Drug Utilization Review Board

Oklahoma Health Care Authority

4545 N. Lincoln Suite 124

Oklahoma City, Oklahoma 73105

OHCA Board Room

Wednesday

April 9, 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 – April 9, 2008**

DATE: April 3, 2008

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

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

Call to Order

Public Comment Forum

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

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

Action Item – Vote to Prior Authorize Tekturna HCT® – **See Appendix C.**

Action Item – Vote to Prior Authorize Narcotic Analgesics – **See Appendix D.**

60 Day Notice to Prior Authorize Osteoporosis Medications – **See Appendix E.**

60 Day Notice to Prior Authorize Topical Antibiotics – **See Appendix F.**

30 Day Notice to Prior Authorize Allegra® ODT / Syrup and Update PBPA Category – **See Appendix G**

30 Day Notice to Prior Authorize Pristiq™ and Update PBPA Category – **See Appendix H.**

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

Future Business

Adjournment

Drug Utilization Review Board

(DUR Board)

Meeting – April 9, 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. March 12, 2008 DUR Minutes – Vote
B. March 13, 2008 DUR Recommendations Memorandum

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

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

A. Retrospective Drug Utilization Review for December 2007
B. Medication Therapy Management Services July 2007 – December 2007
C. Medication Coverage Activity Audit for March 2008
D. Help Desk Activity Audit for March 2008

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

5. Vote to Prior Authorize Tekturna HCT® – See Appendix C.

A. Product Summary
B. COP Recommendations

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

6. Vote to Prior Authorize Narcotic Analgesics – See Appendix D.

A. COP Recommendations

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

7. 60 Day Notice to Prior Authorize Osteoporosis Medications – See Appendix E.

A. Utilization Review
B. COP Recommendations
C. Product Overview
D. Potential Savings

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

8. 60 Day Notice to Prior Authorize Topical Antibiotics – See Appendix F.

A. Utilization Review
B. Product Overview
C. COP Recommendations
D. Potential Savings

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

9. 30 Day Notice to Prior Authorize Allegra® ODT and Syrup and Update PBPA Category– See Appendix G.

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

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

10. 30 Day Notice to Prior Authorize Pristiq™ and Update PBPA Category – See Appendix H.

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

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

11. FDA and DEA Updates – See Appendix I.

12. Future Business

A. Oral Antifungals
B. Methylphenidate Follow-Up
C. Asthma Utilization Review
D. Hemophilia Review
E. New Product Reviews

13. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES of MEETING of MARCH 12, 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	
Shellie Gorman, Pharm.D.; 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: Christine Le and Mark Glenn	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, Senior Pharmacy Financial Analyst		X

OTHERS PRESENT:

Jacque Collier, Abbott Labs	Aaron Walker, Schering Plough	Donna Erwin, BMS
Linda Camo, BMS	Joseph Medina, Sepracor	Brian Shank, Astra Zeneca
William Dozier, Gilead	Amie Gardiner, Purdue	Cathy Hollen, Lilly
Pat Trahen, Taro	Ron Schnare, Shire	Mark DeClerk, Lilly
Janie Huff, TAP	Rebecca King, Taro	Jim Dunlap, Lilly
Kim Greenberg, Amylin	Cheryl McIntosh	

PRESENT FOR PUBLIC COMMENT:

Lorraine Wilson, M.D.; Novartis — Agenda Item No. 7

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

1A: Roll Call

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

ACTION: NONE REQUIRED.

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

Lorraine Wilson, M.D.; Novartis, for Agenda Item 7.

ACTION: NONE REQUIRED.

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

3A: February 13, 2008 DUR Minutes

Dr. Kuhls moved to approve minutes as amended (corrections were noted in red; Agenda Item No. 3 and Agenda Item No. 13); seconded by Dr. Bell.

ACTION: MOTION CARRIED.

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

4A: Retrospective Drug Utilization Review Report: November 2007

4B: Retrospective Drug Utilization Review Response: August 2007

4C: Medication Coverage Activity Audit: February 2008

4D: Help Desk Activity Audit: February 2008

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

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 5: **VOTE TO PRIOR AUTHORIZE COMBIGAN™**

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

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

ACTION: MOTION CARRIED.

AGENDA ITEM NO. 6: **30-DAY NOTICE TO PRIOR AUTHORIZE NARCOTIC ANALGESICS**

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

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 7: **30-DAY NOTICE TO PRIOR AUTHORIZE TEKTURNA HCT®**

For Public Comment; Dr. Lorraine Wilson: Good evening. I'm Lorraine Wilson. I'm a nephrologist here in Oklahoma City. I've practiced many years, and the focus of my practice is the treatment of chronic kidney disease and hypertension, and I educate many physicians in the state on the treatment of hypertension, and I've been asked today to help update you on the use of aliskiren in the treatment of hypertension and I how I see it being used presently. Just to briefly touch on the scope of the problem, for those of you who aren't quite as familiar with the problem, 64 million Americans are hypertensive. Only half of the people we treat get to goal, so half of the people that are on medication don't reach their goal and one out of five deaths in the United States is directly related to high blood pressure. So there is a big surge now to try to get our patients to goal and that has changed dramatically in the last several years. It's currently recommended goal blood pressure be 130/80 for high risk patients. If we have a patient that we see in the office that has a blood pressure of more than 20 points above 130, we know it's going to take two to four drugs to get them to goal. That's statistically been proven in many, many, many studies. So the focus of our, the thrust of our therapy right now is on combination medications. To help our patients succeed. We have had little in the way of new medications in the last ten years. The focus for my practice and many, many physicians who deal with hypertensive patients, diabetic patients, kidney disease patients, and cardiovascular patients is manipulation of the renin-angiotensin-aldosterone system, the RAS system. We have had two classes of drugs to deal with the RAS system. ACE inhibitors, which have been around for 25 years, and ARB's – angiotensin receptor blockers – which were introduced in the 1990's. We've had no new classes of drugs since the mid-90's until aliskiren was approved last year by the FDA. It works in a completely different fashion than the ACE inhibitors and the ARB drugs. And I have a schematic there which you may want to look at if you don't remember the RAS system and how it works. But renin acts on angiotensinogen to produce angiotensin-1. The ability of renin to do that is measured by PRA. We measure PRA indication, we're measuring that activity. Tekturna sits in

the binding pocket for renin and prevents that from happening and it's very effective. The ACE's and ARB's incompletely block the production of angiotensin-2. And we have learned that in combination with ACE's and ARB's, aliskiren the new drug, has additive effects. If aliskiren is added to an ARB you have an additional 30% reduction in blood pressure. If it's added to an ACE, you have 40% additional reduction in blood pressure. And if it's added to a thiazide diuretic, you have 50% additional reduction in blood pressure. So, if I see a patient in my office that has a blood pressure of 160/90, for example, they're overweight, they're diabetic, they have cardiovascular disease, I know that up titration with one drug will not get them to therapy, usually. If I step up from their ACE to a hydrochlorothiazide I'm not going to get them to therapy statistically, as been statistically shown. So what we would like to ask is that the patients that we see that are at risk, that are already on an ACE or an ARB, that they be allowed to use the fixed combination of aliskiren HCT rather than step-titrating to hydrochlorothiazide first, not reaching the goal and having to come back a month or two later and titrate up again. So it shortens the time in which we get the patient to goal and it's more effective than the current titration method.

Dr. Kuhls: I have a question. If you have one of these heart patients coming in to you de novo, and you already know that it's going to probably take multiple drugs, that's what you said, wouldn't you initially try to add a diuretic initially to your therapy to begin with, as primary therapy. I know you don't see a lot of patients in primary care being treated the first time, your patient population is different, but in the out-patient general setting, if you do think that you have a very complicated patient, multiple risk factors, you think that it's going to be hard to treat their hypertension, wouldn't you do one of your ACE's or whatever with a diuretic, thiazide diuretic, to begin with?

Dr. Wilson: If I saw a patient de novo with new onset hypertension and they were 160/90 I know right off the bat that I need two drugs to get ..... a minimum of two drugs, and probably, statistically speaking, three. If they're diabetic, possibly four. So yes, I'm going to start with two drugs and many times that is going to include a diuretic, but not always. If they have gout, if they have a sulfa allergy, if they don't want to take a diuretic. There are many patients who I've put on a fixed dose but not necessarily with a diuretic.

Dr. Kuhls: Right. But, then with that argument is going second right to Tekturna with diuretic, you have the same risk factors in that gout patient.

Dr. Wilson: Yeah, I thought you were asking me a different question.

Dr. Kuhls: Well, I'm asking you ..... many of the patients that you're going to consider doing Tekturna with diuretic are already going to be the patients that are high risk and have failed and that many of those patients are already going to have had thiazide diuretic with whatever their primary other agent, whatever that physician wants to choose.

Dr. Wilson: And then it's a moot issue, because according to this algorithm, you have the ability to add Tekturna on. If they're already on the diuretic, then you pass go, and you can go to Tekturna.

Dr. Kuhls: Exactly.

Dr. Wilson: Yes, yes. But if you have the patient that's coming to you and is not on a diuretic, they're on lisinopril, and their blood pressure's 160/90, I know that adding the diuretic alone is not going to get me to 130/80, so rather than add the diuretic, wait 30 days, come back and add another drug, what I'm asking you to consider is not to cut out that middle step, and add the Tekturna HCT to the lisinopril .....

Dr. Kuhls: I understand that.

Dr. Wilson: Yeah.

Dr. Kuhls: But I think many patients, I don't do a lot of hypertension compared to others in this room, but most patients already, the routine patient, I don't want to talk about gout, some of the contraindications to diuretics have already been, had diuretic therapy with whatever.

Dr. Wilson: Right, and then .....

Dr. Kuhls: Then it's moot.

Dr. Wilson: Then it's moot, because you're free to use whatever's available on the next tier.

Dr. Kuhls: Right.

Dr. McNeill: I would imagine that probably 90% or greater would already be on a diuretic.

Dr. Wilson: Not necessarily.And that's probably going to change from practice to practice, but many on a diuretic. I wouldn't, I don't know what those statistics are.

Dr. McNeill: Thank you, Dr. Wilson.

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

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 8: **FISCAL YEAR 2007 ANNUAL REVIEW**

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

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 9: **UTILIZATION REVIEW OF TOPICAL ANTIBIOTICS**

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

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 10: **VOTE ON NEW QUANTITY LIMITS & ANNUAL REVIEW OF OSTEOPOROSIS MEDICATIONS / BONE RESORPTION SUPPRESSION AGENTS**

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

AGENDA ITEM NO. 11: **ANNUAL REVIEW OF NASAL ALLERGY PRODUCTS**

Materials included in agenda packet; presented by Dr. Moore. Motion was made to update category to three tiers.
Dr. Kuhls moved to approve; seconded by Dr. Rhymer.
ACTION: MOTION CARRIED.

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

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

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

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

13A: Oral Allergy Follow-Up
13B: Methylphenidate Follow-Up
13C: Qualaquin Annual Review
13D: Oral Antifungals
13E: New Product Reviews
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 14: **ADJOURNMENT**

The meeting was adjourned at 7:10 p.m.

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: March 13, 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 March 12, 2008

Recommendation 1: Vote to Prior Authorize Combigan™

MOTION CARRIED by unanimous approval.

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. Information regarding need for use of combination product over single ingredient products must also be provided.

Recommendation 2: Vote on Quantity Limits for Bone Resorption Suppression Agents

MOTION CARRIED by unanimous approval.

1. Etidronate (Didronel): Maximum of 6 months of treatment per year.
    a. 200mg tablet 75 tablets per 30 days
    b. 400mg tablet 150 tablets per 30 days
2. Zoledronic Acid (Reclast): 5mg (100ml) per 365 days.

The DUR Board also recommends further review of this category for possible inclusion in the Product Based Prior Authorization Program.

Recommendation 3: Annual Review of Nasal Allergy Products

MOTION CARRIED by unanimous approval.

The DUR Board recommends the following changes to the Nasal Allergy Product Based Prior Authorization Category:

Nasal Allergy Products		
Tier 1	***Tier 2***	***Tier 3***
Corticosteroids		**Omnaris™**
fluticasone		**Nasonex®**
flunisolide		**Veramyst™**
		Beconase® AQ
Other		**Nasacort® AQ**
ipratropium bromide		**Rhinocort® AQ**
		Astelin®

1. The following criteria are required for approval of a Tier 2 product (or a Tier 3 product if no Tier 2 exists):
    a. Documented adverse effect or contraindication to the preferred products.
    b. Failure with at least two Tier 1 medications defined as no beneficial response after at least two weeks each of use during which time the drug has been titrated to the recommended dose (~~at least one trial must be a corticosteroid~~ all available Tier 1 corticosteroids should be tried prior to approval of higher Tiered products).
2. The following criteria are required for approval of a Tier 3 product:
    a. All Tier 2 criteria must be met.
    b. Failure with all available Tier 2 products defined as no beneficial response after at least two weeks each of use during which time the drug has been titrated to the recommended dose.
3. Approvals will be for the duration of three months, except for members with chronic diseases such as asthma or COPD, in which case authorizations will be for the duration of one year.

Appendix B

Retrospective Drug Utilization Review Report

Claims Reviewed for December 2007

Module	**Drug Interaction**	**Duplication of Therapy**	**Drug-Disease Precautions**	**Dosing & Duration**
Total # of messages returned by system when no limits were applied	31,412	48,489	794,608	27,475
Limits which were applied	Established, Major, Males and Females, Age 19-37	Narcotics, Males and Females, Age 22-24	Contraindicated, Males and Females, Age 36-42, Asthma	High Dose only, 44-150 year old, male and females, Abilify and Geodon
Total # of messages after limits were applied	48	140	58	7
Total # of members reviewed after limits were applied	48	105	36	7

LETTERS			
Prescribers		**Pharmacies**	
Sent	**Responded**	**Sent**	**Responded**
154		71	

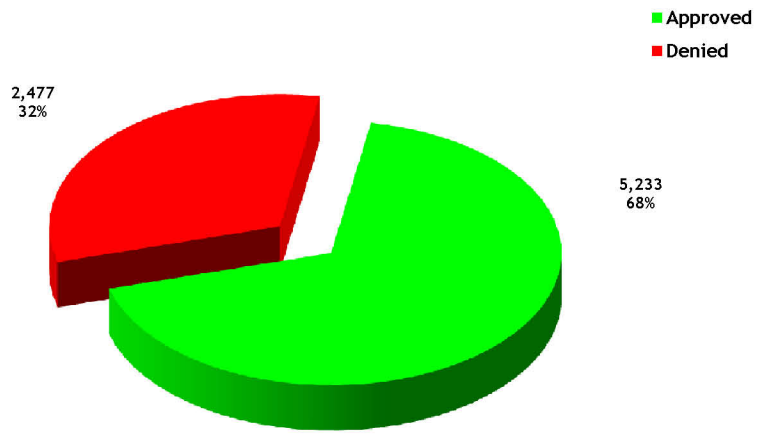
Medication Therapy Management Services Program

FY '08 Quarters 1 and 2

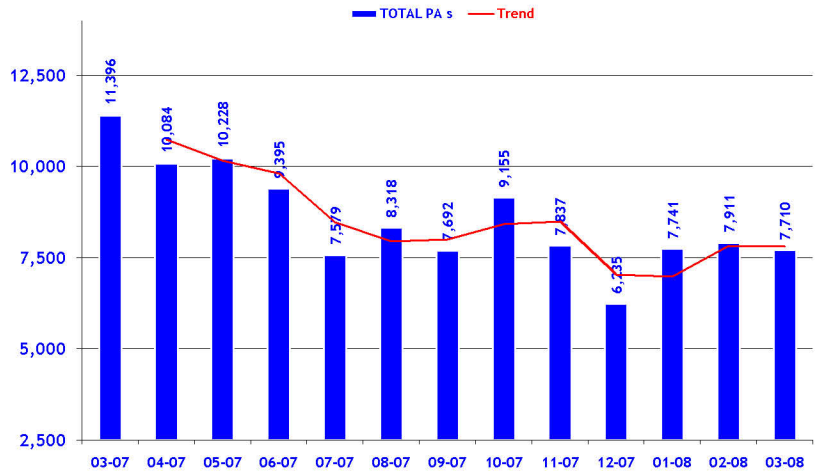
July 2007 – December 2007

	Member Profiles Reviewed		Prior Authorizations				Communications	
Month	**New Members**	**Established Members**	**Total**	**Approved**	**Denied**	**Incomplete**	**Letters**	**Calls**
July 2007	15	13	213	144	15	54	25	7
August 2007	20	11	325	185	19	121	62	5
Sept 2007	15	15	204	139	20	45	62	8
1st Quarter	**50**	**39**	**742**	**468**	**54**	**220**	**149**	**20**
October 2007	20	10	275	189	20	66	86	9
November 2007	8	26	197	138	25	34	115	7
Dec 2007	14	25	186	110	50	26	107	6
2nd Quarter	**42**	**61**	**658**	**437**	**95**	**126**	**308**	**22**
Totals	**126**	**100**	**1,400**	**905**	**149**	**346**	**551**	**42**

PRIOR AUTHORIZATION ACTIVITY REPORT
March 2008



PRIOR AUTHORIZATION REPORT
March 2007 – March 2008



Activity Audit for
March 01, 2008 Through March 31, 2008

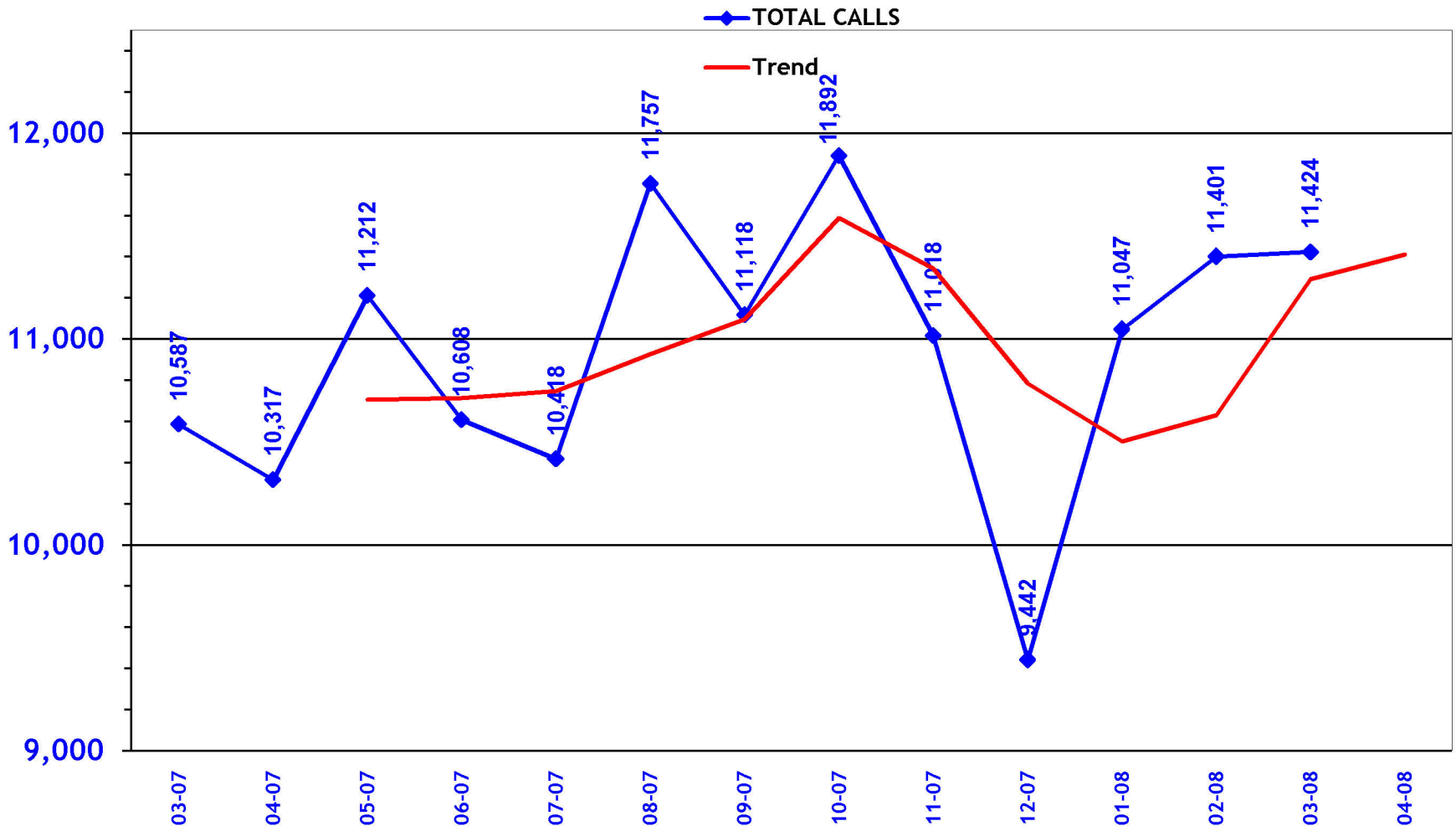
	Average Length of Approvals in Days	Approved	Denied	Total
ACE Inhibitors	87	11	8	19
Angiotensin Receptor Antagonist	299	26	79	105
Antidepressant	259	210	304	514
Antihistamine	95	383	301	684
Antiulcers	6	10	3	13
Anxiolytic	94	2691	369	3060
Calcium Channel Blockers	93	5	4	9
Growth Hormones	165	27	0	27
HTN Combos	225	5	12	17
Insomnia	109	31	15	46
Nsaids	251	29	71	100
Plavix	130	176	22	198
Stimulant	217	654	325	979
Others	102	973	964	1937
Emergency PAs		2	0	2
Total		**5233**	**2477**	**7710**
Overrides				
Brand	185	29	17	46
Dosage Change	18	324	20	344
Ingredient Duplication	23	23	6	29
Lost/Broken Rx	20	77	2	79
Nursing Home Issue	11	61	1	62
Other	30	20	10	30
Quantity vs. Days Supply	218	279	134	413
Stolen	31	3	2	5
Wrong D.S. on Previous Rx	0	0	4	4
Overrides Total		**793**	**190**	**983**

Denial Reasons

Lack required information to process request.	2287
Unable to verify required trials.	837
Not an FDA approved indication/diagnosis.	209
Considered duplicate therapy. Member has a prior authorization for similar medication.	146
Does not meet established criteria.	49
Requested dose exceeds maximum recommended FDA dose.	40
Member has active PA for requested medication.	26
Medication not covered as pharmacy benefit.	11
Duplicate Requests	467
* Changes to existing	558

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

CALL VOLUME MONTHLY REPORT
March 2007 – March 2008



04-06 thru 03-07: corrected totals

Appendix C

Vote to Prior Authorize Tekturna HCT® (aliskiren and hydrochlorothiazide)

Oklahoma Health Care Authority
April 2008

Manufacturer	Novartis Pharmaceuticals
Classification	Direct Renin Inhibitor and Diuretic Combination
Status:	Prescription Only

Summary

Tekturna HCT® is a combination dose form of the direct renin inhibitor aliskiren and the diuretic hydrochlorothiazide. It was approved by the FDA on January 23, 2008. It is indicated for the treatment of hypertension. Because it is a fixed dose combination, it is not recommended for initial therapy. Tekturna HCT® is dosed once daily and may be titrated up to a maximum dose of 300/25mg a day. It may be administered with other antihypertensive medications.

Tekturna HCT® is contraindicated in patients with anuria or hypersensitivity to sulfonamide-derived drugs. The most common side effects of therapy are dizziness and diarrhea. The usual warnings and concerns seen with HCTZ monotherapy also apply with Tekturna HCT®.

Recommendations

The College of Pharmacy recommends adding Tekturna HCT® to the Antihypertensive PBPA Category as a tier-3 agent with Tekturna® and the following criteria:

1. FDA approved indication.
2. Recent trial, within the previous 6 months and at least 4 weeks in duration, of an ACE inhibitor (or an ARB if previous trial of an ACEI) and a diuretic, used concomitantly at recommended doses, that did not yield adequate blood pressure control.

Reference

Tekturna HCT® Product Information. Novartis Pharmaceuticals. January 2008.

Appendix D

Vote to Prior Authorize Narcotic Analgesics

Oklahoma HealthCare Authority
April 2008

This category was introduced for possible inclusion in the Product Based Prior Authorization program in September 2007. See the September, February and March DUR packets for complete discussion of this category. This notice is presented to meet the statutory requirements of 63 O.S. Sec. 5030.5.

Recommendations

The College of Pharmacy recommends adding the Narcotic Analgesics to the Product Based Prior Authorization Program.

Tier 1	Tier 2	Tier 3	Oncology Only
All Immediate Release Narcotics Not Listed in Higher Tier*	**Long-Acting**		
	Morphine ER* Duragesic® Patches†	Kadian® Avinza® Opana® ER Oxycontin®	
	Short Acting		
	Xodol® Opana®		Actiq® Fentora®

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

Recommended Criteria:

1. Tier 2 agents will only be approved after:
    a. A minimum 30 day documented trial/titration period of at least two Tier 1 agents in the past 90 days or
    b. Clinically appropriate pain therapy requiring time-released medication.

    In either case, diagnosis should be for pain related to a chronic condition.
2. Tier 3 agents will only be approved after:
    a. A minimum 30 day documented trial period of at least two Tier 2 agents in different classes in the past 90 days or
    b. Documented allergy or contraindication to all Tier 2 agents.
3. Members with an oncology related diagnosis will be exempt from the prior authorization process, quantity and dosage limits would still apply.
4. Actiq® and Fentora® are only approved for oncology related diagnoses.
5. Only 1 long-acting and 1 short-acting agent can be used concurrently regardless of diagnosis (methadone is included in this criteria).

Appendix E

60 Day Notice to Prior Authorize Osteoporosis Medications

Oklahoma Health Care Authority

April 2008

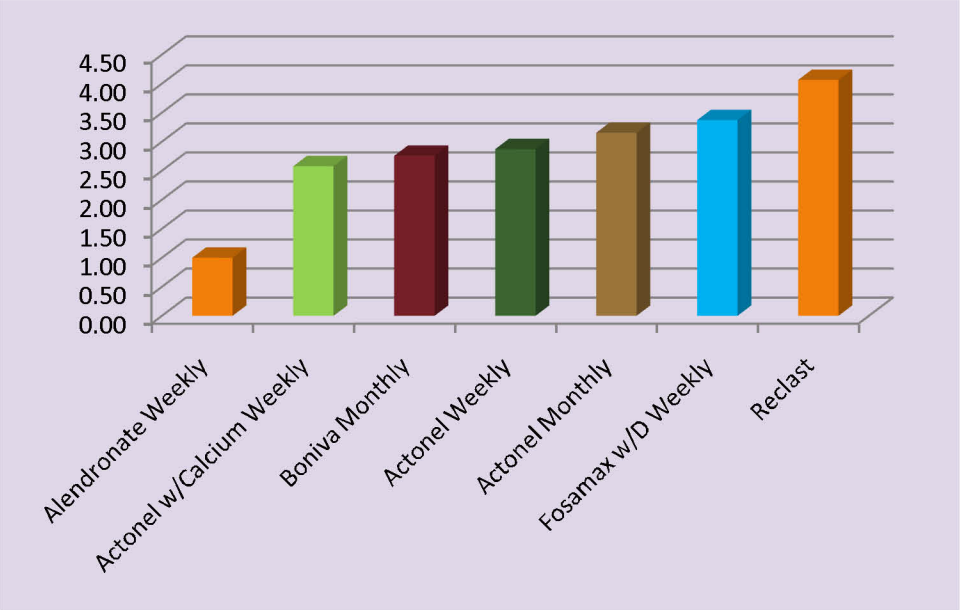
This category was introduced for possible inclusion in the Product Based Prior Authorization program in March 2008. See the March DUR packet for a more complete discussion of the category. This notice and statement of potential economic impact are presented to meet the statutory requirements of 63 O.S. Sec. 5030.5.

Total Reimbursement – July 2007 through December 2007

RANK CLAIMS	RANK COST	GENERIC NAME	CLAIMS	UNITS	DAYS	MEMBERS	COST	UNITS / DAY	CLAIMS / CLIENT	COST / DAY	PERCENT COST
1	1	Alendronate	1,575	34,148	49,683	465	$139,609.28	0.69	3.39	$2.81	32.97%
6	2	Teriparatide	121	363	3,420	29	$87,245.39	0.11	4.17	$25.51	20.60%
3	3	Ibandronate	665	986	27,095	249	$77,761.03	0.04	2.67	$2.87	18.36%
2	4	Risedronate	831	4,776	25,135	212	$72,823.78	0.19	3.92	$2.90	17.20%
4	5	Alendronate + D	260	1,128	8,052	76	$22,283.63	0.14	3.42	$2.77	5.26%
5	6	Calcitonin	208	823	6,226	71	$12,896.10	0.13	2.93	$2.07	3.05%
7	7	Pamidronate	47	437	49	12	$8,275.65	8.92	3.92	$168.89	1.95%
9	8	Etidronate	6	540	180	1	$1,674.66	3	6	$9.30	0.40%
8	9	Risedronate + Calcium	12	312	336	4	$934.05	0.93	3	$2.78	0.22%
		Total	**3,725**	**43,513**	**120,176**	**1,065**	**$423,503.57**	**0.36**	**3.5**	**$3.52**	

Market Analysis

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.



Recommendations:

The College of Pharmacy recommends adding the Osteoporosis Medications to the Product Based Prior Authorization Program.

Tier 1*	Tier 2	Tier 3
Alendronate (Fosamax)		Ibandronate (Boniva)
Calcium + Vitamin D		Risedronate (Actonel)
		Zoledronic acid (Reclast)

*Branded products will require a brand name override.

Recommended Criteria:

1. FDA approved diagnosis.
2. Recent 180-day trial (within the previous 365 days) of all available Tier 1 medications at maximum recommended dose. Calcium and Vitamin D should also be used in combination with a biphosphonate at recommended dosage for member's age group (see Attachement 1).
3. Most recent BMD (T-Score at or below -2.5) results should be submitted.
4. Approval will be for 1 year.
5. No concomitant use of biphosphonate therapy will be approved. No additional biphosphonate may be approved for 365 days following zoledronic acid infusion.
6. Clinical Exceptions:
    a. FDA approved non-osteoporosis diagnosis.
    b. Risedronate may be approved for members with high risk for gastric side effects.
7. Reclast will be exempt from prior authorization for a diagnosis of Paget's disease or for osteoporosis if secondary diagnosis meets criteria (see Attachment 2).

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 products to a Tier 1 product of 100%, it is estimated that approximately 500 petitions would be required. The proposed tier changes would affect approximately 50 % 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 $3,660 and $7,085 annually. Anticipated actual administrative cost to the program is projected to be less than $5,000.

Potential Program Savings

Potential net ingredient savings to the program based on recommended tiers and a potential shift of 100% of market share from Tier 3 to Tier 1 is estimated to be $175,050 annually. Additionally a further savings of approximately $80,016 per year will be saved due to the addition of generic alendronate to the market. The cost of adding Calcium and Vitamin D to each member's therapy is estimated to be $59,974. This results in a net savings of $195,092 annually over 2007 spending.

Total Potential Savings

Potential Net Ingredient Savings:	$ 195,092		$ 195,092
Potential Administrative Cost:	$- 7,085		$- 3,660
Total Potential Annual Savings:	**$ 188,007**	**to**	**$ 191,432**
Percent of Current Reimbursement		**~ 22 %**	

Attachment 1

Dietary Reference Intakes for Vitamin D (Based on absence of adequate exposure to sunlight.)				
	Life Stage Group	RDA/AI (IU)	UL (IU)	Adverse effects of excessive consumption
Infants	0-6 mo	200	1000	Elevated plasma 25 (OH) D concentration causing hypercalcemia
	7-12 mo	200	1000	
Children	1-3 yrs	200	2000	
	4-8 yrs	200	2000	
Males	9-13	200	2000	
	14-18	200	2000	
	19-30	200	2000	
	31-50	200	2000	
	50-70	400	2000	
	> 70	600	2000	
Females	9-13	200	2000	
	14-18	200	2000	
	19-30	200	2000	
	31-50	200	2000	
	50-70	400	2000	
	>70	600	2000	
Pregnant or Lactating	≤18	200	2000	
	19-30	200	2000	
	31-50	200	2000	

Dietary Reference Intakes for Calcium				
	Life Stage Group	RDA/AI (mg)	Upper Limit (mg)	Adverse Effects of excessive consumption
Infants	0-6 months	210	ND	Kidney stones, hypercalcemia, renal insufficiency, milk alkali syndrome, possible CV risks
	7-12 months	270	ND	
Children	1-3 yrs	500	2500	
	4-8 yrs	800	2500	
Males	9-13 yrs	1300	2500	
	14-18 yrs	1300	2500	
	19-30 yrs	1000	2500	
	31-49 yrs	1000	2500	
	50-70 yrs	1200	2500	
	> 70 yo	1200	2500	
Females	9-13 yrs	1300	2500	
	14-18 yrs	1300	2500	
	19-30 yrs	1000	2500	
	31-50 yrs	1000	2500	
	50-70 yrs	1200	2500	
	>70 yrs	1200	2500	
Pregnant or Lactating	≤18 yrs	1300	2500	
	19-30 yrs	1000	2500	
	31-50 yrs	1000	2500	

United States Department of Agriculture. Dietary Reference Intake Tables. United States Department of Agriculture. http://www.iom.edu/Object.File/Master/7/294/0.pdf. http://www.iom.edu/Object.File/Master/7/296/webtablevitamins.pdf. Published 2001. Accessed March 13, 2008.

Attachment 2

Reclast Coverage Guidelines

Reclast will be covered for postmenopausal osteoporosis in women who have the following secondary diagnoses:

- Severe esophageal disease (e.g., ulcerations, strictures):
  - ICD-9 codes 530.0, 530.20-530.21, 530.3 and 710.1
- Inability to take anything by mouth:
  - ICD-9 codes 530.87, V44.1, V45.72 and V45.75
- Inability to sit or stand for prolonged periods.
  - ICD-9 code V49.84.
- Inability to take an oral bisphosphonate for other special medical circumstances that justify the method of administration:
  - ICD-9 codes 995.29 and V12.79.

Member must have osteoporosis as evidenced by a spine, hip or pelvis Bone Mineral Density (BMD) T-score less than -2.5.

http://www.trailblazerhealth.com/Tools/Local%20Coverage%20Determinations/Default.aspx?ID=2084

Attachment 3

Osteoporosis and Bone Resorption Suppression Products

	FDA Approved Indication		Unlabeled or Other Uses	Efficacy	Side Effects	Contraindications	Level of Evidence
	Prevention	*Treatment*					
Calcium/VitaminD	Osteoporosis	Osteoporosis	Dietary Supplement, Antacid	Reduce rate of bone loss and fractures in women more than 5 years postmenopausal; effective beyond 75 years of age; WHI study indicates 29% reduction in hip fractures; Vitamin D_3 (cholecalciferol) preferred over Vitamin D_2 (ergocalciferol)	Bloating, gas, and constipation. Reduced side effects with calcium citrate.	Urinary calcium excretion >300mg/24 hours uncontrolled with thiazide diuretics. WHI study indicates 17% increase kidney stones	1B Relatively safe and effective in long-term use
Bisphophonates Fosamax (alendronate, alendronate w/ Vitamin D)	Osteoporosis (recently diagnosed)	Osteoporosis (Post-menopausal and gluco-corticoid induced)	Dietary Supplement of Vitamin D_3	Reduce the risk of spine, hip and non spine fractures by 50%. Increase BMD at spine and hip by 5 to 10%.	Dysphagia, esophagitis, esophageal or gastric ulcer. Take with 8 oz. water on empty stomach. Remain sitting or standing for 30 minutes on empty stomach.	Active upper gastrointestinal disease, hypersensitivity, hypocalcemia. Severe renal insufficiency require dose adjustment. Pregnancy **C**.	2B Evidence available at 7 year efficacy.
Actonel (Risedronate, risedronate w/calcium carbonate)	Osteoporosis (recently diagnosed)	Osteoporosis (Post-menopausal and gluco-corticoid induced, Men) Paget's Disease	Dietary Supplement of Calcium Carbonate	Reduce risk of spine fractures by 40%; Hip and non spine by 30%.	(see above)	(see above) Avoid if Creatine clearance is <30ml/minute.	2B Evidence available at 3 year efficacy.
Aredia (pamidronate)	n/a	Cancer related hyper-calcemia Osteolytic bone lesions Paget's Disease	Treatment of pediatric osteoporosis, treatment of osteogenesis imperfecta	Not FDA approved but often used in patients who cannot tolerate oral treatment. Improves BMD but fracture prevention lacks supporting evidence.	(see above) plus fatigue, fever, insomnia, anemia, dyspnea, cough, myalgia.	Hypersensitivity, Pregnancy **D**.	2B Patients who cannot tolerate oral products or cannot absorb due to GI disorders.
Boniva (Ibandronate)	Treatment and prevention of osteoporosis	Treatment and prevention of osteoporosis	Hypercalcemia of malignancy; corticosteroid-induced	Increases BMD(1.8 to 3%), reduce the risk of new vertebral fractures versus placebo.	(see above) plus dyspepsia, back pain. Ibandronate should be taken in an upright position with a full	Hypersensitivity, Pregancy risk factor **C**. Avoid if creatine clearance is	2B A reduction in hip fracture risk has

	in postmenopausal females	in postmenopausal females	osteoporosis; Paget's disease; reduce bone pain and skeletal complications from metastatic bone disease		glass (6-8 oz) of plain water and the patient should avoid lying down for 60 minutes to minimize the possibility of GI side effects.	<30ml/minute.	not been established in randomized trials.
Reclast (Zoledronic acid)	n/a	Treatment of hypercalcemia of malig-nancy (albumin-corrected serum calcium ≥12 mg/dL), multiple myeloma, bone metastases of solid tumors, Paget's disease of bone, postmenopausal osteoporosis	Prevention of bone loss associated with aromatase inhibitor therapy in postmenopausal women with breast cancer; prevention of bone loss associated with androgen deprivation therapy in prostate cancer	3 yr Horizon Pivotal Trial shown 70% reduction in vertebral fracture and 41 % in hip fracture, compared to placebo. Maintain adequate hydration (2-3 L/day of fluids) unless instructed to restrict fluid intake. **Note:** Patients should receive a daily calcium supplement and multivitamin containing vitamin D For those that cannot oral bisphophonates or inability to sit or stand upright.	An acute reaction (eg, arthralgia, fever, flu-like symptoms, myalgia) may occur within the first 3 days following infusion; usually resolves within 3-4 days of onset, although may take up to 14 days to resolve. Hypertension, Fever, headache, arthralgia, myalgia, nausea, dizziness, fatigue, atrial fibrillation.	Pregnancy risk factor **D**,**Renal deterioration: Single and multiple infusions have been associated with renal deterioration, resulting in renal failure and dialysis; has occurred in patients with normal and impaired renal function. Aspirin-sensitive asthma: Use with caution in patients with aspirin-sensitive asthma; may cause bronchoconstriction.	2B However, long-term safety data beyond three years in patients with osteoporosis is lacking.
Didronel (Etidronate)	Heterotopic ossification due to spinal cord injury or after total hip replacement. Hyper-calcemia of malignancy	Symptomatic treatment of Paget's disease; Treatment of heterotopic ossification due to spinal cord injury or after total hip replacement	Postmenopausal osteoporosis	2/3 decrease in clinically important heterotopic bone formation; Retards progression of immature lesions and decreases severity by 50%, persisting through 9 months.	Diarrhea, nausea, bone pain.	Hypersensitivity to bisphosphonates or any component of the formulation; overt osteomalacia	2C
Calcitonin	n/a	Treatment of Paget's disease of bone (osteitis deformans); adjunctive therapy for hypercalcemia; treatment of osteoporosis	n/a	Reduce the risk of spine fracture by 21%. Increase in BMD.	Rhinitis, epistaxis, nausea, flushing. GI symptoms not as common with nasal route.	Hypersensitivity. Pregnancy risk factor **C**.	2B

		in women >5 years postmenopause					
Hormone Therapy Estrogen, Estrogen/medroxy progesterone	Osteoporosis (postmenopausal)	n/a	Least preferred. No longer first-line agent.	Reduce the risk of spine and hip fractures by 34% with estrogen/medroxyprogesterone. 39%decrease in risk with estrogen alone. Treatment >7yrs = 50% lower risk.	Hyperplasia, carcinoma, Irregular vaginal bleeding, cholelithiasis, fluid retention, mastalgia, headache, abdominal pain, thromboembolism.	Pregnancy, breast cancer, neoplasia, undiagnosed genital bleeding, thromboembolic disease,hypersensitivity. Increase in triglycerides.	2A Risk for breast cancer, heart attack, stroke, and venous thromboembolism.
Forteo (teriparatide)	n/a	Treatment of osteoporosis in post-menopausal women at high risk of fracture; treatment of primary or hypogonadal osteoporosis in men at high risk of fracture	n/a	Reduce spine fractures by 65% and nonspine fractures by 54% after 19 months of therapy. Increased bone density in lumbar spine and neck in men over 11 months 9-13% and 3-6% respectively. Reduces bone resorption. Anabolic effects resulting in increased bone density.	Leg cramps and dizziness. Nausea, orthostatic hypotension, arthralgia, depression, vertigo, gastrointestinal dyspepsia, rash, and asthenia. Monitor for hypercalcemia or hypercalciuria.	Contraindicated in Paget's disease, patients with open epiphysis, history of irradiation of skeleton, elevation of alkaline phosphatase of skeletal origin. Pregnancy risk factor C. Caution in patients with urolithiasis, hx of skeletal metastases.	2B Limit 2 year treatment.
Selective Estrogen Receptor Modulators Evista (Raloxifene)	Osteoporosis Risk reduction for invasive breast cancer in post-menopausal women with osteoporosis and in postmenopausal women with high risk for invasive breast cancer	Osteoporosis	**Evista(Raloxifene)** 60mg/day.	Reduce spine fractures by 50% with 3 year treatment. Increased BMD by 2.7% in spine and 2.4 % neck.	Hot flashes and deep vein thrombosis. Peripheral edema,	Pregnancy risk factor X, hypersensitivity, current thromboembolic disease. Prolonged immobilization. Avoid ampicillin and cholestyramine use.	2B Has shown reduction in LDL and total cholesterol by 7 to 11%. MORE study shown 76% reduction in breast cancer. Efficacy and safety up to 3 yrs..
Combination				Insufficient			

Recommendation grades

1. Strong recommendation: Benefits clearly outweigh the risks and burdens (or vice versa) for most, if not all, patients
2. Weak recommendation: Benefits and risks closely balanced and/or uncertain

Evidence grades

A. High-quality evidence: Consistent evidence from randomized trials, or overwhelming evidence of some other form
B. Moderate-quality evidence: Evidence from randomized trials with important limitations, or very strong evidence of some other form
C. Low-quality evidence: Evidence from observational studies, unsystematic clinical observations, or from randomized trials with serious flaws

Appendix F

60 Day Notice to Prior Authorize Topical Antibiotics

Oklahoma Health Care Authority
April 2008

This category was introduced for possible inclusion in the Product Based Prior Authorization program in March 2008. See the March 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

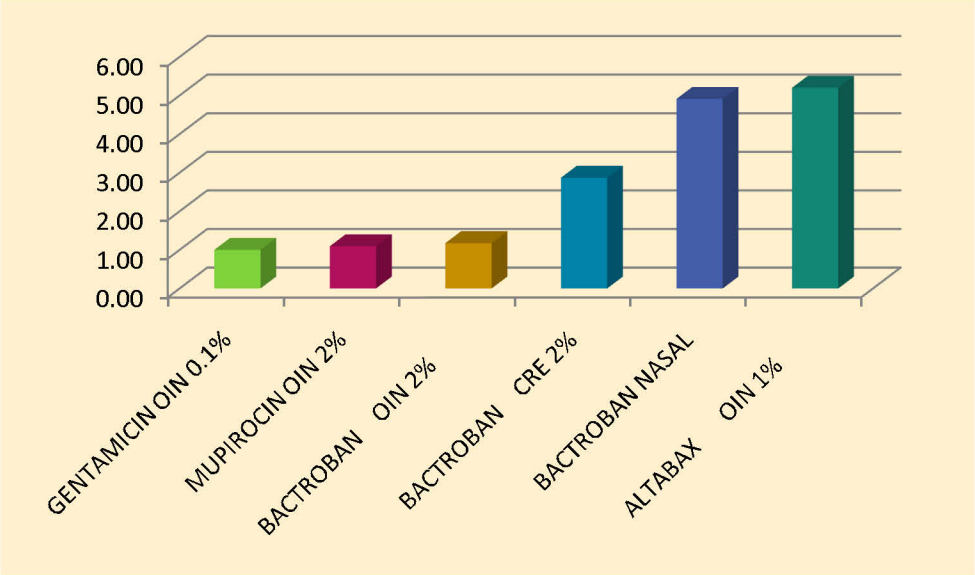
RANK CLAIMS	RANK COST	PRODUCT NAME	CLAIMS	UNITS	DAYS	MEMBERS	COST	UNITS / DAY	CLAIMS/ CLIENT	COST / DAY	PERCENT COST
2	1	BACTROBAN CRE 2%	4,758	120,893	52,580	4,092	$297,888.47	2.3	1.16	$5.67	40.64%
3	2	ALTABAX OIN 1%	2,984	43,938	25,233	2,508	$237,628.10	1.74	1.19	$9.42	32.42%
1	3	MUPIROCIN OIN	9,426	227,421	104,025	7,996	$168,594.98	2.19	1.18	$1.62	23.00%
4	4	BACTROBAN OIN NASAL 2%	239	3,139	2,239	193	$24,323.63	1.4	1.24	$10.86	3.32%
5	5	GENTAMICIN	168	4,477	1,523	104	$2,385.96	2.94	1.62	$1.57	0.33%
6	6	CORTISPORIN OIN 1%	18	252	166	15	$1,020.04	1.52	1.2	$6.14	0.14%
7	7	CORTISPORIN CRE 0.5%	16	164	166	10	$975.57	0.99	1.6	$5.88	0.13%
9	8	POLYSPORIN	2	165	20	2	$71.93	8.25	1	$3.60	0.01%
8	9	TRIPLE ANTIB OIN	3	210	21	3	$16.12	10	1	$0.77	0.00%
10	10	BACITR ZINC OIN	1	453	30	1	$6.86	15.1	1	$0.23	0.00%
		Total	**17,615**	**401,112**	**186,003**		**$732,911.66**	**2.16**	**1.24**	**$3.94**	

Indications

Drug	Indication
Gentamicin	▪ Infection of skin and/or subcutaneous tissue ▪ Staphylococcal infectious disease
Mupirocin	▪ Impetigo ▪ Methicillin resistant Staph aureus infection, colonization ▪ Secondary infection – skin lesion
Retapamulin	▪ Impetigo due to S. aureus (methacillin – susceptible only) or S. pyogenes
Neomycin/Polymixin B/HC	▪ Treatment of corticosteroid responsive dermatoses with secondary infection.

Market Analysis

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



Efficacy and Safety:

The efficacy of topical Bactroban® ointment (mupirocin) in impetigo was tested in two studies. In the first, patients with impetigo were randomized to receive either Bactroban® ointment or vehicle placebo t.i.d. for 8 to 12 days. Clinical efficacy rates at end of therapy were 71% for Bactroban® ointment (n=49) and 35% for vehicle placebo (n=51). Pathogen eradication rates in the evaluable populations were 94% for Bactroban® ointment and 62% for vehicle placebo. In the second study, patients with impetigo were randomized to receive either Bactroban® ointment t.i.d. or 30 to 40 mg/kg oral erythromycin ethylsuccinate per day for 8 days. There was a follow-up visit 1 week after treatment ended. Clinical efficacy rates at the follow-up visit were 93% for Bactroban ointment (n=29) and 78.5% for erythromycin (n=28).[1]

Altabax™ was evaluated in a placebo-controlled study that enrolled adult and pediatric patients 9 months of age and older for treatment of impetigo. The success rate for the Clinical Per Protocol Populations was 89.5% (n=124) for the Altabax™ treated patients versus 53.2% (n=62) for placebo. The success rate for the Clinical Intent to Treat Population was 85.6% (n=139) for Altabax™ treated patients versus 52.1% (n=71) for placebo.[2]

The decision on how to treat Impetigo depends on the number of lesions, location and the need to limit spread of infection to others. Currently the standard of care is mupirocin. Patients who have numerous lesions or who are not responding to topical agents should receive oral antimicrobials effective against both *S. aureus* and *S. pyogenes* (A-1).[3] Because resistence to mupirocin has been noted, newer agents should be reserved for more resistant cases.

Recommendations:

The College of Pharmacy recommends creating a Product Based Prior Authorization category for this group of medications with the following tier structure and criteria:

Tier 1*	Tier 2	Tier 3
Mupirocin Oint 2% Gentamicin Oint 0.1% Gentamicin Cream 0.1% Gentamicin Powder Cortisporin Oint 1%† Cortisporin Cream 0.5%†	Supplemental Rebated Tier 3	Bactroban Cream 2% Centany Kit 2% Altabax Oint 1%

*Branded products will require a Brand Name Override when generic versions are available.
†Products will remain Tier 1 as long as federal rebate does not decrease.

Criteria:

- A 5-day trial of a Tier 1 medication (must include mupirocin) within the last month is required before a Tier 2 medication (or a Tier 3 medication if no Tier 2 exists) can be approved.
- Member must have a 5-day trial with a Tier 1 and a Tier 2 medication prior to receiving authorization for a Tier 3 medication.
- Clinical exception for drug allergy to all applicable lower tiered products or a unique indication not covered by all available lower tiered products.
- Prior authorization will be for a maximum of 10 days.

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 products to a Tier 1 product of 75%, it is estimated that approximately 4,500 petitions would be required. The proposed tier changes would affect approximately 45 % 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 $32,940 and $63,765 annually. Anticipated actual administrative cost to the program is projected to be less than $20,000.

Potential Program Savings

Potential net ingredient savings to the program based on recommended tiers and a potential shift of 75% of market share from Tier 3 to Tier 1 is estimated to be $399,349.58 annually.

Total Potential Savings

Potential Net Ingredient Savings:	$ 399,350		$ 399,350
Potential Administrative Cost:	$- 63,765		$- 32,940
Total Potential Annual Savings:	**$ 335,585**	**to**	**$ 366,410**
Percent of Current Annual Reimbursement	**~ 29.8 %**	**to**	**~ 32.6 %**

References

1. Bactroban ointment®, Product Information. GlaxoSmithKline, 2001.
2. Altabax™, Product Information. GlaxoSmithKline, 2007.
3. Stevens DL, Bisno AL, Chambers HF, et al. Practice Guidelines for the Diagnosis and Management of Skin and Soft-Tissue Infections. Clinical Infectious Disease 2005;41:1373-1406.

Appendix G

30 Day Notice to Prior Authorize Allegra Syrup and ODT Tablets and Update PBPA Category

Oklahoma Health Care Authority

April 2008

Current Criteria of Oral Allergy Prior Authorization Category

ORAL ALLERGY MEDICATIONS		
Tier 1	**Tier 2**	**Tier 3**
OTC Loratadine*	fexofenadine (generic tabs)	cetirizine (Zyrtec)**
		desloratadine (Clarinex)**
		fexofenadine (Allegra)
		levocetirizine (Xyzal)†
* For members 21 years and older, loratadine is available with prior authorization after documented trial of a non-loratadine OTC product. Loratadine does not require PA for members under age 21. ** Zyrtec and Clarinex syrup are available without PA for members age 6 months to 2 years. †Xyzal not covered for members under age 6.		

Approval Criteria:

- A 14 day trial of OTC loratadine within the last month is required before a Tier 2 medication can be approved.
- OTC loratadine and a Tier 2 product must be tried for 14 days each within the last 60 days before a Tier 3 medication can be approved.
- Diagnosis must be for a chronic allergic condition.
- Clinical exception for members with asthma.
- Prior authorization will be for 90 days, except for members with asthma. Authorization for members with asthma will be for 360 days.

Economic Impact of Changes

Total petitions submitted (cetirizine and loratadine) for this category during CY07- 11,660:

Approved *6,465*
Denied 4,201
Incomplete 994

Of these 11,660 petitions received, 844 members >21 that were denied cetirizine or loratadine. (201 of these members were also on nasal steroids.)

Potential cost for removal of non-loratadine OTC trial from step therapy for adults:

Potential Costs for 1 claim to 12 claims per year for 844 members:

$ 7,427.20 to $ 90,645.60 per year*

Total impact for removal of non-loratadine trial for Duals cannot be determined.

(*Based on an average cost per claim of $8.80 for OTC loratadine or OTC cetirizine and assuming all members were denied due to lack of non-loratadine OTC trial.)

Recommendations

ORAL ALLERGY MEDICATIONS		
Tier 1	**Tier 2**	**Tier 3**
OTC loratadine*	fexofenadine (generic tabs)	desloratadine (Clarinex)**
OTC cetirizine*		fexofenadine (Allegra)†
		levocetirizine (Xyzal)‡
* For members 21 years and older, OTC loratadine and OTC cetirizine is available with prior authorization. OTC loratadine and OTC cetirizine do not require PA for members under age 21. ** Clarinex and Allegra syrups are available without PA for members age 6 months to 2 years. †Includes new Allegra syrup and ODT formulations. ‡Xyzal not covered for members under age 6.		

Approval Criteria:

- A 14 day trial each of OTC loratadine and cetirizine within the last month is required before a Tier 2 medication can be approved.
- All Tier 2 products must be tried for 14 days each within the last 60 days before a Tier 3 medication can be approved.
- Diagnosis must be for a chronic allergic condition.
- Clinical exception for members with asthma.
- Prior authorization will be for 90 days, except for members with asthma. Authorization for members with asthma will be for 360 days.

Appendix H

30 Day Notice to Prior Authorize Pristiq™ (desvenlafaxine) and Update PBPA Category

Oklahoma Health Care Authority

April 2008

Manufacturer	Wyeth Pharmaceuticals Inc.
FDA Classification	Oral Antidepressant
Status	Prescription only

Summary[1]

- Pristiq is an extended-release selective serotonin and norepinephrine reuptake inhibitor (SNRI) indicated for the treatment of major depressive disorder (MDD) in adults.[1]
- It is the major active metabolite, O-desmethylvenlafaxine, of the antidepressant, venlafaxine.
- Available in 50 mg and 100 mg tabs.
- For initial or maintenance treatment.

Cost Comparison

	EAC/unit	SMAC/Unit	$/Month* (30 day supply)
Pristiq™ tab 50 mg	$3.75		$116.65
Pristiq™ tab 100 mg	$3.75		$116.65
Effexor XR™ tab 37.5 mg	$2.79		$87.85
Effexor XR™ tab 75 mg	$3.12		$97.75
Effexor XR™ tab 150 mg	$4.24		$131.35
Venlafaxine 25 mg		$1.31	$43.45
Venlafaxine 37.5 mg		$1.37	$45.25
Venlafaxine 50 mg		$1.43	$47.05
Venlafaxine 75 mg		$1.51	$49.45
Venlafaxine 100 mg		$1.60	$52.15

*includes $4.15 dispensing fee. 30 day supply is calculated for one unit per day due to varying doses of the immediate release meds.

Current Prior Authorization Criteria

Antidepressants	
PA Criteria: The following are criteria for approval of a Tier 2 Product: ➢ Documented adverse effect, drug interaction, or contraindication to the Tier 1 products. ➢ Failure with a Tier 1 medication defined as no beneficial or minimally beneficial response after at least 4 weeks of continuous use within the last 6 months. ➢ Unique indication not covered by a Tier 1 product. ➢ Previously stabilized on Tier 2 product. ➢ Petition for a tier 2 medication may be submitted for consideration when a unique member specific situation exists or prescription by a psychiatrist.	
Tier 1	**Tier 2**
Dual Acting Antidepressants	
Any Tier 1 SSRI or • trazodone (Desyrel) • venlafaxine (Effexor) • mirtazapine (Remeron, Remeron SolTab) • bupropion (Wellbutrin, Wellbutrin SR, **Wellbutrin XL**)	• duloxetine (Cymbalta) • venlafaxine (Effexor XR) • nefazodone (Serzone)
SSRIs (Selective Serotonin Reuptake Inhibitors)	
• citalopram (Celexa) • fluoxetine (Prozac) • fluvoxamine (Luvox) • paroxetine (Paxil, **Paxil CR**) • sertraline (Zoloft)	• citalopram (Celexa liquid) • escitalopram (Lexapro tabs & liquid) • fluvoxamine (Luvox CR) • fluoxetine (Sarafem) • fluoxetine (40mg capsules) • fluoxetine (Prozac weekly) • paroxetine (Pexeva)
Monoamine Oxidase Inhibitors	
	• selegiline transderm (Emsam) • phenelzine (Nardil) • tranylcypromine(Parnate) • selegiline (Zelapar)

Note: Supplemental rebates indicated by blue color.

Recommendations

The College of Pharmacy recommends three tiers for the Antidepressant PBPA Category and the placement of Pristiq™ in Tier 3 of the Dual Acting Antidepressants. A quantity limit of one unit per day would be also applied.

Tier 1	Tier 2	Tier 3
Dual Acting Antidepressants		
Any Tier 1 SSRI or • trazodone (Desyrel) • venlafaxine (Effexor) • mirtazapine (Remeron, Remeron SolTab) • bupropion (Wellbutrin, Wellbutrin SR, **Wellbutrin XL**)	Supplemental Rebate	• duloxetine (Cymbalta) • venlafaxine (Effexor XR) • nefazodone (Serzone) • desvenlafaxine (Pristiq)
SSRIs (Selective Serotonin Reuptake Inhibitors)		
• citalopram (Celexa) • fluoxetine (Prozac) • fluvoxamine (Luvox) • paroxetine (Paxil, **Paxil CR**) • sertraline (Zoloft)	Supplemental Rebate	• citalopram (Celexa liquid) • escitalopram (Lexapro tabs & liquid) • fluvoxamine (Luvox CR) • fluoxetine (Sarafem) • fluoxetine (40mg capsules) • fluoxetine (Prozac weekly) • paroxetine (Pexeva)
Monoamine Oxidase Inhibitors		
		• selegiline transderm (Emsam) • phenelzine (Nardil) • tranylcypromine(Parnate) • selegiline (Zelapar)

Note: Supplemental rebates indicated by blue color.

The following are criteria for approval of a Tier 2 product (or Tier 3 if no Tier 2 exists):

1. Documented adverse effect, drug interaction, or contraindication to the Tier 1 products.
2. Failure with at least two Tier 1 medications defined as no beneficial or minimally beneficial response after at least 4 weeks of continuous use within the last 6 months (must have at least 1 Tier 1 from same class).
3. Unique indication not covered by a Tier 1 product.
4. Previously stabilized on Tier 2 product (or Tier 3 product).
5. Petition for a Tier 2 medication may be submitted for consideration when a unique member specific situation exists or prescription by a psychiatrist.

The following criteria apply to Tier 3 products when a Tier 2 product exists.

1. Failure with all Tier 2 products available in the class (as defined above).
2. Unique indication not covered by a Tier 2 product.
3. Previously stabilized on Tier 3 product.
4. Petition for a Tier 3 medication may be submitted for consideration when a unique member specific situation exists or prescription by a psychiatrist.

Product Information

Dosing

- The recommended dose is 50 mg once daily.
- Additional benefit was not seen with doses greater than 50 mg.
- Gradual withdrawal at discontinuation of therapy will reduce or eliminate the incidence of symptoms including dizziness, nausea, insomnia, anxiety, fatigue, and others.

Warnings

- There is a **black box warning** regarding clinical worsening and increased suicidal risk in children, adolescents, and young adults.
- Pristiq is not approved for use in children.
- Concomitant use of MAOI's is contraindicated due to the increased risk of serotonin syndrome.
- SSRI's, other SNRI's, or triptans can be used concurrently with Pristiq, but the patient must be monitored closely for symptoms of serotonin syndrome.

Pharmacokinetics[1,2]

	Pristiq (desvenlafaxine)	Effexor XR (venlafaxine)
Protein binding	30%	27%
Half-Life	11 hrs	5 hrs
Time to Peak Concentration	7.5 hrs	5.5 hrs
Metabolism	conjugation	CYP2D6

- May be taken without regard to food
- Dose adjustment is not required for patients with mild to moderate renal insufficiency. For those with severe renal impairment (CrCl <50 ml-min), the dose is 50 mg every other day.

Adverse Events

Common (>5%) side effects include:

Nausea	Hyperhidrosis	Decreased appetite	Specific male sexual
Dizziness	Constipation	Anxiety	function disorders
Insomnia	Somnolence		

REFERENCES

1. Pristiq™ Product information, Wyeth Pharmaceuticals
2. Effexor XR™ product information, Wyeth Pharmaceuticals.

Appendix I

Early Communication About an Ongoing Safety Review of Montelukast (Singulair)

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 product and the emerging safety issue. Nor does it mean that FDA is advising health care professionals to discontinue prescribing this product. FDA is considering, but has not reached a conclusion about whether this information warrants any regulatory action. FDA intends to update this document when additional information or analyses become available.

FDA is investigating a possible association between the use of Singulair and behavior/mood changes, suicidality (suicidal thinking and behavior) and suicide. Singulair is a medicine in the drug class known as leukotriene receptor antagonists. Singulair is used to treat asthma and the symptoms of allergic rhinitis (sneezing, stuffy nose, runny nose, itching of the nose) and to prevent exercise-induced asthma.

Over the past year, the maker of Singulair, Merck & Co, Inc., has updated the prescribing information and patient information for Singulair to include the following post-marketing adverse events: tremor (March 2007), depression (April 2007), suicidality (suicidal thinking and behavior) (October 2007), and anxiousness (February 2008).

In February 2008, FDA and Merck discussed how best to communicate these labeling changes to prescribers and patients. Merck plans to highlight the recent changes in the prescribing information in face-to-face interactions with prescribers and provide prescribers with patient information leaflets about Singulair. The Singulair website includes the most current prescribing information and patient information for Singulair (www.singulair.com).

FDA is working with Merck to further evaluate a possible link between the use of Singulair and behavior/mood changes, suicidality and suicide in response to inquiries received by FDA. FDA has requested that Merck evaluate Singulair study data for more information about suicidality and suicide. FDA is reviewing the postmarketing reports it has received of behavior/mood changes, suicidality and suicide in patients who took Singulair.

Due to the complexity of the analyses, FDA anticipates that it may take up to 9 months to complete the ongoing evaluations. As soon as this review is complete, FDA will communicate the conclusions and recommendations to the public.

Singulair is an effective medicine that is indicated for the treatment of asthma and symptoms of allergic rhinitis. Patients should not stop taking Singulair before talking to their doctor if they have questions about this new information. Until further information is available, healthcare professionals and caregivers should monitor patients taking Singulair for suicidality (suicidal thinking and behavior) and changes in behavior and mood.

Other leukotriene modifying medications include zafirlukast (Accolate), which is also a leukotriene receptor antagonist and zileuton (Zyflo and Zyflo CR), which is a leukotriene synthesis inhibitor. FDA is reviewing postmarketing reports it has received of behavior/mood changes, suicidality and suicide in patients who took Accolate, Zyflo, and Zyflo CR and will assess whether further investigation is warranted.

This early communication is in keeping with FDA's commitment to inform the public about its ongoing safety reviews of drugs.

The FDA urges both healthcare professionals and patients to report side effects from the use of Singulair, Accolate, Zyflo, and Zyflo CR to the FDA's MedWatch Adverse Event Reporting program

- on-line at [www.fda.gov/medwatch/report.htm];
- by returning the postage-paid FDA form 3500 [available in PDF format at [www.fda.gov/medwatch/getforms.htm] to 5600 Fishers Lane, Rockville, MD 20852-9787;
- faxing the form to 1-800-FDA-0178; or
- by phone at 1-800-332-1088

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PDF requires the free Adobe Acrobat Reader

Date created: March 27, 2008

Early Communication about an Ongoing Safety Review of Ziagen (Abacavir) and Videx (Didanosine)

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

FDA has been made aware of recent findings from analyses of data collected from "*The Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D) Study*". The D:A:D Study is a large observational study of 33,347 HIV-1 infected patients living in North America, Europe and Australia. Patients in this study are being followed to evaluate the short- and long-term adverse effects of treatment with anti-HIV drugs.

Analyses of data collected through February 1, 2007 examined the risk of myocardial infarction (heart attack) in patients taking selected HIV drugs from the class of drugs known as nucleoside reverse transcriptase inhibitors (NRTIs): zidovudine, stavudine, abacavir, didanosine, and lamivudine. The analyses, specifically, describe the relative risk of heart attack among cumulative use, recent use (currently using or use within the past 6 months), and past use (last use greater than 6 months ago) of these drugs.

These analyses showed that recent use of abacavir or didanosine was associated with an increased risk of heart attack. Patients taking either of these drugs had a greater chance of developing a heart attack than patients taking other medications. The risk did not appear to increase over time, but remained stable and appeared to be reversible after abacavir or didanosine were stopped.

In late 2007, GlaxoSmithKline (GSK), the manufacturer of abacavir, received the preliminary findings from the D:A:D Study analyses and conducted a search of their own clinical study databases. The results of the GSK analysis are inconclusive, but did not show an increased risk. Bristol Myers Squibb (BMS), the manufacturer of didanosine, conducted an analysis of their clinical databases, and similarly, found no increased risk for heart attack with didanosine use. The results of the BMS analysis are also inconclusive.

Key findings from the D:A:D Study are as follows:

- The excess risk of heart attack in patients taking at least some NRTIs appears to be greater in patients with other risk factors for heart disease. Risk factors include a history of heart disease, high cholesterol, high blood pressure, diabetes, smoking, and age.
- Certain analyses found the risk of heart attack increased by 49% in patients taking didanosine and increased by 90% in patients taking abacavir.
- The increased risk for heart attack remained stable over the course of treatment and the effect was not seen 6 months after stopping the drugs.

FDA currently believes analyses conducted with D:A:D Study data are incomplete; no analyses were conducted evaluating the risk of heart attack when patients take tenofovir or emtricitabine, two other drugs in the class of NRTIs. However, FDA continues to evaluate the overall risks and benefits of abacavir and didanosine. This evaluation may result in the need to revise labeling for the products. Until this evaluation is complete, healthcare providers should evaluate the potential risks and benefits of each HIV-1 antiretroviral drug their patients are taking, including abacavir and didanosine.

This early communication is in keeping with FDA's commitment to inform the public about ongoing safety reviews of drugs. FDA will work with the manufacturers of abacavir and didanosine to fully evaluate the risks and benefits associated with the use of these products as part of an HIV treatment regimen. As soon as this process is complete, FDA will communicate the conclusions and recommendations to the public.

The FDA urges healthcare professionals to promptly report serious and unexpected adverse reactions associated with abacavir to the FDA MedWatch reporting program, as described below.

- online at www.fda.gov/medwatch/report.htm
- by returning the postage-paid FDA form 3500 (available in PDF format at www.fda.gov/medwatch/getforms.htm) to 5600 Fishers Lane, Rockville, MD 20852-9787
- faxing the form to 1-800-FDA-0178
- by phone at 1-800-332-1088

Consumer Information Sheet for Ziagen

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PDF requires the free Adobe Acrobat Reader

Date created: March 27, 2008

Early Communication about an Ongoing Safety Review of Tiotropium (marketed as Spiriva HandiHaler)

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

The manufacturer of Spiriva HandiHaler, Boehringer Ingelheim, recently informed the FDA that ongoing safety monitoring has identified a possible increased risk of stroke in patients who take this medicine. Spiriva HandiHaler contains tiotropium bromide and is used to treat bronchospasm associated with chronic obstructive pulmonary disease (COPD). Additional information is needed to further evaluate this preliminary information about stroke in patients who take Spiriva HandiHaler.

Boehringer Ingelheim reported to the FDA that it has conducted an analysis of the safety data from 29 placebo controlled clinical studies ("pooled analysis"). In 25 of the clinical studies, patients were treated with Spiriva HandiHaler. In the other 4 clinical studies patients were treated with another formulation of tiotropium approved in Europe, Spiriva Respimat. The 29 clinical studies included approximately 13,500 patients with COPD. Based on data from these studies, the preliminary estimates of the risk of stroke are 8 patients per 1000 patients treated for one year with Spiriva, and 6 patients per 1000 patients treated for one year with placebo. This means that the estimated excess risk of any type of stroke due to Spiriva is 2 patients for each 1000 patients using Spiriva over a one year period.

It is important to interpret these preliminary results with caution. FDA has not confirmed these analyses. Pooled analyses can provide early information about potential safety issues. However, these analyses have inherent limitations and uncertainty that require further investigation using other data sources. This early communication is in keeping with FDA's commitment to inform the public about its ongoing safety reviews of drugs.

FDA is working with Boehringer Ingelheim to further evaluate the potential association between Spiriva and stroke. FDA has requested additional information and is currently reviewing post-marketing adverse event reports with Spiriva. In addition, the manufacturer of Spiriva has conducted a large study called UPLIFT (Understanding the Potential Long-Term Impacts on Function with Tiotropium), which is a large four year study that will provide additional long term safety data with Spiriva and additional insight into the risk of stroke or other safety findings with tiotropium. The data from UPLIFT is expected to be available in June 2008. Once Boehringer Ingelheim provides FDA with the UPLIFT study data, FDA will analyze the data and communicate its conclusions and recommendations to the public.

Spiriva HandiHaler is an effective medicine that is indicated for the long-term, once daily, maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema. Patients should not stop taking Spiriva HandiHaler before talking to their doctor if they have questions about this new information.

The FDA urges both healthcare professionals and patients to report side effects from the use of Spiriva HandiHaler to the FDA's MedWatch Adverse Event Reporting program

- online at www.fda.gov/medwatch/report.htm;
- by returning the postage-paid FDA form 3500 available in PDF format at www.fda.gov/medwatch/getforms.htm to 5600 Fishers Lane, Rockville, MD 20852-9787;
- faxing the form to 1-800-FDA-0178; or
- by phone at 1-800-332-1088

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PDF requires the free Adobe Acrobat Reader

Date created: March 18, 2008

IMPORTANT DRUG WARNING

SUBJECT: Additional Trials Showing Increased Mortality and/or Tumor Progression with EPOGEN®/PROCRIT® and Aranesp®

March 7, 2008

Health Care Professional's Name
Address

Dear Health Care Professional:

On November 8, 2007, the Aranesp® and EPOGEN®/PROCRIT® labeling were revised to describe the results of six studies showing increased mortality and more rapid tumor progression in patients with cancer receiving ESAs. This letter is to alert you that information from two additional trials have been included in the product labels as described below.

Based on the results of these studies, the **Boxed Warnings** section of the EPOGEN®/PROCRIT® and Aranesp® prescribing information has been revised as follows:

Cancer:

- ESAs shortened overall survival and/or time to tumor progression in clinical studies in patients with ~~advanced~~ breast, non-small cell lung, head and neck, lymphoid, and cervical cancers when dosed to target a hemoglobin of ≥ 12 g/dL.

Additional modification made to the product labels are summarized as follows:

WARNINGS: Increased Mortality and/or Tumor Progression section

- Updated table

Study / Tumor / (n)	Hemoglobin Target	Achieved Hemoglobin (Median Q1,Q3)	Primary Endpoint	Adverse Outcome for ESA-containing Arm
Chemotherapy				
Cancer Study 1 Metastatic breast cancer (n=939)	12-14 g/dL	12.9 g/dL 12.2, 13.3 g/dL	12-month overall survival	Decreased 12-month survival
Cancer Study 2 Lymphoid malignancy (n=344)	13-15 g/dL (M) 13-14 g/dL (F)	11.0 g/dL 9.8, 12.1 g/dL	Proportion of patients achieving a hemoglobin response	Decreased overall survival
Cancer Study 3 Early breast cancer (n=733)	12.5-13 g/dL	13.1 g/dL 12.5, 13.7 g/dL	Relapse-free and overall survival	Decreased 3 yr. relapse-free and overall survival

Cancer Study 4 Cervical Cancer (n=114)	12-14 g/dL	12.7 g/dL 12.1, 13.3 g/dL	Progression-free and overall survival and locoregional control	Decreased 3 yr. progression-free and overall survival and locoregional control
Radiotherapy Alone				
Cancer Study 5 Head and neck cancer (n=351)	≥15 g/dL (M) ≥14 g/dL (F)	Not available	Locoregional progression-free survival	Decreased 5-year locoregional progression-free survival Decreased overall survival
Cancer Study 6 Head and neck cancer (n=522)	14-15.5 g/dL	Not available	Locoregional disease control	Decreased locoregional disease control
No Chemotherapy or Radiotherapy				
Cancer Study 7 Non-small cell lung cancer (n=70)	12-14 g/dL	Not available	Quality of life	Decreased overall survival
Cancer Study 8 Non-myeloid malignancy (n=989)	12-13 g/dL	10.6 g/dL 9.4, 11.8 g/dL	RBC transfusions	Decreased overall survival

The label has been updated based on an interim analysis for Cancer Study 3 (the 'PREPARE' study). The study is ongoing and data collection and follow-up continue. The following new text describing this study has been added to the **WARNINGS: Increased Mortality and/or Tumor Progression** section of the labels:

> Cancer Study 3 (the 'PREPARE' study) was a randomized controlled study in which Aranesp® was administered to prevent anemia conducted in 733 women receiving neo-adjuvant breast cancer treatment. An interim analysis was performed after a median follow-up of approximately 3 years at which time the survival rate was lower (86% vs. 90%, HR 1.42, 95% CI: 0.93, 2.18) and relapse-free survival rate was lower (72% vs. 78%, HR 1.33, 95% CI: 0.99, 1.79) in the Aranesp®-treated arm compared to the control arm.

The label has been updated based on additional follow-up of Cancer Study 4 (protocol GOG 191)[1] which was terminated prematurely in late 2003 following an unplanned review of safety data undertaken by the Gynecologic Oncology Group (GOG) at the request of Johnson & Johnson Pharmaceutical Research & Development (J&JPRD). The following new text describing this study has been added to the **WARNINGS: Increased Mortality and/or Tumor Progression** section of the labels:

> Cancer Study 4 (protocol GOG 191) was a randomized controlled study that enrolled 114 of a planned 460 cervical cancer patients receiving chemotherapy and radiotherapy. Patients were randomized to receive Epoetin alfa to maintain hemoglobin between 12 and 14 g/dL or to transfusion support as needed. The study was terminated prematurely due to an increase in thromboembolic events in Epoetin alfa-treated patients compared to control (19% vs. 9%).

Both local recurrence (21% vs. 20%) and distant recurrence (12% vs. 7%) were more frequent in Epoetin alfa-treated patients compared to control. Progression-free survival at 3 years was lower in the Epoetin alfa-treated group compared to control (59% vs. 62%, HR 1.06, 95% CI: 0.58, 1.91). Overall survival at 3 years was lower in the Epoetin alfa-treated group compared to control (61% vs. 71%, HR 1.28, 95% CI: 0.68, 2.42).

Amgen and Ortho Biotech are disseminating this important new prescribing information to inform prescribing healthcare professionals about the safety of Aranesp® and EPOGEN®/PROCRIT®. Over the coming weeks, our field forces will be calling on healthcare professionals and will communicate this important new safety information. Prescribing healthcare professionals are encouraged to review the full prescribing information, including the patient package insert, with patients in order to make appropriate treatment decisions based on the benefit-risk profile of these products. Copies of the revised prescribing information and patient package insert for Aranesp® and EPOGEN®/PROCRIT® are enclosed and available on Amgen's website at www.amgen.com and Ortho Biotech's website at www.procrit.com.

Should you have any questions, require further information on product safety, or wish to report adverse patient experiences:

For Aranesp® and EPOGEN®, please contact Amgen's Medical Information Connection™ at 1-800-77-AMGEN.

For PROCRIT®, please contact Ortho Biotech's Medical Information at 1-888-227-5624.

Alternatively, adverse events may be reported to FDA's MedWatch reporting system

- by phone (1-800-FDA-1088), by facsimile (1-800-FDA-0178),
- online (https://www.accessdata.fda.gov/scripts/medwatch/) or
- mailed, using the MedWatch for FDA 3500 postage paid form, to the FDA Medical Products Reporting Program, 5600 Fishers Lane, Rockville, MD 20852-9787

Sincerely,

Sean E. Harper, MD Senior Vice President, Global Development and Chief Medical Officer Amgen	Craig Tendler, MD Vice President, Medical Affairs Ortho Biotech

References:

1. Thomas G, Ali S, Hoebers F, et al. Phase III trial to evaluate the efficacy of maintaining hemoglobin levels above 120 g/dL with erythropoietin vs above 100 g/dL without erythropoietin in anemic patients receiving concurrent radiation and cisplatin for cervical cancer. Gynecol Oncol 2007.