICAL ANTIFUNGALS**

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

Dr. Kuhls moved to approve recommendations as submitted; seconded by Dr. Muchmore.

ACTION: MOTION CARRIED.

AGENDA ITEM NO. 7: **VOTE TO PRIOR AUTHORIZE SOMA® 250 MG**

Materials included in agenda packet; presented by Dr. Le.
Dr. Gourley moved to approve; seconded by Dr. Meece.
ACTION: MOTION CARRIED.

AGENDA ITEM NO. 8: **VOTE ON TO PRIOR AUTHORIZE AZOR™ AND UPDATE ANTIHYPERTENSIVE PRIOR AUTHORIZATION CRITERIA**

Materials included in agenda packet; presented by Dr. Moore.
Dr. Meece moved to approve; seconded by Dr. Bell.
ACTION: MOTION CARRIED.

AGENDA ITEM NO. 9: **COUGH AND COLD COVERAGE REVIEW**

Materials included in agenda packet; presented by Dr. Gorman.
Dr. Kuhls moved to approve; seconded by Dr. Feightner.*
*With the addition of liquid decongestants, ages 6-12 yrs; three 4 oz units per year.
ACTION: MOTION CARRIED.

AGENDA ITEM NO. 10: **FY07 ANNUAL REVIEW**

Tabled to February 13, 2008 meeting.
ACTION: TABLED.

AGENDA ITEM NO. 11: **ANNUAL REVIEW OF AMITIZA®, LOTRONEX® AND ZELNORM®**

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

AGENDA ITEM NO. 12: **ANNUAL REVIEW OF IMMUNOMODULATORS ELIDEL® AND PROTOPIC®**

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

AGENDA ITEM NO. 13: **FDA & DEA UPDATES**

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

AGENDA ITEM NO. 14: **FUTURE BUSINESS**

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

14A: **Narcotic Utilization Follow-Up**
14B: **Erythropoiesis-Stimulating Agents Follow-Up**
14C: **Osteoporosis Utilization Review**
14D: **Antihistamine Follow-Up**
14E: **Exubera® Annual Review**
14F: **Insomnia PBPA Annual Review**
14G: **New Product Reviews**
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 15: **ADJOURNMENT TO EXECUTIVE SESSION**

The meeting was adjourned to Executive Session as authorized by the Open Meetings Act, Okla. State § 307 (8)(4), (7).

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

Memorandum

Date: January 10, 2008

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

From: Shellie Gorman, Pharm.D.
Drug Utilization Review Manager
Pharmacy Management Consultants

Subject: DUR Board Recommendations from Meeting of January 09, 2008.

Recommendation 1: Vote on 2008 Meeting Dates

MOTION CARRIED by unanimous approval.

Meetings are held the second Wednesday of each month.

JANUARY 9, 2008
FEBRUARY 13, 2008
MARCH 12, 2008
APRIL 9, 2008
MAY 14, 2008
JUNE 11, 2008
JULY 9, 2008
AUGUST 13, 2008
SEPTEMBER 10, 2008
OCTOBER 8, 2008
NOVEMBER 12, 2008
DECEMBER 10, 2008

Recommendation 2: Vote to Prior Authorize Topical Antifungals

MOTION CARRIED by unanimous approval.

The following Tier 1 drug list has been reviewed and determined to be an acceptable combination for use as initial therapy for the majority of members. The College of Pharmacy recommends this list to the Drug Utilization Review Board based on cost and clinical effectiveness for approval before referral to the Oklahoma Healthcare Authority.

Tier 1	Tier 2
Ciclopirox	Ciclopirox sol, shampoo, & gel **(Penlac® and Loprox®)**
Clotrimazole and Clotrimazole/Betamethasone	Miconazole/Zinc Oxide/White petrolatum **(Vusion®)**
Econazole	Oxiconazole **(Oxistat®)**
Ketoconazole	Sertaconazole nitrate **(Ertaczo®)**
Nystatin and Nystatin/Triamcinolone	Butenafine **(Mentax®)**
Hydrocortisone/Iodoquinol	Ketoconazole gel **(Xolegel™)**
All available generic antifungal products	Ketoconazole gel + 1% pyrithione zinc shampoo **(Xolegel™ DUO)**
	Naftifine **(Naftin®)**
	Sulconazole **(Exelderm®)**
	Terbinafine **(Lamisil® Spray)**
	Clotrimazole **(Lotrimin Lotion 1%)**
	Ketoconazole Foam 2% **(Extina®)**

Approval Criteria:

1. Approval of a branded antifungal product will be granted following trials of at least two other Tier 1 topical antifungal products within the last 30 days.

2. For treatment of Onychomycosis, a trial of oral antifungals (6 weeks for fingernails and 12 weeks for toenails) will be required in order for approval of Penlac®.

Recommendation 3: Vote to Prior Authorize Soma® 250

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Soma® 250mg with the following criteria:

1. Must provide detailed documentation regarding member's inability to use other skeletal muscle relaxants including carisoprodol 350mg, and specific reason member cannot be drowsy for even a short time period. Member must not have other sedating medications in current claims history.

2. A diagnosis of acute musculoskeletal pain, in which case, the approval will be for 14 days per 365 day period. Conditions requiring chronic use will not be approved.

Recommendation 4: Vote to Prior Authorize Azor™ and Update Antihypertensive PA Criteria

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends placing Azor™ in the PBPA program as a Tier 3 ARB. A Quantity limit of one unit per day would be applied. The College also recommends applying the following criteria to the ARB and ARB Combination category.

ANTI-HYPERTENSIVE MEDICATIONS		
ARB AND ARB COMBINATION		
Tier 1	**Tier 2**	**Tier 3**
All Tier 1 ACEIs	Supplemental Rebated Tier 3	All ARBs and ARB/HCTZ combos
		Exforge® (amlodipine/valsartan)
		Azor™ (amlodipine/olmesartan)

To qualify for a Tier 2 antihypertensive medication (or Tier 3 medication when no Tier 2 medications exist) there must be

- documented inadequate response to two Tier 1 medications, or
- adverse drug reaction to all Tier 1 class of medications, or
- previous stabilization on the Tier 2 medication, or
- a unique indication for which the Tier 1 antihypertensives lack

To qualify for a Tier 3 antihypertensive medication there must be

- documented inadequate response to two Tier 1 medications and documented inadequate response to all available Tier 2 medications, or
- adverse drug reaction to all Tier 1 or Tier 2 classes of medications, or
- previous stabilization on the Tier 3 medication, or
- a unique indication for which the lower tiered antihypertensives lack

Recommendation 4: Cough and Cold Coverage Update

MOTION CARRIED by unanimous approval.

New Coverage of OTC Cold Products:

1. Liquid decongestant products are covered for children 6 through 12 years of age. Single ingredient Ibuprofen and acetaminophen liquid products are covered for children through 12 years of age.

2. Maximum quantity of 120 ml for a total of 3 claims per year for this category.

3. There is no requirement for a prescription.

Recommendation 4: Annual Review of Amitiza®, Lotronex®, and Zelnorm®

NO ACTION REQUIRED.

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

Recommendation 4: Annual Review of Immunomodulators

NO ACTION REQUIRED.

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

Appendix B

Retrospective Drug Utilization Review Report

Claims Reviewed for October 2007

Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
Total # of messages returned by system when no limits were applied	41,469	65,567	1,049,412	31,634
Limits which were applied	Established, Major, Males and Females, Age 66-150	Narcotics, Males and Females, Age 16-18	Contraindicated, Males and Females, Age 16-21, Asthma	High Dose only, 0-21 year old, male and females, Abilify and Geodon
Total # of messages after limits were applied	4	178	89	7
Total # of members reviewed after limits were applied	4	145	75	7

LETTERS			
Prescribers		**Pharmacies**	
Sent	**Responded**	**Sent**	**Responded**
111		29	

Retrospective Drug Utilization Review Report

Claims Reviewed for June 2007

Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
Limits which were applied	Established, Major, Males and Females, Age 19-40	Antiplatelet agents, Males and Females, Age 0-150	Contraindicated, Chronic Kidney Disease, Males and Females, Age 0-150	High Dose only, Digitalis, Age 0-150

Response Summary (Prescriber)
Letters Sent: 55
Response Forms Returned: 28

The response forms returned yielded the following results:

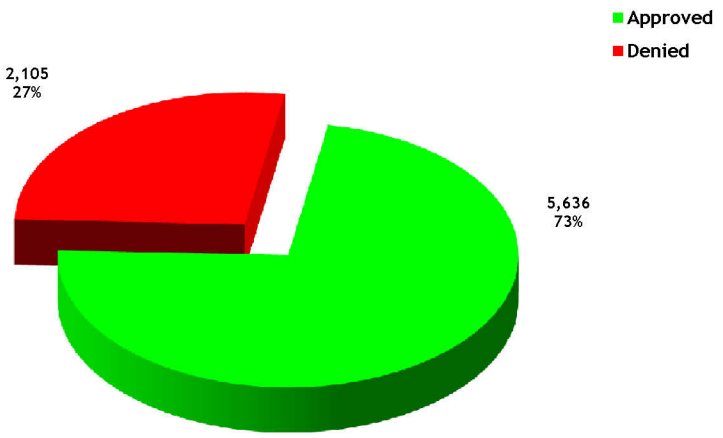
0 (0%)	*Record Error—Not my patient.*
5 (18%)	*No longer my patient.*
2 (7%)	*Medication has been changed prior to date of review letter.*
7 (25%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
8 (29%)	*I am aware of this situation and will plan to continue monitoring therapy.*
6 (21%)	*Other*

Response Summary (Pharmacy)
Letters Sent: 42
Response Forms Returned: 25

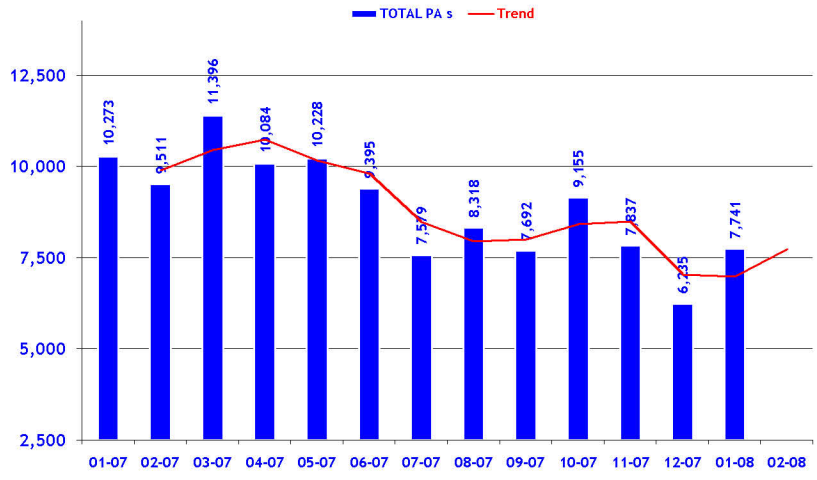
The response forms returned yielded the following results:

0 (0%)	*Record Error—Not my patient.*
2 (8%)	*No longer my patient.*
4 (16%)	*Medication has been changed prior to date of review letter.*
4 (16%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
9 (36%)	*I am aware of this situation and will plan to continue monitoring therapy.*
6 (24%)	*Other*

PRIOR AUTHORIZATION ACTIVITY REPORT
January 2008



PRIOR AUTHORIZATION REPORT
January 2007 – January 2008



Activity Audit for

January 01, 2008 Through January 31, 2008

	Average Length of Approvals in Days	Approved	Denied	Total
ACE Inhibitors	107	11	4	15
Angiotensin Receptor Antagonist	358	50	39	89
Antidepressant	271	224	332	556
Antihistamine	97	474	289	763
Antiulcers	18	18	1	19
Anxiolytic	93	2,827	395	3,222
Calcium Channel Blockers	124	6	1	7
Growth Hormones	170	25	2	27
HTN Combos	189	10	12	22
Insomnia	103	55	23	78
Nsaids	331	31	75	106
Plavix	301	154	24	178
Stimulant	210	664	156	820
Others	115	1,085	752	1,837
Emergency PAs		2	0	2
Total		**5,636**	**2,105**	**7,741**
Overrides				
Brand	257	34	23	57
Dosage Change	15	339	23	362
High Dose	198	2	0	2
Ingredient Duplication	3	1	1	2
Lost/Broken Rx	16	85	7	92
Nursing Home Issue	15	78	2	80
Other	27	36	7	43
Quantity vs. Days Supply	238	226	113	339
Stolen	6	6	2	8
Wrong D.S. on Previous Rx	2	1	2	3
Overrides Total		**807**	**179**	**986**

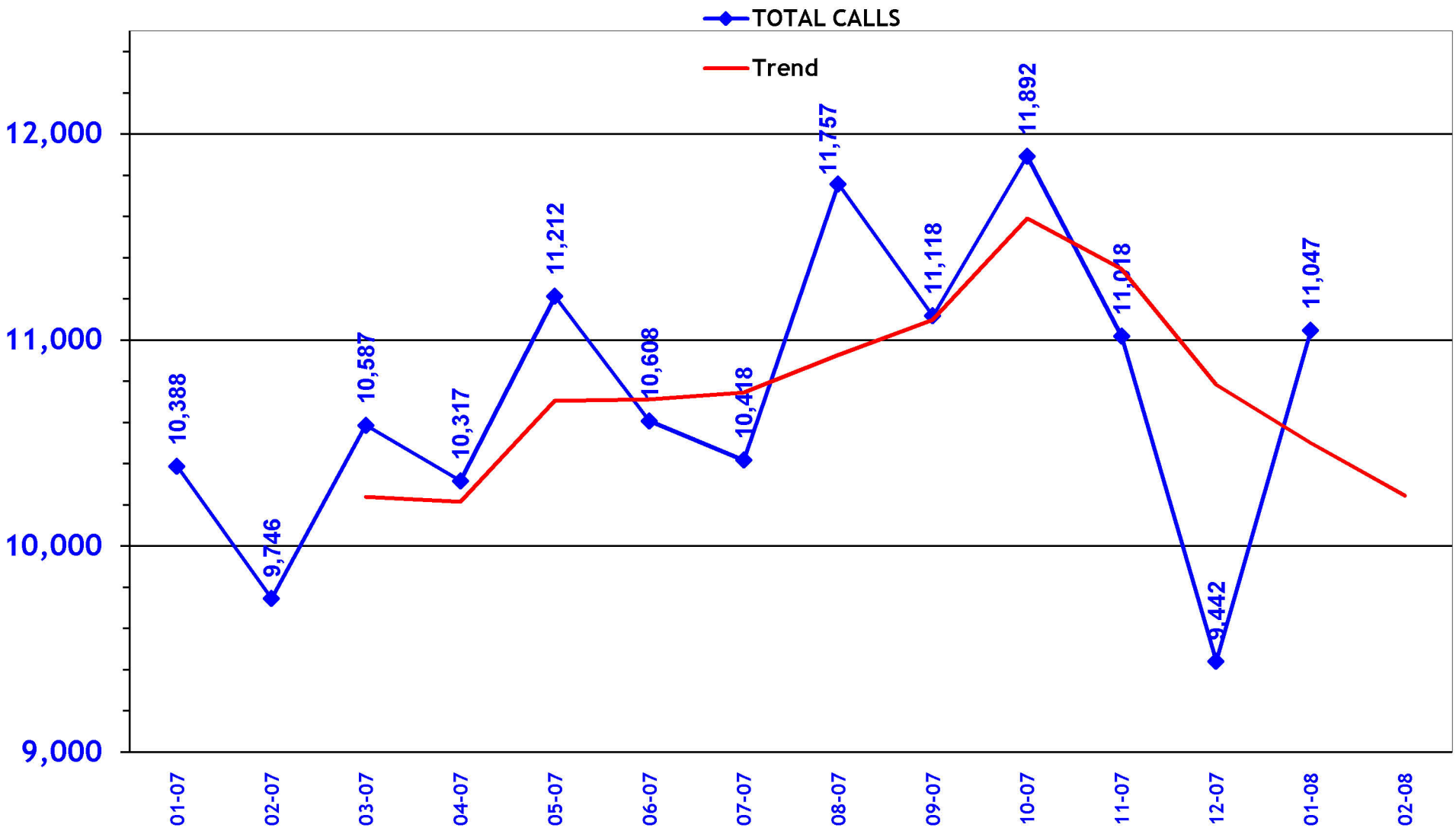
Denial Reasons

Lack required information to process request.	1,976
Unable to verify required trials.	747
Considered duplicate therapy. Member has a prior authorization for similar medication.	145
Does not meet established criteria.	133
Not an FDA approved indication/diagnosis.	130
Requested dose exceeds maximum recommended FDA dose.	71
Member has active PA for requested medication.	22
Medication not covered as pharmacy benefit.	6

Duplicate Requests	404
* Changes to existing	728

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

CALL VOLUME MONTHLY REPORT
January 2007 – January 2008



04-06 thru 03-07: corrected totals

Appendix C

60 Day Notice to Prior Authorize Narcotic Analgesics

Oklahoma HealthCare Authority, February 2008

This category was introduced for possible inclusion in the Product Based Prior Authorization program in September 2007. See the September DUR packet for a more complete discussion of the category. This notice and statement of potential economic impact are presented to meet the statutory requirements of 63 O.S. Sec. 5030.5.

Total Reimbursement – January 2007 through June 2007

BRAND NAME	CLAIMS	UNITS	DAYS	MEMBERS	COST	UNITS / DAY	CLAIMS/ CLIENT	COST/ DAY	PERCENT COST
Fentanyl	3,416	34,418	97,406	1,316	$ 680,038.61	0.35	2.60	$ 6.98	20.46%
Duragesic	57	565	1,650	23	$ 13,080.53	0.34	2.48	$ 7.93	0.39%
Morphine ER	921	77,528	27,173	305	$ 95,688.00	2.85	3.02	$ 3.52	2.88%
Kadian	514	28,307	14,819	159	$ 159,614.03	1.91	3.23	$10.77	4.80%
Avinza	458	14,875	13,615	185	$ 104,127.10	1.09	2.48	$ 7.65	3.13%
Oxycontin	8,837	560,773	258,604	3,630	$2,196,617.15	2.17	2.43	$ 8.49	66.08%
Opana ER	256	14,440	7,184	137	$ 75,143.33	2.01	1.87	$10.46	2.26%
TOTAL	**14,459**	**730,906**	**420,451**	**5,755**	**$3,324,308.75**	**1.74**		**$7.91**	**100.00%**

Diagnoses

The ten most frequent diagnoses found for these members from January 2006 through June 2007 are listed in the table below. There were also a total of 1,807 members with a cancer related diagnosis.

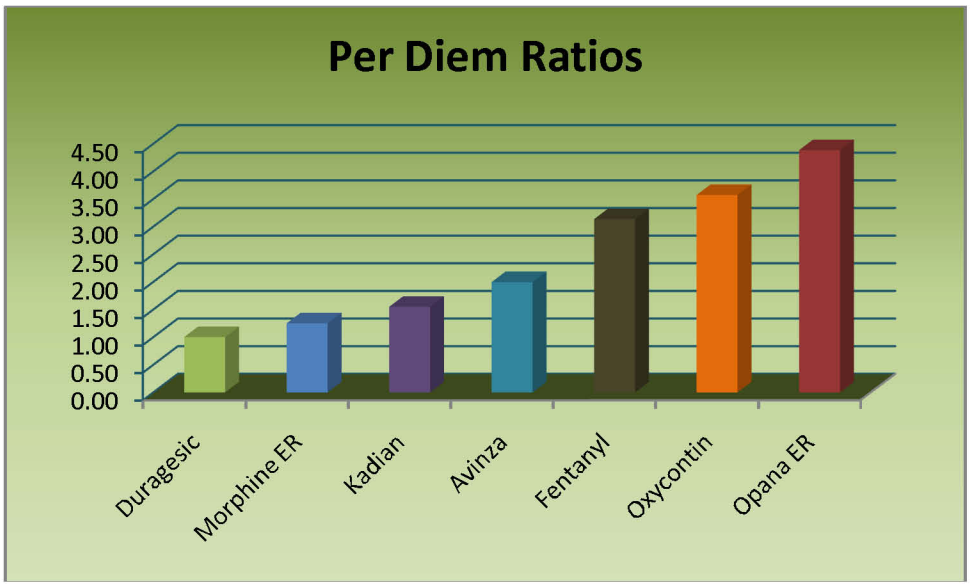
ICD-9	Description	Members
401.90	UNSPECIFIED ESSENTIAL HYPERTENSION	1,898
724.20	LUMBAGO	1,869
305.10	NONDEPENDENT TOBACCO USE DISORDER	1,753
724.50	UNSPECIFIED BACKACHE	1,604
786.50	UNSPECIFIED CHEST PAIN	1,500

729.50	PAIN IN SOFT TISSUES OF LIMB	1,430
311.00	DEPRESSIVE DISORDER, NOT ELSEWHERE CLASSIFIED	1,402
789.00	ABDOMINAL PAIN, UN SPECIFIED SITE	1,381
786.05	SHORTNESS OF BREATH	1,182
300.00	ANXIETY STATE, UNSPECIFIED	1,174

Market Analysis

Currently two morphine extended release products are available as generic products, along with the fentanyl patch. In the next few years there are patent expirations scheduled for Oxycontin, Kadian, and Opana ER. Three new strengths of Oxycontin are now available: 15, 30 and 60 mg.

The following graph shows the ratio of the least expensive per diem (after rebates and dispensing fees have been removed). The lowest bar indicated the lowest ingredient per diem. The ratio does not reflect actual dollar amounts but is a comparison of each product to the lowest.



Efficacy and Safety[1]:

The Oregon Evidence-based Practice Center completed a drug class review on long-acting narcotic analgesics in April 2006. The group reviewed 25 randomized trials involving this class. There were only 5 trials that compared two drugs to each other: three with transdermal

[1] Chou R. Drug Class Review on Long-Acting Opioid Analgesics. Final Report. 2006. Available at: http://www.ohsu.edu/drugeffectiveness/reports/final.crm.

fentanyl and long-acting morphine, one with once-daily morphine and a twice daily morphine, and one with long-acting oxymorphone to long-acting oxycodone.

On the issue of comparative effectiveness, all drugs were found to be effective and there was no evidence to support the use of one long-acting product over another. There was insufficient head-to-head trial data to indicate whether one product was better than another based on withdrawal rates except for the transdermal fentanyl compared to long-acting morphine which had a higher rate of withdrawal for fentanyl, but a lower rate of constipation. All of the head-to-head trials excluded patients at risk for addiction or abuse. Two retrospective trials found long-acting oxycodone had a higher rate of constipation than transdermal fentanyl.

The group summarized that there is insufficient evidence to prove that one product is either safer or more effective than another.

Recommendations:

The College of Pharmacy recommends adding the long-acting narcotic analgesics to the Product Based Prior Authorization Program.

Tier 1	Tier 2	Tier 3
Morphine ER*	Avinza	Oxycontin
Duragesic†	Kadian	Opana ER
Fentanyl Patches		

*Branded products will require a brand name override.
†Product would move to Tier 2 or Tier 3 if current manufacturer's federal rebate status changes.

Recommended Criteria:

1. Failure of all Tier 1 products is required prior to receiving authorization for a Tier 2 product.
2. Failure of all Tier 2 products is required prior to receiving authorization for a Tier 3 product.
3. Failure is defined as continued breakthrough pain at the highest available dosage form of product.
4. Non-cancer clients must have attempted short-acting pain management regimens, including appropriate adjunct therapies.
5. Must be for ongoing continuous therapy, not on an as needed basis.

Potential Secondary Costs

Overall efficacy is considered to be equal across this class, but drug selection requires individual patient history which includes, but is not limited to: other illnesses, disease risk factors, and current symptoms.

Potential Administrative Costs

Based on a potential shift of proposed Tier 3 and Tier 2 products to a Tier 1 product of 45%, it is estimated that approximately 2,500 petitions would be required. The proposed tier changes would affect approximately 70 % of the total population for this PBPA category.

Previously, it has been theorized that total cost per petition to the *healthcare system* (includes cost to physicians, pharmacists, and program) is between $7.32 and $14.17. Total cost per petition to the *healthcare system* is estimated to be between $18,300 and $35,425 annually. Anticipated actual administrative cost to the program is projected to be less than $20,000.

Potential Program Savings

Potential pharmacy reimbursement savings to the program based on recommended tiers and a potential shift of 45% of market share from Tier 3 and Tier 2 to Tier 1 is estimated to be $1,177,407 annually.

Total Potential Savings

Potential Reimbursement Savings:	$ 1,177,407		$ 1,177,407
Potential Administrative Cost:	$ 35,425		$ 18,300
Total Potential Reimbursement Savings:	**$ 1,141,982**	**to**	**$ 1,159,107**

Percent of Current Reimbursement **~ 17.2 %**

Appendix D

30 Day Notice to Prior Authorize
Combigan (TM) (Brimonidine Tartrate and Timolol Maleate)[1]
Anti-Glaucoma Agents
Oklahoma Health Care Authority
February 2008

Manufacturer Allergan
Classification Alpha[2] Agonist/Nonselective Beta-Blocker; Anti-Glaucoma
Status: prescription only

Summary

Combigan(TM) (Brimonidine Tartrate and Timolol Maleate) 0.2%/0.5% received FDA approval on October 31, 2007 for the treatment of elevated intraocular pressure (IOP) in patients with glaucoma or ocular hypertension who require adjunctive or replacement therapy due to inadequately controlled IOP. Both active ingredients are commercially available as single-agent products. The IOP-lowering of COMBIGAN(TM) ophthalmic solution dosed twice a day was slightly less than that seen with the concomitant administration of timolol maleate ophthalmic solution 0.5% dosed twice a day and brimonidine tartrate ophthalmic solution 0.2% dosed three times per day.(2)

Brimonidine 0.2% is selective agonist for alpha$_2$-receptors which causes reduction of aqueous humor formation and increased uveoscleral outflow. Timolol maleate blocks both beta$_1$- and beta$_2$-adrenergic receptors which reduce intraocular pressure by reducing aqueous humor production or possibly outflow. In addition, this component reduces blood pressure by blocking adrenergic receptors and decreasing sympathetic outflow, producing a negative chronotropic and inotropic activity by blocking beta$_1$-adrenergic receptors.

Cost Comparison

	EAC / mL	SMAC / mL	Daily Dose[2]	Cost (5 ml)
Brimonidine tartrate 0.2%	$5.73	$3.05	1 drop TID	$15.25
Timolol Maleate 0.5%	$3.89	$0.62	1 drop BID	$ 3.10
Brimonidine tartrate 0.2%/Timolol Maleate 0.5%	$12.45	n/a	1 drop BID	$62.25

2 Based on # drops per mL of solution and average daily dose (brimonidine=25 drops/ml,timolol=32 drops/ml, Combigan=29.6)

Recommendations

The College of Pharmacy recommends placement of Combigan(TM). (Brimonidine Tartrate and Timolol Maleate) 0.2%/0.5% into the tier-2 products in the Anti-Glaucoma PBPA category.

PA Criteria

1. FDA approved diagnosis.
2. Member must attempt at least one Tier-1 trial of a minimum of 4 weeks duration within the last 90 days. Tier-1 trial must include both brimonidine tartrate and timolol maleate in combination.
3. Approval may be granted if there is a documented adverse effect, drug interaction, or contraindication to Tier-1 products.
4. Member must have had a comprehensive dilated eye exam within the last 365 day period as recommended by the National Institute of Health.
5. Approval duration will be for 1 year.

Tier 1	Tier 2
Beta-Blockers	
Betagan 0.25%,0.5% (Levobunolol) Optipranolol 0.3% (Metipranolol) Timoptic, Betimol, Istalol, Timoptic Ocudose, Timoptic XE 0.25,0.5% (Timolol Maleate) Cartrol, Ocupress 1% (Carteolol) Betoptic-S 0.5% (betaxolol)	Betoptic-S (betaxolol) Cosopt (Dorzolamide and Timolol)* Timoptic 0.5% Dropperette
Prostaglandin Analogs	
Xalatan (Latanoprost)** Travatan, Travatan Z (Travoprost)	Lumigan (Bimatoprost)
Adrenergic Agonists#	
Propine (Dipivefrin)	
Alpha-2 Adrenergic Agonists	
Brimonidine 0.2%	Alphagan P 0.1, 0.15% (Brimonidine) Iopidine 1% Apraclonidine
Carbonic Anhydrase Inhibitor@	
Cosopt (Dorzolamide and Timolol)*	Azopt (Brinzolamide) Trusopt (Dorzolamide)
Cholinergic Agonists[1]/Cholinesterase Inhibitors[2]	
Isopto Carpine, Pilopine HS 0.5,1,2,4,6 %(Pilocarpine)	Isopto, Miostat 1.5, 3% (Carbachol)[1] Phospholine Iodide (Echothiophate Iodide)[2]
Combination Products	
	Brimonidine 0.2%/Timolol Maleate 0.5% (Combigan)*

Blue indicates Tier-1 due to Supplemental Rebate Participation

@ Oral formulations of Carbonic Anhydrase Inhibitors also available

*Combination product

**Tentative generic approval by FDA 03/09/2007; supplemental rebate agreement participation

Dosage Forms

Combigan ophthalmic solution is available as brimonidine tartrate 0.2%/timolol maleate 0.5% in a 5ml bottle

Indication

Reduction of intraocular pressure (IOP) in patients with glaucoma or ocular hypertension.

Dosage

Ophthalmic: Children ≥2 years and Adults: Instill 1 drop into affected eye(s) twice daily

Pregnancy Risk Factor C

Contraindications

Hypersensitivity to brimonidine, timolol, or any other component of the formulation; current or history of bronchial asthma, severe chronic obstructive pulmonary disease (COPD); sinus bradycardia, second- or third-degree atrioventricular block, overt cardiac failure, cardiogenic shock. Also see individual agents.

Precautions and Adverse Effects

Inadvertent contamination of multiple-dose ophthalmic solutions has the potential to cause bacterial keratitis.

Use of agents that reduce/suppress aqueous humor production has been associated with choroidal detachment after filtration procedures. Discontinue use in patients with chronic or recurrent choroidal detachment.

May enhance orthostatic hypotension. Use cautiously.

Disease-related concerns:

- Angle-closure glaucoma: This medication not for use alone to treat acute angle-closure glaucoma (has no effect on papillary constriction).

- Bronchospastic disease: In general, patients with bronchospastic disease (eg, asthma, COPD) should not receive beta-blockers; if used at all, should be used cautiously with close monitoring.

- Conduction abnormalities: Consider pre-existing conditions such as sick sinus syndrome before initiating.

• Diabetes: Use with caution in patients with diabetes mellitus; may potentiate hypoglycemia and/or mask signs and symptoms.

• Heart failure: Use with caution in patients with compensated heart failure and monitor for a worsening of the condition.

• Hepatic impairment: Use with caution in patients with hepatic impairment; not studied.

• Myasthenia gravis: Use with caution in patients with myasthenia gravis; may worsen myasthenia-related muscle weakness.

• Psychiatric disease: Use with caution in patients with a history of psychiatric illness; may cause or exacerbate CNS depression.

• Renal Impairment: Use with caution in patients with renal impairment; not studied.

• Thyrotoxicosis: Signs of hyperthyroidism (eg, tachycardia) may be masked by beta-blockers. Avoid abrupt withdrawal if thyrotoxicosis is suspected (may precipitate thyroid storm).

• Vascular disease: Use with caution in patients with cerebral/coronary insufficiency as well as peripheral vascular disease (including Raynaud's, thromboangiitis obliterans).

Side Effects

>10%	Conjunctival hyperemia, burning sensation
1% to 10%	Hypertension,somnolence,headache,depression,xerostomia,weakness,stinging, pruritus, allergic conjunctivitis, conjunctival folliculosis, blurred vision, blepharitis, corneal erosion, dry eyes, epiphora, eye discharge, eyelid edema, eyelid erythema, superficial punctuate keratitis, eye pain, foreign body sensation, eye irritation, eyelid pruritus

Drug Interactions

Timolol: Substrate of CYP2D6 (major); Inhibits CYP2D6 (weak)

Patient Information

May cause drowsiness. Can be absorbed by contact lenses. Remove lenses before the application and do not reinsert for at least 15 minutes. May cause redness and burning. Breast-feeding is not recommended. Safety and efficacy have not been established in children <2 years of age; use in children <2 years of age is not recommended.

REFERENCE

Combigan(TM). (Brimonidine Tartrate and Timolol Maleate) 0.2%/0.5% Product Information. Lexicomp. Accessed 2008.

Appendix E

Drug Utilization Review – Beta-Blockers
Oklahoma Health Care Authority
February 2008

Introduction

Cardiovascular disease is a leading cause of death in adults in the United States. Hypertension is estimated to affect almost 65 million individuals nationwide and 1 billion worldwide. Implementing early hypertension treatment can slow disease progression and delay the development of heart attack, heart failure, stroke, kidney disease, and blindness. Beta-blockers have been a mainstay of first-line pharmacologic treatment for primary uncomplicated hypertension. Clinical evidence has shown beta-blockers to be effective in hypertension, post myocardial infarction, angina pectoris, heart failure, dysrhythmias, migraines, hypertrophic obstructive cardiomyopathy, and preventing premature death. Beta-blockers have been commonly used as primary prevention of coronary heart disease. Current clinical literature remains inadequate to support these agents as a first-line therapy for specific indications for the prevention of cardiovascular events. Newer beta-blocker agents have been developed which may have more favorable outcomes in reducing morbidity and mortality.

Background[1]

Blood Pressure	Systolic Blood Pressure	Diastolic Blood Pressure
Normal	<120	and <80
Pre-hypertension	120-139	or 80-89
Stage 1	140-159	or 90-99
Stage 2	≥160	or ≥ 100

It is estimated 30% patients are unaware they have hypertension. The systolic blood pressure becomes more indicative of cardiovascular risk with patients over the age of 50. Systolic blood pressure is more difficult to control compared to diastolic blood pressure.

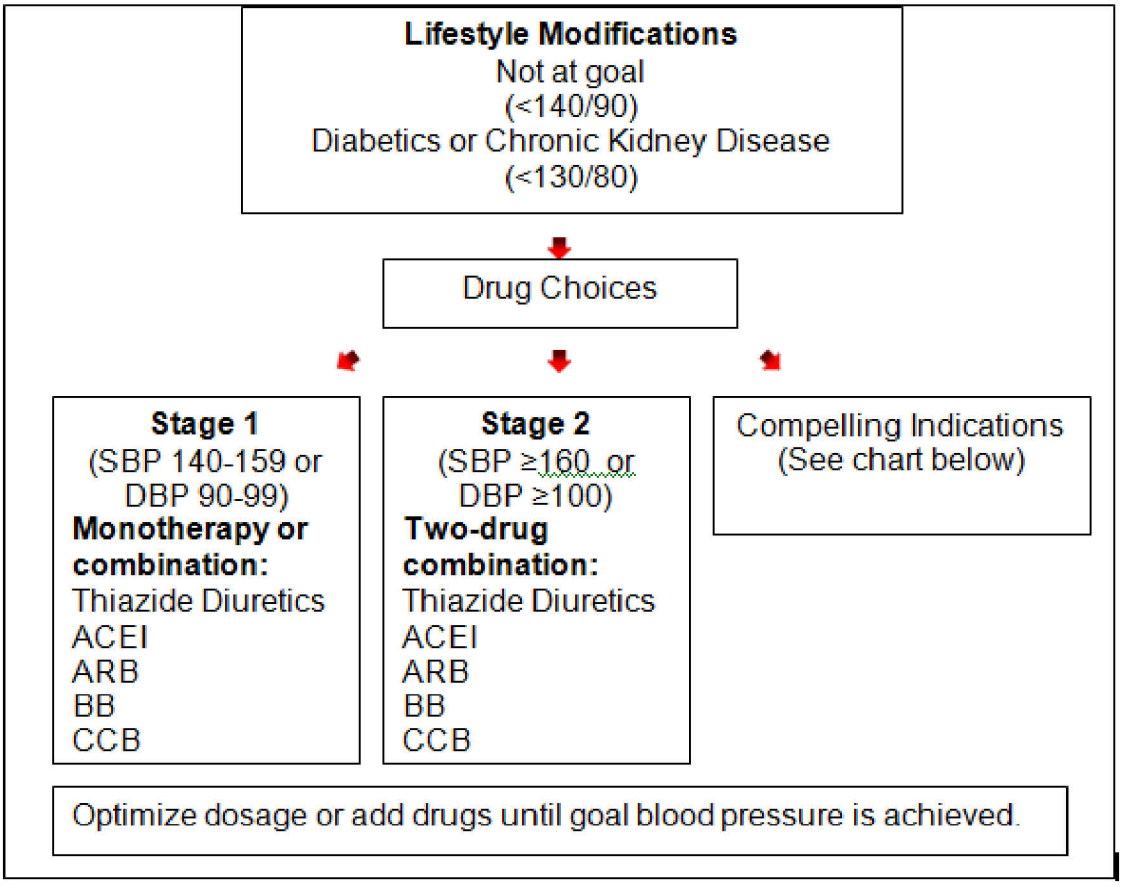
Most patients often require two or more medications to control their hypertension. Those patients who are unable to control blood pressure with three medications at full doses are categorized as having resistant hypertension.

Purpose: Evaluate current utilization and prescribing trends of beta-blockers among SoonerCare members to assess whether a PBPA category would improve member health outcomes while minimizing health care costs.

Why: Ensure members are receiving appropriate care based on clinical literature and recent evidence regarding the safe and effective use of beta-blockers. Cost-effective use of beta-blockers and newer available agents can prevent cardiovascular disease progression while reducing the overall use of medical services and health care costs.

Treatment[1,4,5]

Treatment Algorithm for Hypertension JNC VII[1]:



Compelling Indications	Recommended Treatment[1]							
	Diuretics	Nitrates Vasodilators	BB	ACEI	ARB	CCB	ALDO/ ANT	
Heart Failure	√	√	√	√	√		√	
Post-MI			√	√			√	
High-risk coronary disease	√		√	√		√		
Diabetes	√		√	√	√	√		
Chronic kidney disease				√	√			
Recurrent stroke prevention	√			√				
Angina Pectoris		√	√			√		
Arrhythmias			√			√		
Isolated Systolic Hypertension	√		√			√		

ACEI=Angiotension converting enzyme inhibitor, ARB=Angiotension receptor blocker, BB=Beta-blocker, CCB=Calcium Channel Blocker, MI=Myocardial Infarction, Aldo/Ant=Aldosterone antagonist

Special Considerations[1,4,5]

Heart Failure

- Asymptomatic individuals with ventricular dysfunction recommend treatment with BB's or ACEI's.
- Symptomatic ventricular dysfunction requires loop diuretics along with ACEI's, BB's, ARB's or Aldosterone antagonists.

Diabetic Hypertension

- Combination of two or more drugs: Thiazide diuretics, BB's, ACEI's, ARB's and CCB's.

Chronic Kidney Disease

- Combination of three or more drugs: usually loop diuretics with other drug classes.
- ACEI's or ARB's favorable effects on progression of diabetic and nondiabetic renal disease.

Cerebrovascular Disease

- Blood pressure control at approximately 160/100 mmHg is appropriate during acute stroke until stabilized or improved.
- Recurrent stroke treated with combination of *ACEI and thiazide diuretic*.

Left ventricular hypertrophy

- Acceptable treatment with all antihypertensive agents except hydralazine and minoxidil.

Peripheral arterial disease

- Any class of antihypertensive drugs in conjunction with aspirin therapy

Hypertension in pregnancy

- Methyldopa, BB's, and vasodilators are preferred medications for the safety of fetus.

Beta-blocker relevant indications

- May be used to treat tachyarrythmias/fibrillation, migraines, thyrotoxicosis (short term), essential tremor, or perioperative hypertension.

Beta Blocker Cardiovascular Considerations[8]

Atrial Fibrillation: Beta-blocker therapy provides effective rate control in patients with atrial fibrillation.

Chronic Stable Angina: Beta-blockers are effective in the treatment of chronic stable angina as monotherapy or when combined with nitrates and/or calcium channel blockers. In patients with severe intractable angina requiring negative cardiac chronotropic medications, pacemaker placement has been carried out to maintain heart rate in the setting of large doses of beta-blockers and/or calcium channel blockers. Beta-blockers are ineffective in the treatment of pure vasospastic (Prinzmetal) angina.

Heart Failure: Strong evidence supports that beta-blocker therapy, without intrinsic sympathomimetic activity (ISA), should be initiated in select patients with **stable** congestive heart failure (NYHA Class II-III). Carvedilol is a nonselective beta-blocker with alpha-blocking and antioxidant properties. To date, carvedilol, sustained release metoprolol, and bisoprolol have demonstrated a beneficial effect on morbidity and mortality. It is important that beta-blocker therapy be instituted initially at very low doses with gradual and very careful titration. Because carvedilol has alpha-adrenergic blocking effects, it may lower blood pressure to a greater extent.

Hypertension: Beta-blocker therapy in the treatment of hypertension has been associated with improved cardiovascular outcomes. According to the 2003 JNC-VII guidelines for the treatment of hypertension, most patients with hypertension will require treatment with at least 2 antihypertensives. First-line therapy for hypertension is a diuretic (eg, hydrochlorothiazide or chlorthalidone). When a diuretic cannot be used or when a compelling indication exists that requires the use of other drugs, other types of antihypertensives may be used (eg, ACEIs, ARBs, beta-blockers, CCBs). Beta-blockers are among the multiple choices of agents that have shown benefit in a number of different patient subtypes. Compelling indications for a beta-blocker include patients with heart failure, postmyocardial infarction, high coronary disease risk, or diabetes. In type 2 diabetic patients, a UK Prospective Diabetes Study Group (UKPDS) trial showed that beta-blocker therapy (atenolol) was as effective as an ACE inhibitor in reducing cardiovascular events and that the benefits of therapy were related more to the degree of antihypertensive efficacy rather than the class of drug used.

Treatment should be targeted to a goal blood pressure of <140/90 mm Hg. If diabetes or renal disease coexists, the blood pressure goal should be <130/80 mm Hg.

ST-Segment Elevation Myocardial Infarction (STEMI): Beta-blockers, without intrinsic sympathomimetic activity (ISA), have been shown to decrease morbidity and mortality when initiated in the acute treatment of STEMI and continued long-term. Oral beta-blockade should be initiated promptly in patients without contraindications (eg, signs of heart failure, evidence of a low output state, risk of cardiogenic shock, or other beta-blocker contraindications) (Class I recommendation). Use of intravenous beta-blockade may be considered and given promptly if the patient is experiencing concomitant hypertension or a tachyarrhythmia (Class IIa recommendation).

Unstable Angina/Non-ST-Segment Elevation MI (UA/NSTEMI): In the treatment of UA/NSTEMI, oral beta-blockade should be initiated within the first 24 hours in patients without contraindications (eg, signs of heart failure, evidence of a low output state, risk of cardiogenic shock, or other beta-blocker contraindications) (Class I recommendation). Use of intravenous beta-blockade should only be considered if the patient is experiencing concomitant hypertension upon presentation (Class IIa recommendation).

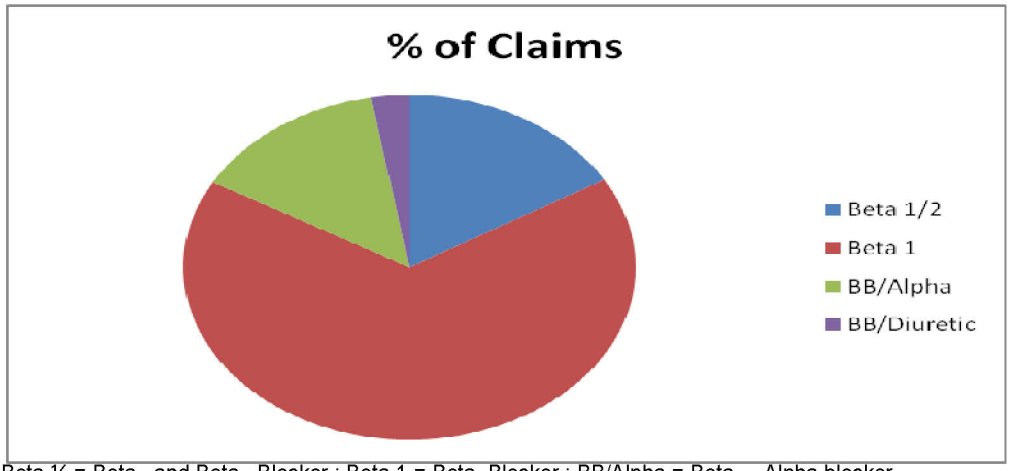
Withdrawal: Beta-blocker therapy should not be withdrawn abruptly, but gradually tapered to avoid acute tachycardia and hypertension.

Cost and Utilization

FY 2006 versus FY 2007			% Change
Cost FY '07		**$1,850,029.22**	**50.2↓**
	Cost FY '06	*$3,714,163.08*	
Claims FY '07		**60,764**	**47.3↓**
	Claims FY '06	*115,346*	
Cost per Claim FY '07		**$30.45**	**5.4↓**
	Cost per Claim FY '06	*$32.20*	
Members FY '07		**13,851**	**54.6↓**
	Members FY '06	30,513	

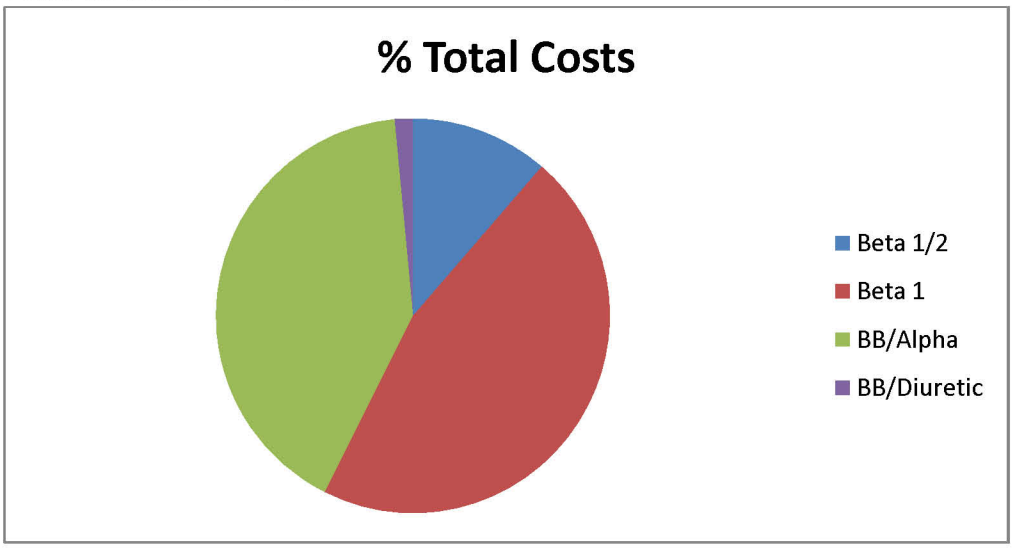
(See back for Individual product utilization)

Market Share of Beta-Blockers



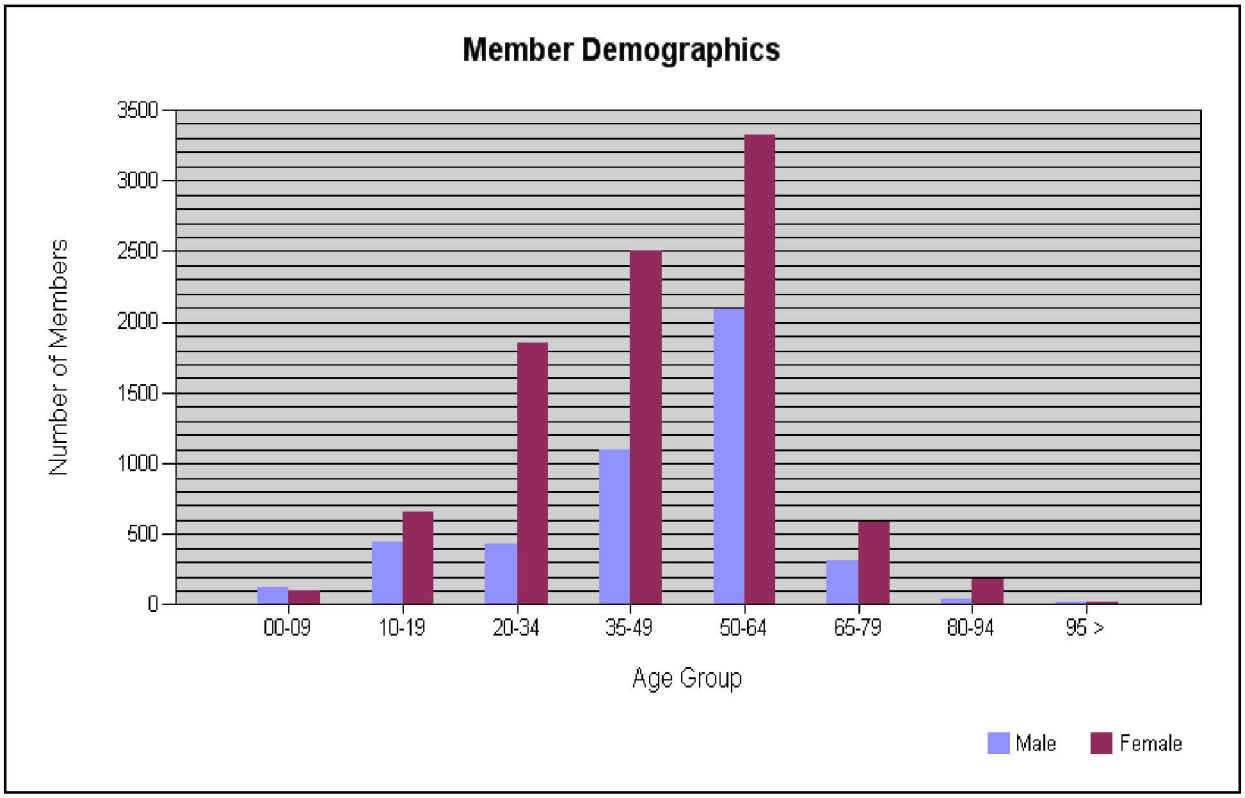
Beta ½ = $Beta_1$ and $Beta_2$ Blocker ; Beta 1 = $Beta_1$ Blocker ; BB/Alpha = $Beta_{1,2}$ Alpha blocker

Total of Costs FY '07

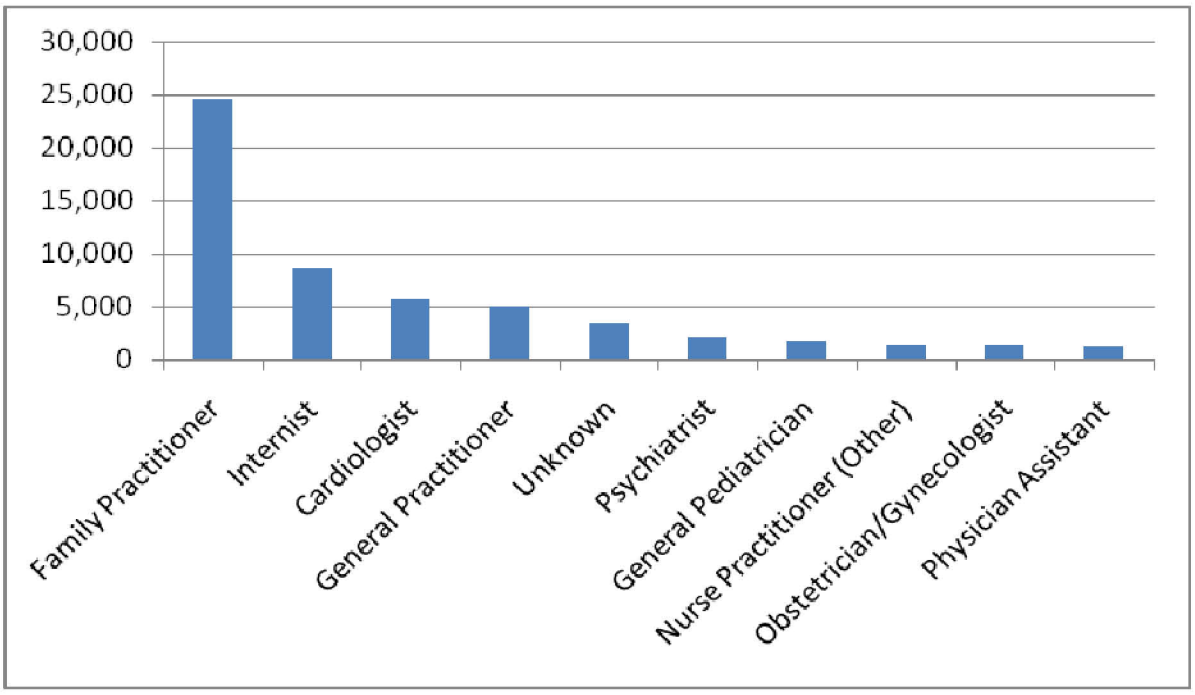


Beta ½ = $Beta_1$ and $Beta_2$ Blocker ; Beta 1 = $Beta_1$ Blocker ; BB/Alpha = $Beta_{1,2}$ Alpha blocker

Age and Gender FY '07



Prescriber Specialty



Update on Market News

October 2006 – FDA approval of Coreg CR(Carvedilol)

December 2007 – New $beta_1$ selective blocker, Bystolic (Nebivolol), receives approval for the treatment of hypertension. In addition, nebivolol can cause vasodilation in patients leading to reduced peripheral vascular resistance.

Recommendation

The College of Pharmacy does not recommend any changes to this class of antihypertensives at this time and will continue to monitor utilization and market changes.

REFERENCES

1. Treatment Guidelines: The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. National Heart, Lung, and Blood Institute December 2003. Available at: http://www.nhlbi.nih.gov/guidelines/hypertension/jnc7full.htm>. Accessed June 1, 2006.
2. Lindholm LH, Carlberg B, Samuelsson O. Should β blockers remain first choice in the treatment of primary hypertension? A meta-analysis. Lancet 2005;366:1545-1553.
3. Beevers DG. The end of β blockers for uncomplicated hypertension? Lancet 2005;366:1510-1512.
4. 2006 AHA/ACC Secondary Prevention Guidelines for Patients with Coronary and Other Vascular Disease: Summary. The Pharmacist's Letter 2006;22(6):220601. Available at: http://www.pharmacistsletter.com/(bi4lpu452al5h355iyda3eax)/home.aspx?li=0&st=0&cs=&s=PL. Accessed online June 1, 2006.
5. APHA Special Report. The Appropriate Use of β blockers in Heart Failure. American Pharmacists' Association, Baltimore MD; 2006.
6. Treatment Guidelines: Drugs for Hypertension. Medical Letter June 2005. Available at: http://www.medicalletter.org. Accessed July 10, 2006.
7. Which Beta-Blocker? The Medical Letter 2001;43(W1097A):9-11. Available at: http://www.medicalletter.org. Accessed July 10, 2006.
8. Product Information Coreg®(Carvedilol) Lexicomp. Accessed 2008.

Beta-Blockers [6,7]

Product	Dosing	Cost[6,7]	Indications*	Cardio-selective	Side Effects**
Beta-Blockers					
Atenolol (25, 50, 100mg) tabs	25-100mg QD-BID	 $21.00	1,2,3	Yes	A
Betaxolol (10, 20mg) tabs	5-40mg QD	 $27.30	1	Yes	A
Bisoprolol (5, 10mg) tabs	5-20mg QD	 $30.60	1	Yes	A
Metoprolol (25, 50, 100mg) tabs (25,50,100,200mg) XL tabs	50-200mg QD-BID	 $14.40 $25.80	1,2,3, 5,11	Yes	A
Nadolol (20, 40, 80, 120mg) tabs	20-320mg QD	 $22.20	1,2,10	No	A
Propranolol (10, 20, 40, 60, 80mg) tabs (60, 80, 120, 160mg) ER caps	40-240mg QD-BID	 $15.60 $33.30	1,2,3,8,10,11, 12,13,14	No	A
Timolol (5, 10, 20mg) tabs	10-60mg BID	 $18.00	1,3,10	No	A
Esmolol (10mg/ml,20mg/ml,250mg/ml)	50-300 mcg/kg/min	N/A	1,4,6,7,11	Yes	A
Sotalol (80, 120, 160, 240mg) tabs	80-640mg BID	$75.00	4,11	No	A
Nebivolol (2.5,5,10mg) tabs	5-40mg QD	$56.40	1	Yes	B
Beta-Blockers with Intrinsic Sympathomimetic Activity (ISA)					
Acebutolol (200, 400mg) caps	200-1200mg QD-BID	$22.20	1,2,4	Yes	B
Carteolol (2.5, 5mg) tabs	2.5-10mg QD	Brand $42.30	1	No	B
Penbutolol (20mg) tabs	10-80mg QD	Brand $51.60	1	No	B
Pindolol (5,10mg) tabs	10-60mg BID	 $42.60	1	No	B
Beta-Blockers with Alpha Blocking Activity					
Carvedilol (3.125, 6.25, 12.5, 25mg) tabs (10,20,40,80 mg CR)	12.5-50mg BID 20mg QD	Brand $106.20 $117.00	1,5	No	C
Labetalol (100, 200, 300mg) tabs	200-1200mg BID	 $23.40	1	No	C
Beta-Blockers and Diuretics Combinations					
Atenolol/Chlorthalidone (50-25, 100-25mg) tabs	50-100mg QD	$11.99	1	Yes	A
Bisoprolol/HCTZ (2.5-6.25,5-6.25,10-6.25mg) tabs	2.5-10mg QD	$22.99	1	Yes	A
Metoprolol/HCTZ (50-25,100-25,100-50mg)	50-100mg QD-BID	N/A	1	Yes	A
Propranolol/HCTZ (40-25, 80-25mg) tabs (80-50,120/50,160/50mg)	80-160mg QD-BID	$11.99 $55.50	1	No	A

Cost for 30 day supply of generic product at lowest daily dosage; Brand cost if generic unavailable

*Indications	
1. Hypertension	8. Cardiac Arrhythmias
2. Angina Pectoris	9. Post Myocardial Infarction
3. Myocardial Infarction	10. Migraine Prophylaxis
4. Ventricular Arrhythmias	11. Atrial Fibrillation
5. Congestive Heart Failure	12. Essential Tremor
6. Supraventricular Tachycardia	13. Hypertrophic Cardiomyopathy
7. Intra- or Post-operative Hypertension	14. Pheochromocytoma

**Side Effects		
A	B	C
Fatigue; depression; bradycardia; impotence; decreased exercise tolerance; congestive heart failure; worsening of peripheral arterial insufficiency; may aggravate allergic reactions; bronchospasm; may mask symptoms of and delay recovery from hypoglycemia; Raynaud's phenomenon; insomnia; vivid dreams or hallucinations; acute mental disorder; increased serum triglycerides, decreased HDL cholesterol; sudden withdrawal may lead to exacerbation of angina and myocardial infarction	Similar to other beta-adrenergic blocking agents, but with less resting bradycardia and lipid changes; acebutolol has been associated with a positive antinuclear antibody test and occasional drug-induced lupus; nebivolol potentially less sexual adverse effects	Similar to other beta-adrenergic blocking agents, but more orthostatic hypotension; hepatotoxicity

Beta-blocker Precautions

- May be less effective in African-American patients
- Use may be associated with higher incidence of development of type 2 diabetes and may mask symptoms of hypoglycemia but this should not deter treatment for select indications in patients with diabetes
- Beta-blocker alone in elderly not as effective as a diuretic monotherapy
- Beta-blockers with intrinsic sympathomimetic activity (ISA both beta agonist and antagonist effects) is contraindicated with angina or history of MI due to possible event reoccurence
- Sudden withdrawal of a beta-blocker in patients with angina pectoris may increase risk of myocardial infarction or cardiac arrhythmia.
- Side effects of beta-blockers may be minimized by gradual titration of dose when initiating therapy.
- **NOT** recommended in patients with asthma, reactive airway disease, second or third degree block when using non-cardioselective beta-blockers.
- Betapace should not be substituted for Betapace AF. Betapace AF is distributed with educational insert specifically for patients with atrial fibriallation/flutter.
- Beta-blocker therapy should be withdrawn gradually to avoid acute tachycardia, hypertension, and/or ischemia.

Beta $_1$ and Beta $_2$ Selective Agents

Product	Claims	Units	Days	Members	Costs	Unit/ day	Claims/ Member	Cost /Day	% Cost
PROPRANOLOL TAB 10MG	2,377	161,056	75,700	772	$15,742.76	2.13	3.08	$0.21	7.52%
PROPRANOLOL TAB 20MG	2,294	156,108	72,010	676	$16,709.44	2.17	3.39	$0.23	7.98%
PROPRANOLOL TAB 40MG	1,698	111,072	56,767	512	$13,433.37	1.96	3.32	$0.24	6.42%
INDERAL LA CAP 80MG	541	22,010	20,423	172	$35,118.35	1.08	3.15	**$1.72**	16.77%
INDERAL LA CAP 60MG	504	19,604	16,275	163	$26,158.59	1.2	3.09	**$1.61**	12.49%
PROPRANOLOL TAB 80MG	329	21,368	10,898	102	$2,841.80	1.96	3.23	$0.26	1.36%
INDERAL LA CAP 120MG	225	10,868	8,775	60	$21,094.36	1.24	3.75	**$2.40**	10.08%
PINDOLOL TAB 10MG	206	10,346	5,938	36	$2,180.59	1.74	5.72	$0.37	1.04%
PROPRANOLOL CAP 80MG ER	200	7,524	7,260	97	$10,627.16	1.04	2.06	**$1.46**	5.08%
PROPRANOLOL 20MG/5ML	197	36,712	5,586	40	$3,357.50	6.57	4.93	$0.60	1.60%
SOTALOL HCL TAB 80MG	188	11,027	6,110	40	$3,617.87	1.8	4.7	$0.59	1.73%
PROPRANOLOL TAB 60MG	170	10,738	5,029	47	$5,556.46	2.14	3.62	**$1.10**	2.65%
PROPRANOLOL CAP 60MG ER	155	5,778	5,200	74	$7,075.45	1.11	2.09	**$1.36**	3.38%
NADOLOL TAB 40MG	153	7,096	6,180	37	$1,678.40	1.15	4.14	$0.27	0.80%
NADOLOL TAB 20MG	142	6,791	5,016	44	$1,299.80	1.35	3.23	$0.26	0.62%
INNOPRAN XL CAP 80MG	123	4,593	4,283	34	$7,087.04	1.07	3.62	**$1.65**	3.39%
INDERAL LA CAP 160MG	96	5,176	4,096	27	$12,906.68	1.26	3.56	**$3.15**	6.16%
PROPRANOLOL CP 120MG ER	81	3,619	3,035	40	$6,208.86	1.19	2.03	**$2.05**	2.97%
INNOPRAN XL CAP 120MG	71	3,924	2,260	9	$6,446.28	1.74	7.89	**$2.85**	3.08%
NADOLOL TAB 80MG	67	3,846	2,493	13	$1,296.98	1.54	5.15	$0.52	0.62%
PINDOLOL TAB 5MG	48	2,391	1,656	14	$452.97	1.44	3.43	$0.27	0.22%
SOTALOL HCL TAB 160MG	41	2,648	1,324	6	$1,194.04	2	6.83	$0.90	0.57%
SOTALOL HCL TAB 120MG	39	2,590	1,193	10	$928.85	2.17	3.9	$0.78	0.44%
PROPRANOLOL CP 160MG ER	33	1,740	1,240	14	$3,865.68	1.4	2.36	**$3.12**	1.85%
TIMOLOL MAL TAB 10MG	17	1,430	495	3	$511.65	2.89	5.67	**$1.03**	0.24%
PROPRANOLOL 40MG/5ML	13	1,410	380	4	$196.37	3.71	3.25	$0.52	0.09%
SORINE TAB 120MG	10	600	300	2	$227.88	2	5	$0.76	0.11%
NADOLOL TAB 160MG	8	430	215	1	$766.78	2	8	**$3.57**	0.37%
NADOLOL TAB 120MG	4	120	150	2	$93.27	0.8	2	$0.62	0.04%
SOTALOL HCL TAB 240MG	3	123	51	1	$442.03	2.41	3	**$8.67**	0.21%
SORINE TAB 160MG	2	120	60	1	$129.34	2	2	**$2.16**	0.06%
SORINE TAB 80MG	2	120	60	1	$110.34	2	2	**$1.84**	0.05%
PROPRANOLOL POW HCL	1	60	30	1	$4.57	2.01	1	$0.15	0.00%
Totals	10,038	633,038	330,488		$209,361.51	1.92	3.89	$0.63	

Beta $_1$ Selective agents

Product	Claims	Units	Days	Members	Costs	Unit/ day	Claims/ Member	Cost /Day	% Cost
METOPROLOL TAB 50MG	7,760	466,116	280,660	1986	$41,090.69	1.66	3.91	$0.15	4.82%
ATENOLOL TAB 50MG	6,428	312,097	257,508	1562	$45,511.89	1.21	4.12	$0.18	5.34%
TOPROL XL TAB 50MG	5,247	234,258	211,812	1408	$215,329.93	1.11	3.73	**$1.02**	25.27%
ATENOLOL TAB 25MG	4,263	200,681	164,518	1190	$28,517.62	1.22	3.58	$0.17	3.35%
TOPROL XL TAB 100MG	3,996	195,426	172,915	961	$259,216.03	1.13	4.16	**$1.50**	30.43%
METOPROLOL TAB 25MG	3,352	185,282	107,914	1056	$18,894.54	1.72	3.17	$0.18	2.22%
METOPROLOL TAB 100MG	3,347	218,577	115,511	779	$22,247.66	1.89	4.3	$0.19	2.61%
ATENOLOL TAB 100MG	1,796	87,862	76,517	427	$17,627.59	1.15	4.21	$0.23	2.07%
TOPROL XL TAB 25MG	1,729	70,901	67,178	621	$65,481.21	1.06	2.78	$0.97	7.69%
METOPROLOL TAB 25MG ER	1,523	62,647	58,310	610	$50,744.61	1.07	2.5	$0.87	5.96%
TOPROL XL TAB 200MG	774	35,968	34,306	189	$75,203.93	1.05	4.1	**$2.19**	8.83%
BISOPROL FUM TAB 5MG	152	5,863	5,548	41	$5,720.07	1.06	3.71	**$1.03**	0.67%
ACEBUTOLOL CAP 200MG	73	4,758	2,229	12	$1,238.90	2.13	6.08	$0.56	0.15%
BISOPROL FUM TAB 10MG	45	2,095	2,020	11	$1,922.25	1.04	4.09	$0.95	0.23%
BETAXOLOL TAB 20MG	16	690	690	2	$867.23	1	8	**$1.26**	0.10%
LOPRESSOR TAB 100MG	14	975	420	1	$1,783.52	2.32	14	**$4.25**	0.21%
BETAXOLOL TAB 10MG	6	90	180	1	$99.66	0.5	6	$0.55	0.01%
TENORMIN TAB 100MG	2	180	180	1	$384.64	1	2	**$2.14**	0.05%
METOPROLOL INJ 1MG/ML	1	80	10	1	$38.90	8	1	**$3.89**	0.00%
METOPROLOL TB 100MG ER	1	30	30	1	$37.91	1	1	**$1.26**	0.00%
Totals	40,525	2,084,576	1,558,456		$851,958.78	1.34	4.42	$0.55	

Beta and Alpha Antagonists

Product	Claims	Units	Days	Members	Costs	Unit /day	Claims/ Member	Cost/ Day	% Cost
COREG TAB 6.25MG	1,859	114,362	61,000	466	$214,335.24	1.87	3.99	**$3.51**	28.16%
COREG TAB 25MG	1,585	108,236	53,463	336	$203,878.96	2.02	4.72	**$3.81**	26.79%
COREG TAB 3.125MG	1,365	81,541	43,232	356	$154,655.53	1.89	3.83	**$3.58**	20.32%
COREG TAB 12.5MG	1,235	74,146	40,035	346	$137,471.02	1.85	3.57	**$3.43**	18.06%
LABETALOL TAB 200MG	1,074	84,397	31,739	466	$19,143.68	2.66	2.3	$0.60	2.52%
LABETALOL TAB 100MG	1,008	59,837	29,555	487	$10,793.90	2.02	2.07	$0.37	1.42%
LABETALOL TAB 300MG	307	20,726	8,693	108	$6,005.94	2.38	2.84	$0.69	0.79%
COREG CR CAP 10MG	29	1,025	965	15	$3,829.06	1.06	1.93	**$3.97**	0.50%
COREG CR CAP 20MG	27	1,140	1,047	17	$4,227.64	1.09	1.59	**$4.04**	0.56%
COREG CR CAP 40MG	25	1,122	1,122	20	$4,173.42	1	1.25	**$3.72**	0.55%
COREG CR CAP 80MG	20	670	670	13	$2,495.88	1	1.54	**$3.73**	0.33%
Totals	8,534	547,202	271,521		$761,010.27	2.02	3.88	$2.80	

Beta-blocker/Diuretic Combo

Product	Claims	Units	Days	Members	Costs	Unit /day	Claims/ Member	Cost/ Day	% Cost
ATENOL/CHLOR TB 50-25MG	517	22,264	20,810	126	$4,561.58	1.07	4.1	$0.22	16.47%
BISOPRL/HCTZ TAB 10/6.25	253	12,111	11,169	54	$2,409.92	1.08	4.69	$0.22	8.70%
ATENOL/CHLOR TB 100-25MG	240	11,740	11,193	65	$2,676.14	1.05	3.69	$0.24	9.66%
BISOPRL/HCTZ TAB 5/6.25MG	233	12,053	11,263	67	$4,024.88	1.07	3.48	$0.36	14.53%
BISOPRL/HCTZ TAB 2.5/6.25	170	8,643	6,973	39	$1,675.68	1.24	4.36	$0.24	6.05%
METOPRL/HCTZ TB 50-25MG	103	3,750	3,295	26	$3,815.64	1.14	3.96	**$1.16**	13.78%
PROPRAN/HCTZ TAB 80/25	37	2,190	1,260	5	$405.63	1.74	7.4	$0.32	1.46%
PROPRAN/HCTZ TAB 40/25	27	1,025	995	7	$174.94	1.03	3.86	$0.18	0.63%
METOPRL/HCTZ 100-25MG	19	1,090	853	8	$1,600.74	1.28	2.38	**$1.88**	5.78%
LOPRESS HCT TAB 50-25MG	15	1,140	750	4	$1,537.90	1.52	3.75	**$2.05**	5.55%
ZIAC TAB 5/6.25MG	14	395	395	1	$940.34	1	14	**$2.38**	3.39%
CORZIDE TAB 40/5	13	530	530	2	$1,142.42	1	6.5	**$2.16**	4.12%
LOPRESS HCT TAB 100/50MG	11	585	450	2	$1,296.06	1.3	5.5	**$2.88**	4.68%
METOPRL/HCTZ T 100-50MG	9	655	550	3	$1,046.88	1.19	3	**$1.90**	3.78%
TENORETIC TAB 50	6	240	240	1	$389.91	1	6	**$1.62**	1.41%
Totals	1,667	78,411	70,726		$27,698.66	1.11	4.23	$0.39	

Appendix F

ERYTHROPOIESIS-STIMULATING AGENTS UTILIZATION REVIEW

Oklahoma Health Care Authority
February 2008

FDA Indications

Procrit® (epoetin alfa)

1. Treatment of Anemia of Chronic Renal Failure Patients
2. Treatment of Anemia in Zidovudine-treated HIV-infected Patients
3. Treatment of Anemia in Cancer Patients on Chemotherapy
4. Reduction of Allogeneic Blood Transfusion in Surgery Patients

Epogen® (epoetin alfa) – same as Procrit

Aranesp® (darbepoetin alfa)

1. Treatment of anemia associated with chronic renal failure (on dialysis and patients not on dialysis)
2. Treatment of anemia in patients with non-myeloid malignancies where anemia is due to the effect of concomitantly administered chemotherapy

Off Label Uses:

- Anemia - Congestive heart failure
- Anemia - Critical illness
- Anemia - Rheumatoid arthritis
- Anemia - Multiple myeloma
- Anemia - Myelodysplastic syndrome
- Anemia due to radiation
- Anemia during the puerperium
- Anemia of chronic disease - Neoplastic disease
- Anemia of prematurity
- Anemia - Hepatitis C, In patients being treated with a combination of ribavirin and interferon alfa or ribavirin and peginterferon alfa
- beta Thalassemia
- Blood unit collection for autotransfusion

Center for Medicare and Medicaid Services (CMS) Guidelines for Medicare B[1]

Chronic Kidney Disease (CKD) related Anemia

EPO and Aranesp are covered under the Part B benefit for the treatment of symptomatic anemia associated with ESRD patients who are on dialysis. Generally, patients should have a hematocrit less than 30% or hemoglobin less than 10 g/dL. ESRD patients who have been receiving EPO/Aranesp therapy should have a hematocrit between 30% and 36%.

Non CKD-related Anemia

CMS has determined that there is sufficient evidence to conclude that erythropoiesis stimulating agent (ESA) treatment is not reasonable and necessary for beneficiaries with certain clinical conditions, either because of a deleterious effect of the ESA on their underlying disease or because the underlying disease increases their risk of adverse effects related to ESA use. These conditions include:

1. Any anemia in cancer or cancer treatment patients due to folate deficiency, B-12 deficiency, iron deficiency, hemolysis, bleeding, or bone marrow fibrosis;
2. The anemia associated with the treatment of acute and chronic myelogenous leukemias (CML, AML), or erythroid cancers;
3. The anemia of cancer not related to cancer treatment;
4. Any anemia associated only with radiotherapy;
5. Prophylactic use to prevent chemotherapy-induced anemia;
6. Prophylactic use to reduce tumor hypoxia;
7. Patients with erythropoietin-type resistance due to neutralizing antibodies; and
8. Anemia due to cancer treatment if patients have uncontrolled hypertension.

Anemia due to Myelosuppressive Anticancer Chemotherapy

CMS has determined that ESA treatment for the anemia secondary to myelosuppressive anticancer chemotherapy in solid tumors, multiple myeloma, lymphoma and lymphocytic leukemia is only reasonable and necessary under the following specified conditions:

1. The hemoglobin level immediately prior to initiation or maintenance of ESA treatment is < 10 g/dL (or the hematocrit is < 30%).
2. The starting dose for ESA treatment is the recommended FDA label starting dose, no more than 150 U/kg/three times weekly for epoetin and 2.25 mcg/kg/weekly for darbepoetin alpha. Equivalent doses may be given over other approved time periods.
3. Maintenance of ESA therapy is the starting dose if the hemoglobin level remains below 10 g/dL (or hematocrit is < 30%) 4 weeks after initiation of therapy and the rise in hemoglobin is > 1g/dL (hematocrit > 3%).
4. For patients whose hemoglobin rises <1 g/dl (hematocrit rise <3%) compared to pretreatment baseline over 4 weeks of treatment and whose hemoglobin level remains <10 g/dL after the 4 weeks of treatment (or the hematocrit is <30%), the recommended FDA label starting dose may be increased once by 25%. Continued use of the drug is not reasonable and necessary if the hemoglobin rises <1 g/dl (hematocrit rise <3 %) compared to pretreatment baseline by 8 weeks of treatment.
5. Continued administration of the drug is not reasonable and necessary if there is a rapid rise in hemoglobin > 1 g/dl (hematocrit > 3%) over 2 weeks of treatment unless the hemoglobin remains below or subsequently falls to < 10 g/dL (or the hematocrit is < 30%). Continuation and reinstitution of ESA therapy must include a dose reduction of 25% from the previously administered dose.
6. ESA treatment duration for each course of chemotherapy includes the 8 weeks following the final dose of myelosuppressive chemotherapy in a chemotherapy regimen.

Other National Guidelines for ESA's[2,3]

- **National Kidney Foundation's** 2006 KDOQI Clinical Practice Guidelines and Clinical Practice Recommendations for Anemia in Chronic Kidney Disease, updated 2007:
  - Defines anemia as: <13.5 g/dL in adult males and <12.0 g/dL in adult females.
  - In patients with CKD target range for hemoglobin (Hb) should be in the range of 11.0 to 12.0 g/dl.
  - Target Hb should not exceed 13.0 g/dL in ESA-treated patients.
- Clinical Practice Guidelines of the **American Society of Clinical Oncology** and the **American Society of Hematology**, updated Aug 2007:
  - Epoetin is recommended for patients with chemotherapy-associated anemia whose Hb is <10 g/dl at a starting dose of 150U/kg three times a week for 4 weeks. Dosing weekly with 40,000U is also acceptable.
  - Darbepoetin is recommended for patients with chemotherapy-associated anemia whose Hb is <10 g/dl at a starting dose of 2.25µg/kg weekly or 500µg every 3 weeks.
  - Target Hb range should not exceed 12 g/dl.
  - For patients whose Hb level fails to respond to adequate doses after 6-8 weeks, continued treatment with epoetin does not appear to be of benefit.
  - Recommend against the use of ESAs to treat anemia associated with malignancy, or the anemia of cancer, among patients with solid or non-myeloid malignancies who are not receiving concurrent chemotherapy.

Recent Developments with Erythropoiesis-Stimulating Agents[4]

On November 8, 2007, the FDA approved new labeling strengthening the boxed warning and warning sections of labeling for epoetin and darbepoetin. This updated labeling is shown at the end of this section.

On November 30, 2007, the FDA was notified by the manufacturer of findings from the Preoperative Epirubicin Paclitaxel Aranesp Study (PREPARE). The PREPARE study enrolled patients with primary breast cancer that were to undergo chemotherapy prior to surgery. These patients were randomly assigned to receive Aranesp or no Aranesp.

On December 4, 2007, the FDA was notified by the manufacturer of findings from the GOG-191 study. This study enrolled patients with cervical cancer treated with chemotherapy and radiation and were assigned to receive ESA or transfusions. The study stopped enrolling patients because of a higher rate of potentially life-threatening blood clots in the patients receiving an ESA.

Both the PREPARE study and the GOG-191 study showed higher rates of death and/or tumor progression in patients receiving ESA compared to those who did not receive ESA therapy.

The FDA is currently reviewing this information and plans to take action as appropriate. The FDA plans to hold a public advisory committee meeting in early 2008 to reevaluate the risk and benefit of ESAs for the treatment of chemotherapy-induced anemia.

Black Box Warning applicable for all epoetin and darbepoetin alfa products (11/8/2007)[5]:

WARNINGS: INCREASED MORTALITY, SERIOUS CARDIOVASCULAR and THROMBOEMBOLIC EVENTS, and TUMOR PROGRESSION

Renal failure: **Patients experienced greater risks for death and serious cardiovascular events when administered erythropoiesis-stimulating agents (ESAs) to target higher versus lower hemoglobin levels (13.5 vs. 11.3 g/dL; 14 vs. 10 g/dL) in two clinical studies. Individualize dosing to achieve and maintain hemoglobin levels within the range of 10 to 12 g/dL.**

Cancer:

- **ESAs shortened overall survival and/or time-to-tumor progression in clinical studies in patients with advanced breast, head and neck, lymphoid, and non-small cell lung malignancies when dosed to a target hemoglobin of > 12 g/dL.**
- **The risks of shortened survival and tumor progression have not been excluded when ESAs are dosed to target a hemoglobin of < 12 g/dL.**
- **To minimize these risks, as well as the risk of serious cardio- and thrombovascular events, use the lowest dose needed to avoid red blood cell transfusions.**
- **Use only for treatment of anemia due to concomitant myelosuppressive chemotherapy.**
- **Discontinue following the completion of a chemotherapy course.**

Perisurgery: **PROCRIT® increased the rate of deep venous thromboses in patients not receiving prophylactic anticoagulation. Consider deep venous thrombosis prophylaxis.**

(See WARNINGS: Increased Mortality, Serious Cardiovascular and Thromboembolic Events, WARNINGS: Increased Mortality and/or Tumor).

Utilization January 1, 2007 thru June 30, 2007

Total Utilization

NAME	CLAIMS	MEMBERS	COST
Darbepoetin	667	195	$962,357.96
Epoetin	791	177	$538,861.17
	1,458	**337**	**$1,501,219.13**

Pharmacy Point-of-Sale claims

BRAND NAME	CLAIMS	UNITS	DAYS	Members	COST	COST/ DAY
Aranesp (darbepoetin)	44	63	1,253	17	$133,638.25	$106.65
Epogen (epoetin)	56	345	1,610	26	$68,446.50	$42.51
Procrit (epoetin)	212	1,064	5,459	76	$224,060.33	$41.04
	312	**1,472**	**8,322**	**102***	**$426,145.08**	**$51.21**

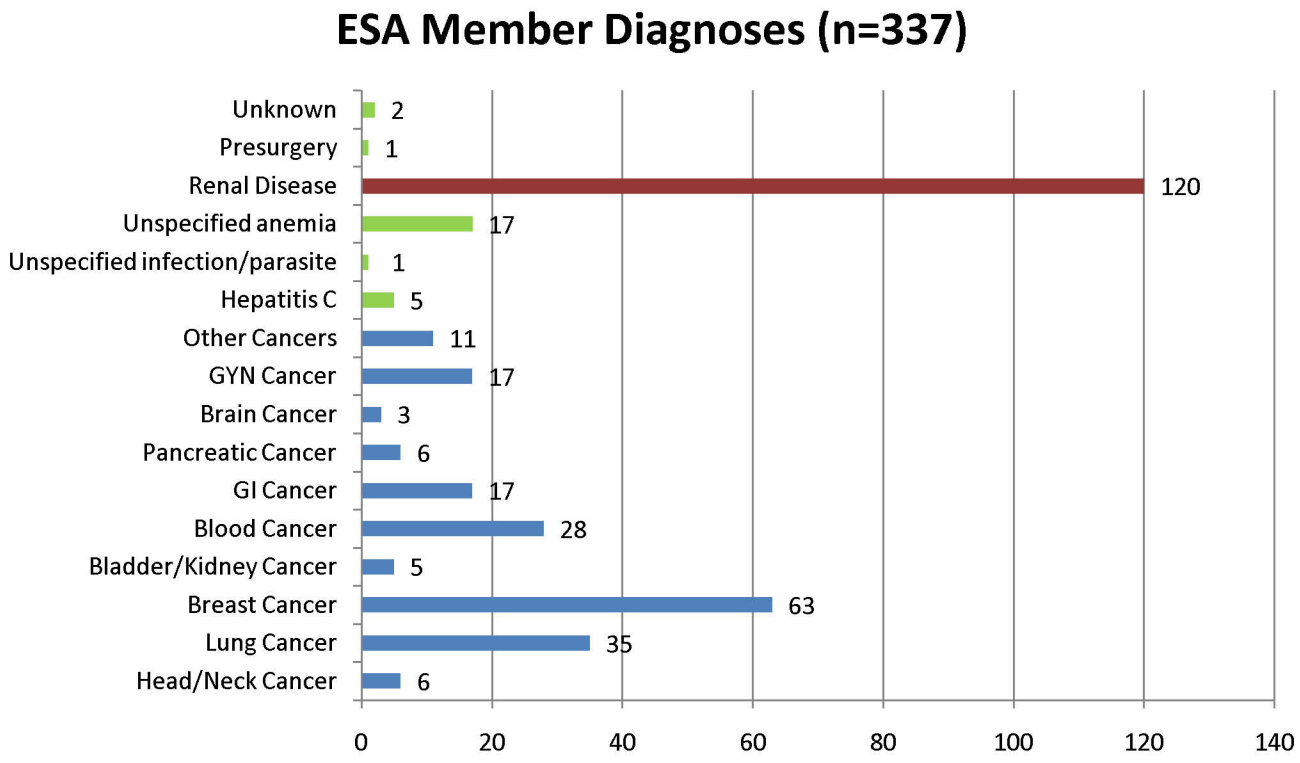
*unduplicated within POS claims

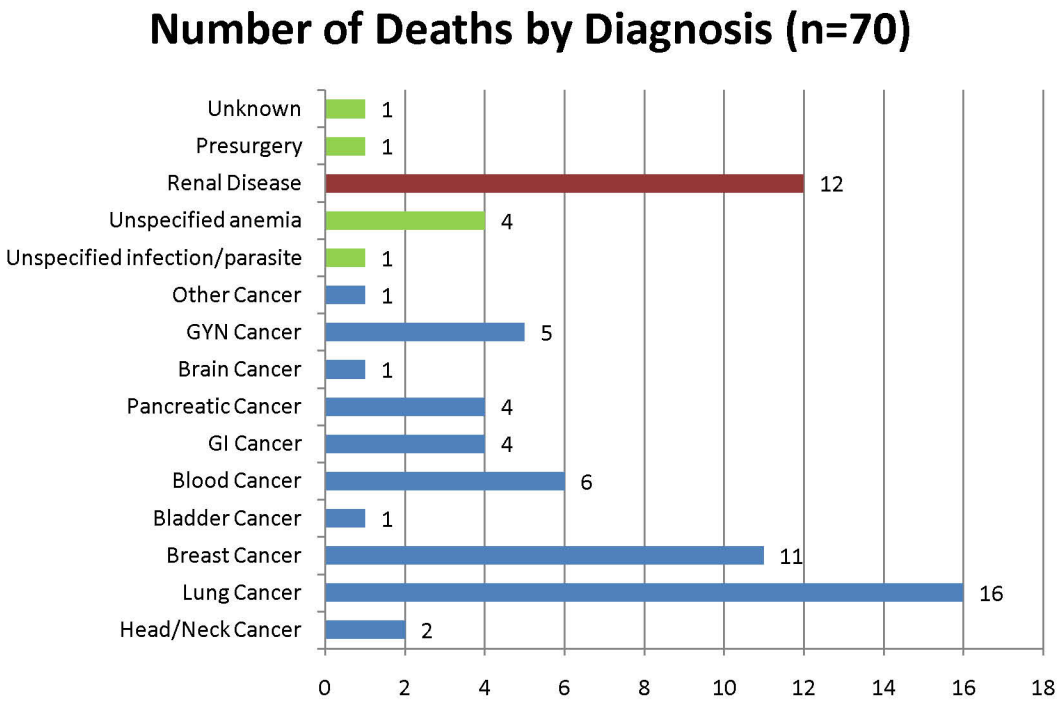
Outpatient 1500 & UB92 claims

HCPCS Code*	CLAIMS	MEMBERS	COST
J0881	609	173	$819,181.51
J0882	14	5	$9,538.20
J0885	398	55	$174,749.51
J0886	125	20	$71,604.83
Totals	1,146	240*	$1,075,074.05

*unduplicated within medical claims

J0881 – Injection, darbepoetin alfa – non-ESRD
J0882 – Injection, darbepoetin alfa – ESRD
J0885 – Injection, epoetin alfa – non-ESRD
J0886 – Injection, epoetin alfa – ESRD (no claims in 2006)





Recommendations

The College of Pharmacy recommends waiting at least 6 months to consider any possible action on Erythropoiesis-Stimulation Agents. This time period should allow the various specialty groups to re-evaluate the use of ESAs based upon recent clinical findings and, if deemed appropriate by those bodies, alter their guidelines for use.

References

1. CMS Manual System. Pub 100-04 Medicare Claims Processing. Transmittal 1307. July 20, 2007
2. National Kidney Foundation, Inc. website www.kidney.org
3. Rizzo Jd, Somerfield MR, Hagerty KL, et al: American Society of Clinical Oncology/American Society of Hematology 2007 Clinical Practice Guideline Update on the Use of Epoetin and Darbepoetin. J Clin Oncol 2007; JCO Early Release 10.1200/JCO.2007.14.3396 on October 22 2007.
4. Food and Drug Administration. Center for Drug Evaluation and Research. Communication about an Ongoing Safety Review. January 3, 2007. http://www.fda.gov/cder/drug/early_comm/ESA.htm
5. Procrit™ package insert. Website available at: http://procrit.com/impor_safe.html

Appendix G

Annual Review of Insomnia Products

Oklahoma Health Care Authority
February 2008

Background

Insomnia prior authorization criteria for calendar year 2006:

- The first 90 therapy days of insomnia medications are covered without prior authorization.
- After the first 90 days, members may continue to receive an insomnia medication if daytime dosing of benzodiazepines do not exceed three times daily. Prior authorization is granted every 90 days as long as the above criterion is met.
- There are currently quantity limits on temazepam, Lunesta®, Rozerem®, Sonata®, Ambien® and Ambien CR®.

As of January 1, 2006, all Dual Eligible members are covered under Medicare Part D except for excluded categories like the benzodiazepines which continue to be covered by Medicaid. Non-benzodiazepine insomnia medications are no longer covered by Medicaid, but fall under Part D coverage.

January 2007 Category Changes

Tier 1[a]	Tier 2
estazolam temazepam flurazepam triazolam zolpidem* Lunesta®* Rozerem®* Ambien CR®*	Sonata®* Restoril® 7.5 and 22.5 mg

Blue indicates tier-1 status due to Supplemental Rebate Participation
[a]Brand products would still require a brand name override.
*Non-benzodiazepine

Tier 2 Insomnia Approval Criteria:

1. Minimum of 30 day trial with at least two Tier 1 products (including zolpidem once generic is available) and clinical documentation of attempts to correct any primary cause for insomnia.

2. FDA approved diagnosis (Ambien CR® only covered for sleep maintenance insomnia). *This criteria not effective while Ambien CR is on tier-one*.
3. No concurrent anxiolytic benzodiazepine therapy greater than TID dosing and no concurrent ADHD medications.
4. Approvals granted for 6 months.

Also, age limits placed based on FDA approved limits and quantity limits of 30 units for a 30 day supply.

Utilization FY07

Product	# of Claims	Total Units	Total Days	Units/Day	Total Cost	Total Members	Per Diem
Ambien 5mg	2,281	57,946	55,852	1	$228,508.99	1,151	$4.09
Ambien 10mg	10,678	289,173	291,466	1	$1,156,331.27	3,826	$3.97
Ambien CR 6.25mg	87	2,513	2,513	1	$8,726.05	30	$3.47
Ambien CR 12.5mg	738	21,420	21,474	1	$71,557.69	201	$3.33
Estazolam 1mg	46	1,558	1,233	1.3	$649.91	16	$0.53
Estazolam 2mg	211	6,629	6,415	1	$3,717.37	49	$0.58
Flurazepam 15mg	133	4,772	3,865	1.2	$850.82	56	$0.22
Flurazepam 30mg	404	12,350	12,204	1	$2,494.46	132	$0.20
Halcion 0.25mg	13	780	390	2	$1,224.15	1	$3.14
Lunesta 1mg	184	5,050	4,939	1	$19,161.07	79	$3.88
Lunesta 2mg	1,464	39,188	39,424	1	$149,196.71	688	$3.78
Lunesta 3mg	2,940	83,352	83,559	1	$315,886.91	1,026	$3.78
Restoril 7.5mg	1,629	46,785	46,784	1	$178,751.88	451	$3.82
Restoril 15mg	4	120	120	1	$586.63	3	$4.89
Restoril 22.5mg	15	450	450	1	$1,717.67	3	$3.82
Restoril 30mg	2	60	60	1	$331.48	1	$5.52
Rozerem	1,736	49,311	49,558	1	$144,109.18	854	$2.91
Sonata 5mg	48	1,095	1,095	1	$3,587.42	23	$3.27
Sonata 10mg	377	12,387	10,569	1.2	$40,882.38	133	$3.87
Temazepam 15mg	9,255	295,268	264,544	1.1	$65,146.94	3,038	$0.25
Temazepam 30mg	10,560	326,525	325,314	1	$69,858.97	2,943	$0.21
Triazolam 0.125mg	111	2,189	1,831	1.2	$814.66	74	$0.44
Triazolam 0.25mg	1,364	38,299	29,948	1.3	$12,262.82	618	$0.41
Zolpidem 5mg	376	9,432	9,252	1	$6,802.21	298	$1.08
Zolpidem 10mg	1,997	54,120	54,397	1	$44,214.12	1,483	$.081
Total	**46,653**	**1,360,772**	**1,317,256**		**$2,527,401.71**	**13,592***	**$1.92**

*Unduplicated members.

Total Cost FY '07	**$2,527,401.71**
Total Cost FY '06	*$3,410,378.93*
Total Claims FY '07	**46,653**
Total Claims FY '07	*60,695*
Total Clients FY '07	**13,592**
Total Clients FY '06	*21,094*
Per Diem FY '07	**$1.92**
Per Diem FY '06	*$1.97*

Total petitions submitted in for this category during specified time period:

Approved	11,028
Denied	2,695
Incomplete	967

Age	Female	Male	Totals
0 to 9	25	33	58
10 to 19	684	477	1,161
20 to 34	2,490	395	2,885
35 to 49	2,654	886	3,540
50 to 64	2,307	1,069	3,376
65 to 79	1,022	470	1,492
80 to 94	742	209	951
95 and Over	81	13	94
Totals	**10,005**	**3,552**	**13,557***

*35 members did not have a gender indicated.

Recommendations

The College of Pharmacy recommends no changes to the current hypnotic prior authorization category:

Appendix H

Prior Authorization Annual Review of Glumetza™ and Fortamet® FY'07

Oklahoma Health Care Authority
February 2008

Category Criteria for FY'07

Approval of Fortamet® and Glumetza™ is based on clinical documentation of inability to take other forms of generic metformin ER (after slow titration of 500 mg ER at 2 week intervals up to 2000 mg daily).

Utilization

For the 2007 fiscal year, 5,991 members received metformin products through the *SoonerCare* program.

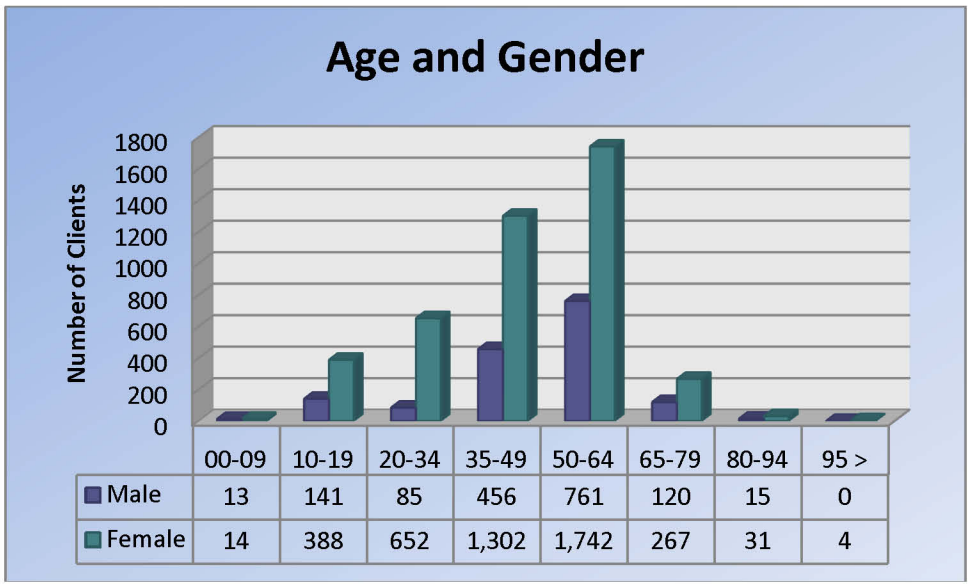
BRAND NAME	CLAIMS	UNITS	DAYS	MEMBERS	COST	UNITS / DAY	COST/ DAY
METFORMIN TAB 500MG	15,789	1,182,555	513,533	3,948	$122,972.91	2.3	$0.24
METFORMIN TAB 1000MG	7,902	523,247	267,290	1,824	$75,187.77	1.96	$0.28
METFORMIN TAB 500MG ER	2,120	165,796	74,434	550	$23,553.71	2.23	$0.32
METFORMIN TAB 850MG	1,589	112,161	53,357	391	$14,345.02	2.1	$0.27
METFORMIN TAB 750MG ER	79	3,985	2,630	31	$1,534.86	1.52	$0.58
FORTAMET TAB 1000MG	49	2,560	1,715	16	$7,035.88	1.49	$4.10
FORTAMET TAB 500MG	45	2,880	1,466	11	$3,465.44	1.96	$2.36
RIOMET SOL	43	15,537	1,151	13	$2,591.24	13.5	$2.25
GLUCOPHAGE TAB 1000MG	28	1,710	740	3	$3,042.25	2.31	$4.11
GLUCOPHAGE TAB XR 500MG	21	2,370	630	2	$2,131.41	3.76	$3.38
GLUMETZA TAB 500MG	5	340	220	3	$383.84	1.55	$1.74
GLUCOPHAGE TAB 500MG	2	200	50	1	$167.94	4	$3.36
	27,672	**2,013,341**	**917,216**		**$256,412.27**	**2.20**	**$0.28**

Fiscal Year	Total Clients	Total Claims	Total Cost	Cost per Claim	Per Diem Cost	Total Days
2006*						
	11,406	46,234	$582,525.26	$12.59	$0.37	1,563,124
2007						
	5,991	27,672	$256,412.27	$9.27	$0.28	917,216
Percent Change	-47.5%	-40.1%	-56.0%	-26.4%	-24.3%	-41.3%

*Includes dual eligibles until December 31, 2005.

Total petitions submitted in for this category during specified time period: 123

Approved *76*
Denied 26
Incomplete 21



Recommendations

The College of Pharmacy recommends continuation of current coverage for Fortamet® and Glumetza™.

Appendix I

FDA News

FOR IMMEDIATE RELEASE
January 18, 2008

Media Inquiries:
Rita Chappelle, 301-827-6242
Consumer Inquiries:
888-INFO-FDA

FDA Approves Update to Label on Birth Control Patch

The U.S. Food and Drug Administration (FDA) today approved additional changes to the Ortho Evra Contraceptive Transdermal (Skin) Patch label to include the results of a new epidemiology study that found that users of the birth control patch were at higher risk of developing serious blood clots, also known as venous thromboembolism (VTE), than women using birth control pills. VTE can lead to pulmonary embolism.

The label changes are based on a study conducted by the Boston Collaborative Drug Surveillance Program (BCDSP) on behalf of Johnson and Johnson. The patch was studied in women aged 15-44. These recent findings support an earlier study that also said women in this group were at higher risk for VTE.

"For women that choose to use contraceptives, it is important that they thoroughly discuss with their health care providers the risks and benefits involved," said Janet Woodcock, M.D., the FDA's deputy commissioner for scientific and medical programs, chief medical officer, and acting director of the Center for Drug Evaluation and Research.

"This is an example of FDA working in tandem with the drug manufacturer to keep the public informed of new safety data and epidemiological studies that may impact health decisions about the use of FDA approved products."

In September 2006, FDA revised the label for Ortho Evra to warn women of the risk of VTE based on two epidemiology studies. One study, conducted by i3 Ingenix, showed that some women using the patch were at a two-fold greater risk of developing VTE. The other study, conducted by BCDSP, showed they were not at increased risk compared to women using birth control pills containing 30-35 micrograms of estrogen and the progestin norgestimate.

Ortho Evra is a prescription patch that releases ethinyl estradiol (an estrogen hormone) and norelgestromin (a progestin hormone) through the skin into the blood stream. Because the hormones are processed by the body differently than hormones from birth control pills, women using the product will be exposed to about 60 percent more estrogen than if they were using typical birth control pills containing 35 micrograms of estrogen. Increased levels of estrogen may increase the risk of side effects, including VTE. Women should discuss with their health care provider the possible increased risk of VTE with Ortho Evra, which is applied once a week, and balance this risk against the increased chance of pregnancy if women do not take their birth control pill daily.

The FDA believes that Ortho Evra is a safe and effective method of contraception when used according to the labeling, which recommends that women with concerns or risk factors for serious blood clots talk with their health care provider about using Ortho Evra versus other contraceptive options.

The Ortho Evra Contraceptive Transdermal Patch is manufactured by Ortho McNeil Pharmaceuticals, a division of Johnson and Johnson.

Consumers with questions regarding this drug or any medications may contact FDA's Division of

Drug Information at: 888-INFO-FDA (888-463-6332), or email to: druginfo@fda.hhs.gov.

To view additional information on the use of Ortho Evra please visit:
www.fda.gov/cder/drug/infopage/orthoevra/default.htm

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FDA News

FOR IMMEDIATE RELEASE
January 17, 2008

Media Inquiries:
Susan Cruzan, 301-827-6242
Consumer Inquiries:
888-INFO-FDA

FDA Releases Recommendations Regarding Use of Over-the-Counter Cough and Cold Products

Products should not be used in children under 2 years of age; evaluation continues in older populations

En Español

The U.S. Food and Drug Administration today issued a Public Health Advisory for parents and caregivers, recommending that over-the-counter (OTC) cough and cold products should not be used to treat infants and children less than 2 years of age because serious and potentially life-threatening side effects can occur from such use. OTC cough and cold products include decongestants, expectorants, antihistamines, and antitussives (cough suppressants) for the treatment of colds.

There are a wide variety of rare, serious adverse events reported with cough and cold products. They include death, convulsions, rapid heart rates, and decreased levels of consciousness.

"The FDA strongly recommends to parents and caregivers that OTC cough and cold medicines not be used for children younger than 2," said Charles Ganley, M.D., director of the FDA's Office of Nonprescription Products. "These medicines, which treat symptoms and not the underlying condition, have not been shown to be safe or effective in children under 2."

The announcement does not include the FDA's final recommendation about use of OTC cough and cold medicines in children ages 2 to 11 years. The agency's review of data for 2-to-11-year-olds is continuing. The FDA is committed to making a timely and comprehensive review of the safety of OTC cough and cold medicines in children. The agency plans to issue its recommendations on use of the products in children ages 2 to 11 years to the public as soon as the review is complete.

Today's statement is based on the FDA's review of data and discussion at a joint meeting of the Nonprescription Drugs and Pediatric Advisory Committees on Oct. 18 and 19, 2007.

Pending completion of the FDA's ongoing review, parents and caregivers that choose to use OTC cough and cold medicines to children ages 2 to 11 years should:

- Follow the dosing directions on the label of any OTC medication,
- Understand that these drugs will NOT cure or shorten the duration of the common cold,
- Check the "Drug Facts" label to learn what active ingredients are in the products because many OTC cough and cold products contain multiple active ingredients, and
- Only use measuring spoons or cups that come with the medicine or those made specially for measuring drugs.

The FDA recommends that anyone with questions contact a physician, pharmacist or other health care professional to discuss how to treat a child with a cough or cold.

For more information and the full list of the FDA's recommendations, visit:

Public Health Advisory: Nonprescription Cough and Cold Medicine Use in Children
http://www.fda.gov/cder/drug/advisory/cough_cold_2008.htm

Questions and Answers for Consumers
http://www.fda.gov/consumer/updates/coughcold011708.html

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FDA Statement

FOR IMMEDIATE RELEASE
January 25, 2008

Media Inquiries:
Susan Cruzan, 301-827-6242
Consumer Inquiries:
888-INFO-FDA

FDA Issues Early Communication about an Ongoing Review of Vytorin

The U.S. Food and Drug Administration today issued an Early Communication regarding the agency's ongoing review of Vytorin based on preliminary results from a recently completed study – the Effect of Combination Ezetimibe and High-Dose Simvastatin vs. Simvastatin Alone on the Atherosclerotic Process in Patients with Heterozygous Familial Hypercholesterolemia (ENHANCE) – on this cholesterol lowering drug. Vytorin contains both Zetia (ezetimibe) and Zocor (simvastatin) in one tablet.

The FDA is informing the public that the agency will conduct a review of Merck and Schering Plough's recent trial once the FDA receives the final study results.

Merck/Schering Plough Pharmaceuticals issued a press release reporting preliminary results of the study and stated that the study demonstrated no significant differences between the combination product and Zocor on the build up of cholesterol plaque in the carotid (neck) arteries. The study was not designed to detect any difference in risk of having a heart attack or stroke between the two treatments. An ongoing trial called -- Improved Reduction of Outcomes: Vytorin Efficacy International Trial (IMPROVE IT) -- is underway which is designed to evaluate the effect of Vytorin versus Zocor on heart disease and stroke.

This Early Communication is in keeping with the FDA's commitment to inform the public about its ongoing review of drugs. Until the FDA reviews the data, the agency advises patients to talk with their health care providers if they have questions about the ENHANCE study.

Full text of the Early Communication about an Ongoing Data Review for the ENHANCE Study can be found at: http://www.fda.gov/cder/drug/early_comm/ezetimibe_simvastatin.htm.

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Suicidality and Antiepileptic Drugs

FDA ALERT [1/31/2008] - The FDA has analyzed reports of suicidality (suicidal behavior or ideation) from placebo-controlled clinical studies of eleven drugs used to treat epilepsy as well as psychiatric disorders, and other conditions. These drugs are commonly referred to as antiepileptic drugs (see the list below). In the FDA's analysis, patients receiving antiepileptic drugs had approximately twice the risk of suicidal behavior or ideation (0.43%) compared to patients receiving placebo (0.22%). The increased risk of suicidal behavior and suicidal ideation was observed as early as one week after starting the antiepileptic drug and continued through 24 weeks. The results were generally consistent among the eleven drugs. Patients who were treated for epilepsy, psychiatric disorders, and other conditions were all at increased risk for suicidality when compared to placebo, and there did not appear to be a specific demographic subgroup of patients to which the increased risk could be attributed. The relative risk for suicidality was higher in the patients with epilepsy compared to patients who were given one of the drugs in the class for psychiatric or other conditions.

All patients who are currently taking or starting on any antiepileptic drug should be closely monitored for notable changes in behavior that could indicate the emergence or worsening of suicidal thoughts or behavior or depression.

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 health care professionals to discontinue prescribing these products. FDA intends to update this document when additional information or analyses become available.

- **Healthcare Professional Information**
  - Information for Healthcare Professionals
- **Other Information**
  - FDA News: FDA Alerts Health Care Providers to Risk of Suicidal Thoughts and Behavior with Antiepileptic Medications

The following is a list of antiepileptic drugs* included in the analyses:

Labeling and approval history from Drugs@FDA.

- Carbamazepine (marketed as Carbatrol, Equetro, Tegretol, Tegretol XR)
- Felbamate (marketed as Felbatol)
- Gabapentin (marketed as Neurontin)
- Lamotrigine (marketed as Lamictal)
- Levetiracetam (marketed as Keppra)
  - Patient Information Sheet
- Oxcarbazepine (marketed as Trileptal)
- Pregabalin (marketed as Lyrica)
- Tiagabine (marketed as Gabitril)
- Topiramate (marketed as Topamax)
- Valproate (marketed as Depakote, Depakote ER, Depakene, Depacon)
- Zonisamide (marketed as Zonegran)

* Some of these drugs are also available in generic form.

FDA News

FOR IMMEDIATE RELEASE
February 1, 2008

Media Inquiries:
Susan Cruzan, 301-827-6242
Rita Chappelle, 301-827-6242
Consumer Inquiries:
888-INFO-FDA

FDA Issues Public Health Advisory on Chantix

Agency requests that manufacturer add new safety warnings for smoking cessation drug

The U.S. Food and Drug Administration (FDA) today issued a Public Health Advisory to alert health care providers, patients, and caregivers to new safety warnings concerning Chantix (varenicline), a prescription medication used to help patients stop smoking.

On Nov. 20, 2007, FDA issued an Early Communication to the public and health care providers that the agency was evaluating postmarketing adverse event reports on Chantix related to changes in behavior, agitation, depressed mood, suicidal ideation, and actual suicidal behavior.

As the agency's review of the adverse event reports proceeds, it appears increasingly likely that there may be an association between Chantix and serious neuropsychiatric symptoms. As a result, FDA has requested that Pfizer, the manufacturer of Chantix, elevate the prominence of this safety information to the warnings and precautions section of the Chantix prescribing information, or labeling. In addition, FDA is working with Pfizer to finalize a Medication Guide for patients. This is an example of FDA working with drug manufacturers throughout products' lifecycles to keep health care professionals and patients informed of new and emerging safety data.

"Chantix has proven to be effective in smokers motivated to quit, but patients and health care professionals need the latest safety information to make an informed decision regarding whether or not to use this product," said Bob Rappaport, M.D., director of the FDA's Division of Anesthesia, Analgesia and Rheumatology Products. "While Chantix has demonstrated clear evidence of efficacy, it is important to consider these safety concerns and alert the public about these risks. Patients should talk with their doctors about this new information and whether Chantix is the right drug for them, and health care professionals should closely monitor patients for behavior and mood changes if they are taking this drug."

Chantix was approved by FDA in May 2006 as a smoking cessation drug. Chantix acts at sites in the brain affected by nicotine and may help those who wish to stop smoking by providing some nicotine effects to ease the withdrawal symptoms and by blocking the effects of nicotine from cigarettes if users resume smoking.

In the Public Health Advisory and a Health Care Professional Sheet that was also issued today, FDA emphasized the following safety information for patients, caregivers, and health care professionals:

Patients should tell their health care provider about any history of psychiatric illness prior to starting Chantix. Chantix may cause worsening of current psychiatric illness even if it is currently under control. It may also cause an old psychiatric illness to reoccur. FDA notes that patients with these illnesses were not included in the studies conducted for the drug's approval.

Health care professionals, patients, patients' families, and caregivers should be alert to and monitor for changes in mood and behavior in patients treated with Chantix. Symptoms may include anxiety, nervousness, tension, depressed mood, unusual behaviors and thinking about or

attempting suicide. In most cases, neuropsychiatric symptoms developed during Chantix treatment, but in others, symptoms developed following withdrawal of varenicline therapy.

Patients should immediately report changes in mood and behavior to their doctor.

Vivid, unusual, or strange dreams may occur while taking Chantix.

Patients taking Chantix may experience impairment of the ability to drive or operate heavy machinery.

FDA will continue to update health care professionals with new information from FDA's continuing review or if new information is received on Chantix and serious neuropsychiatric symptoms. FDA may consider requesting further revisions to the labeling or taking other regulatory action as the agency's continuing reviews and conclusions warrant.

For more information:
http://www.fda.gov/cder/drug/infopage/varenicline/default.htm

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