Drug Utilization Review Board

Oklahoma Health Care Authority

4545 N. Lincoln Suite 124

Oklahoma City, Oklahoma 73105

OHCA Board Room

Wednesday

January 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 – January 9, 2008**

DATE: January 2, 2008

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

Enclosed are the following items related to the January 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 on 2008 DUR Meeting Dates **– See Appendix C.**

Action Item – Vote to Prior Authorize Topical Antifungals **– See Appendix D.**

Action Item – Vote to Prior Authorize Soma® 250mg **– See Appendix E.**

Action Item – Vote to Prior Authorize Azor™ and Update Antihypertensive Prior Authorization Criteria – **See Appendix F.**

Action Item - Cough and Cold Coverage Review

Fiscal Year 2007 Annual Review **– See December 2007 DUR Meeting Packet – See Appendix G.**

Action Item – Annual Review of Amitiza®, Lotronex® and Zelnorm®**– See Appendix H.**

Action Item – Annual Review of Immunomodulators: Elidel® and Protopic®**– See Appendix I.**

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

Future Business

Adjourn to Proposed Executive Session as Recommended by the General Counsel and Authorized by the Open Meetings Act, 25 Okla. State. § 307 (8)(4),(7). The Executive Session will take place at OHCA, 4545 N. Lincoln, Suite 124, Oklahoma City, OK, 73105.

Drug Utilization Review Board

(DUR Board)

Meeting – January 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. November 14, 2007 DUR Minutes – Vote
B. November 21, 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 August 2007
B. Retrospective Drug Utilization Review for September 2007
C. Retrospective Drug Utilization Review Response for May 2007
D. Retrospective Drug Utilization Review Response for June 2007
E. Medication Coverage Activity Audit for November 2007
F. Medication Coverage Activity Audit for December 2007
G. Help Desk Activity Audit for November and December 2007

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

5. Action Item – Vote on 2008 DUR Meeting Dates – See Appendix C.

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

6. Action Item – Vote to Prior Authorize Topical Antifungals – See Appendix D.

A. COP Recommendations
B. PA Criteria

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

7. Action Item – Vote to Prior Authorize Soma® 250mg – See Appendix E.

A. Product Summary
C. COP Recommendations

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

8. Action Item – Vote to Prior Authorize Azor™ and Update Antihypertensive Prior Authorization Criteria **– See Appendix F.**

A. Product Summary
B. COP Recommendations

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

9. Action Item – Cough and Cold Coverage Review

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

10. FY07 Annual review – See Appendix G.

A. Pharmacy Claims by Therapeutic Category
B. Top 100 Medications by Pharmacy Reimbursement
C. Top 50 Medications by Claims

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

11. Action Item: Annual Review of Amitiza®, Lotronex® and Zelnorm® – See Appendix H.

A. Product Overview
B. Current PA Criteria
C. Utilization Review
D. COP Recommendations

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

12. Action Item: Annual Review of Immunomodulators: Elidel® and Protopic® – See Appendix I.

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

13. FDA and DEA Updates – See Appendix J.

14. Future Business

A. Narcotic Utilization Follow-Up
B. Erythropoiesis-Stimulating Agents Follow-Up
C. Osteoporosis Utilization Review
D. Antihistamine Follow-Up
E. Exubera® Annual Review
F. Insomnia PBPA Annual Review
G. New Product Reviews

15. Adjournment to Proposed Executive Session as Recommended by the General Counsel and Authorized by the Open Meetings Act, Okla. State. § 307 (8)(4), (7).

The Executive Session will take place at OHCA, 4545 N. Lincoln, Suite 124, Oklahoma City, OK 73105.

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES of MEETING of NOVEMBER 14, 2007

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.; 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: Melissa Williams, CheHou Tse	X	

OKLAHOMA HEALTH CARE AUTHORITY STAFF:	PRESENT	ABSENT
Alex Easton, M.B.A.; Pharmacy Operations Manager		X
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

OTHERS PRESENT:

Bobby White, UCB	Donna Erwin, BMS	Tracy Copeland, Daiichi Sankyo
Ron Schnare, Shire	Rachelle Wan, Amgen	Vince Morrison, Forest
Mark DeClerk, Lilly	Kristen Thomas, Adams RT	Richard Ponder, Johnson & Johnson

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 the absence of a quorum, but a quorum was established upon the late arrival of another DUR Board Member.

ACTION: NONE REQUIRED.

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

There were no speakers for Public Comment.

ACTION: NONE REQUIRED.

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

3A: October 10, 2007 DUR Minutes

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

ACTION: MOTION CARRIED.

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

4A: Retrospective Drug Utilization Review Report: July 2007

4B: Retrospective Drug Utilization Review Response: April 2007

4C: Medication Coverage Activity Audit: October 2007

4D: Help Desk Activity Audit: October 2007

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

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 5: **COUGH AND COLD COVERAGE UPDATE**

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

Dr. Nesser will investigate rebate and coverage of sodium bicarbonate rinse/nasopharyngeal sprays. Dr. Kuhls recommended the OHCA perform a QA audit of high number of claims.

Dr. Gourley moved to approve; seconded by Dr. Muchmore.*

* Discontinue OTC coverage for all ages except for single ingredient ibuprofen and acetaminophen liquid products. Coverage will be for age 12 years and under only with a maximum of three claims per year for each product.

ACTION: MOTION CARRIED.

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE XYZAL®; VOTE TO UPDATE ORAL ALLERGY PBPA CATEGORY**

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

Update PBPA category update for Oral Allergy products and prior authorize Xyzal®: Dr. Gourley moved to approve recommendations as submitted; seconded by Dr. Meece.

ACTION: MOTION CARRIED.

Remove prior authorization of OTC loratadine for adults: Dr. Feightner moved to table this motion to allow COP to further research the economic impact; seconded by Dr. Kuhls.

ACTION: MOTION TABLED.

AGENDA ITEM NO. 7: **VOTE TO PRIOR AUTHORIZE NUVIGIL™**

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

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

ACTION: MOTION CARRIED.

AGENDA ITEM NO. 8: **VOTE ON CHANGES TO INGREDIENT DUPLICATION PRODUR MODULE**
Materials included in agenda packet; presented by Dr. Gorman.
Dr. Meece moved to approve; seconded by Dr. Muchmore.
ACTION: MOTION CARRIED.

AGENDA ITEM NO. 9: **30-DAY NOTICE TO PRIOR AUTHORIZE TOPICAL ANTIFUNGALS**
Materials included in agenda packet; presented by Dr. Patel.
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 10: **30-DAY NOTICE TO PRIOR AUTHORIZE AZOR™**
Materials included in agenda packet; presented by Dr. Moore.
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 11: **30-DAY NOTICE TO PRIOR AUTHORIZE SOMA ® 250 MG**
Materials included in agenda packet; presented by Dr. Le.
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 12: **ANNUAL REVIEW OF MUSCLE RELAXANTS**
Materials included in agenda packet; presented by Dr. Le.
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**
14A: Narcotic Utilization Follow-Up
14B: Erythropoiesis-Stimulating Agents Follow-Up
14C: Osteoporosis Utilization Review
14D: Elidel/Protopic Annual Review
14E: Amitiza® Annual Review
14F: New Product Reviews
14G: Annual Reviews
Materials included in agenda packet; submitted by Dr. Graham.
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 15: **ADJOURNMENT**
The meeting was declared adjourned.

The University of Oklahoma College of Pharmacy

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

Memorandum

Date: November 21, 2007, 2007

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 November 14, 2007.

Recommendation 1: Vote to Update Cough and Cold Coverage

MOTION CARRIED by unanimous approval.

The College of Pharmacy has the following recommendations for the Cough and Cold products:

1. Discontinue OTC coverage of cough and cold products. Single ingredient ibuprofen and acetaminophen liquid products would still be covered for age 12 and under.
2. Only allow a maximum of 3 claims per year for this category.

Additional DUR Board recommendations:

1. OHCA review members with excessive utilization and notify the primary physicians. The members should also be investigated for fraud and abuse.
2. Review possible coverage of nasal wash products.

Recommendation 2: Vote to Update Oral Allergy PBPA Category

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following:

I. Restructuring of Category

Tier 1	Tier 2	Tier 3
• Over-the-counter loratadine* • Zyrtec and Clarinex syrup for members 6 months to 2 years of age	• Fexofenadine Tabs	• Zyrtec • Clarinex • Allegra • Xyzal

* For members 21 years of age and older, loratadine is available with prior authorization AFTER documented trial of a non-loratadine OTC product.

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.

II. Prior Authorization of XYZAL®

Placing XYZAL® in the PBPA as a tier-3 agent. In addition to current tier-3 criteria, member must also be greater than 6 years of age.

MOTION TABLED by unanimous approval.

The DUR Board recommends removal of the prior authorization restrictions for loratadine for members 21 years of age and over. The College of Pharmacy will research this and report back to the DUR Board.

Recommendation 3: Vote to Prior Authorize Nuvigil

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends placing Nuvigil™ into the ADHD/Narcolepsy PBPA category as a Tier 3. Approval would require a diagnosis of obstructive sleep apnea/hypopnea syndrome (with documentation of prior attempts and continuation of standard treatment, i.e. CPAP), narcolepsy or shift work sleep disorder. A quantity limit of 30 units for a 30 day supply and age restriction of 18 or older would also be applied. If approved, the initial approval would be for 3 months, beyond that additional information from the physician about the member's response to the medication would be required for long term authorization.

Recommendation 4: Vote on Changes to Ingredient Duplication Module

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends reconfiguring the module to review only claims for duplication of hydrocodone with acetaminophen.

1. Turn off all ingredients which are active in the module except H3AJ – Hydrocodone.
2. Set module to deny new claims within 90% of the day supply from the initial claim.
3. Approval of multiple hydrocodone claims would require prior authorization.

Recommendation 4: Annual Review of Muscle Relaxants

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 August 2007

Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
Total # of messages returned by system when no limits were applied	39,527	62,640	975,332	31,634
Limits which were applied	Established, Major, Males and Females, Age 41-50	Narcotics, Males and Females, Age 0-10	Contraindicated, Males and Females, Age 0-150, Chronic Ischemic Heart Disease	High dose, 0-6 year old, male and females, Antitussives
Total # of messages after limits were applied	98	54	20	50
Total # of members reviewed after limits were applied	98	46	20	50

LETTERS			
Prescribers		**Pharmacies**	
Sent	**Responded**	**Sent**	**Responded**
62		67	

Retrospective Drug Utilization Review Report

Claims Reviewed for September 2007

Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
Total # of messages returned by system when no limits were applied	36,933	58,998	946,336	31,634
Limits which were applied	Established, Major, Males and Females, Age 51-65	Narcotics, Males and Females, Age 11-15	Contraindicated, Males and Females, Age 0-15, Asthma	High dose, 0-150 year old, Male and Females, Androgens and Anabolic Steroids
Total # of messages after limits were applied	121	116	301	7
Total # of members reviewed after limits were applied	121	90	263	7

LETTERS			
Prescribers		**Pharmacies**	
Sent	**Responded**	**Sent**	**Responded**
90		60	

Retrospective Drug Utilization Review Report

Claims Reviewed for May 2007

Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
Limits which were applied	Established, Major, Males and Females, Age 66-150	Amphetamines/Stimulants, Males and Females, Age 10-15, Duplication in extended release products only	Contraindicated, Pregnancy, Females, Age 17-18	High Dose, Benzodiazepines, Males and Females, Age 0-18

Response Summary (Prescriber)
Letters Sent: 53
Response Forms Returned: 40

The response forms returned yielded the following results:

7 (18%)	*Record Error—Not my patient.*
1 (3%)	*No longer my patient.*
3 (8%)	*Medication has been changed prior to date of review letter.*
2 (5%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
22 (55%)	*I am aware of this situation and will plan to continue monitoring therapy.*
5 (13%)	*Other*

Response Summary (Pharmacy)
Letters Sent: 70
Response Forms Returned: 50

The response forms returned yielded the following results:

0 (0%)	*Record Error—Not my patient.*
1 (2%)	*No longer my patient.*
8 (16%)	*Medication has been changed prior to date of review letter.*
7 (14%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
24 (48%)	*I am aware of this situation and will plan to continue monitoring therapy.*
10 (20%)	*Other*

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 0-18	Amphetamines/Stimulants, Males and Females, Age 16-21	Contraindicated, Pregnancy, Females, Age 19	High Dose and Duration, Oxazolidinones (Zyvox), Males and Females, Age 0-150

Response Summary (Prescriber)
Letters Sent: 124
Response Forms Returned: 72

The response forms returned yielded the following results:

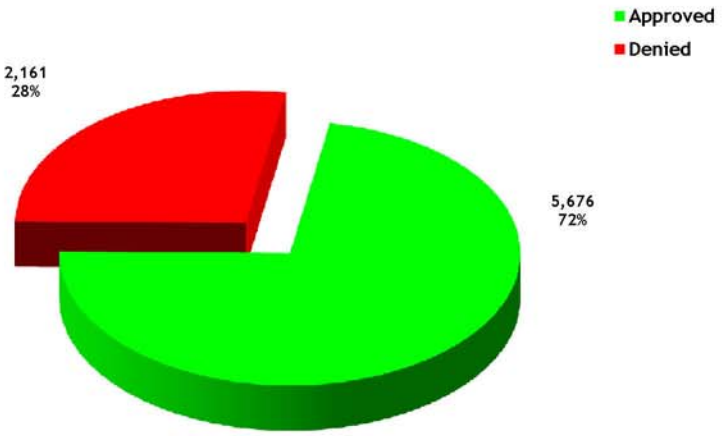
11 (15%)	*Record Error—Not my patient.*
6 (8%)	*No longer my patient.*
3 (4%)	*Medication has been changed prior to date of review letter.*
8 (11%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
29 (40%)	*I am aware of this situation and will plan to continue monitoring therapy.*
15 (21%)	*Other*

Response Summary (Pharmacy)
Letters Sent: 121
Response Forms Returned: 56

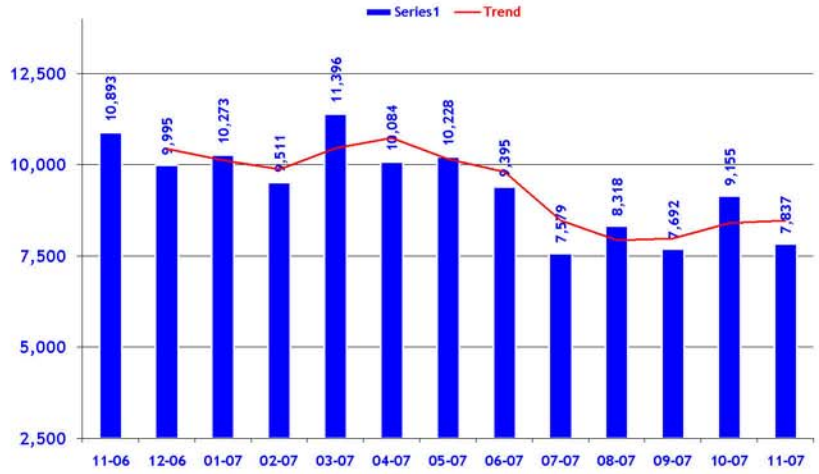
The response forms returned yielded the following results:

1 (2%)	*Record Error—Not my patient.*
3 (5%)	*No longer my patient.*
4 (7%)	*Medication has been changed prior to date of review letter.*
18 (32%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
23 (41%)	*I am aware of this situation and will plan to continue monitoring therapy.*
7 (13%)	*Other*

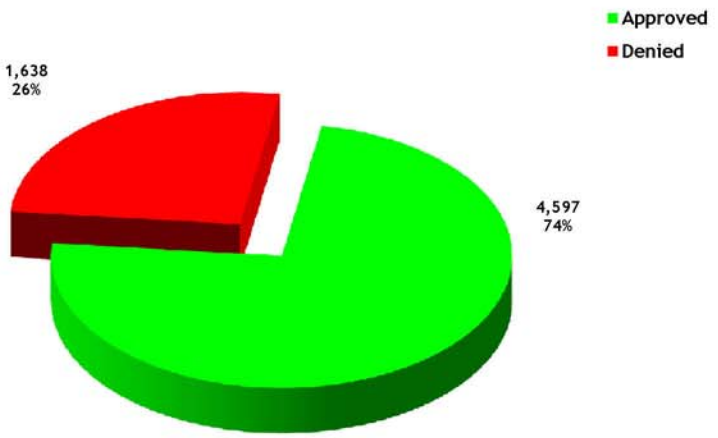
PRIOR AUTHORIZATION ACTIVITY REPORT
November2007



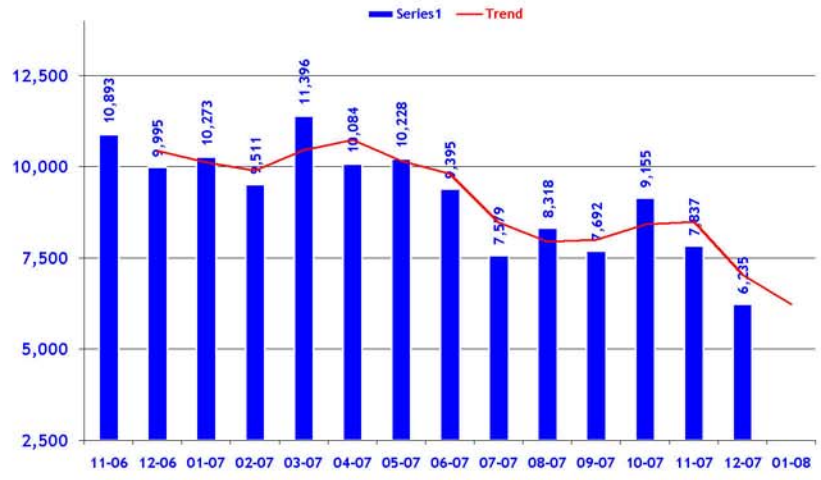
PRIOR AUTHORIZATION REPORT
November 2006 – November 2007



PRIOR AUTHORIZATION ACTIVITY REPORT
December 2007



PRIOR AUTHORIZATION REPORT
November 2006 – December 2007



Activity Audit for

November 01, 2007 Through November 30, 2007

	Average Length of Approvals in Days	Approved	Denied	Total
ACE Inhibitors	80	18	6	24
Angiotensin Receptor Antagonist	338	39	39	78
Antidepressant	290	210	365	575
Antihistamine	104	463	325	788
Antiulcers	23	11	3	14
Anxiolytic	94	2,853	357	3,210
Calcium Channel Blockers	129	6	2	8
Growth Hormones	177	37	2	39
HTN Combos	301	10	4	14
Insomnia	100	51	26	77
Nsaids	298	29	68	97
Plavix	243	123	22	145
Stimulant	200	628	191	819
Others	116	1,197	751	1,948
Emergency PAs		1	0	1
Total		**5,676**	**2,161**	**7,837**
Overrides				
Brand	309	25	28	53
Dosage Change	22	367	20	387
Lost/Broken Rx	15	93	5	98
Nursing Home Issue	19	112	4	116
Other	14	25	7	32
Quantity vs. Days Supply	213	218	146	364
Stolen	12	5	1	6
Wrong D.S. on Previous Rx	0	0	2	2
Overrides Total		**845**	**213**	**1,058**

Denial Reasons

Lack required information to process request.	2,053
Unable to verify required trials.	643
Considered duplicate therapy. Member has a prior authorization for similar medication.	136
Does not meet established criteria.	124
Not an FDA approved indication/diagnosis.	117
Requested dose exceeds maximum recommended FDA dose.	60
Member has active PA for requested medication.	26
Medication not covered as pharmacy benefit.	7
Duplicate Requests	452
* Changes to existing	588

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

Wednesday, December 5, 2007

Activity Audit for

December 01, 2007 Through December 31, 2007

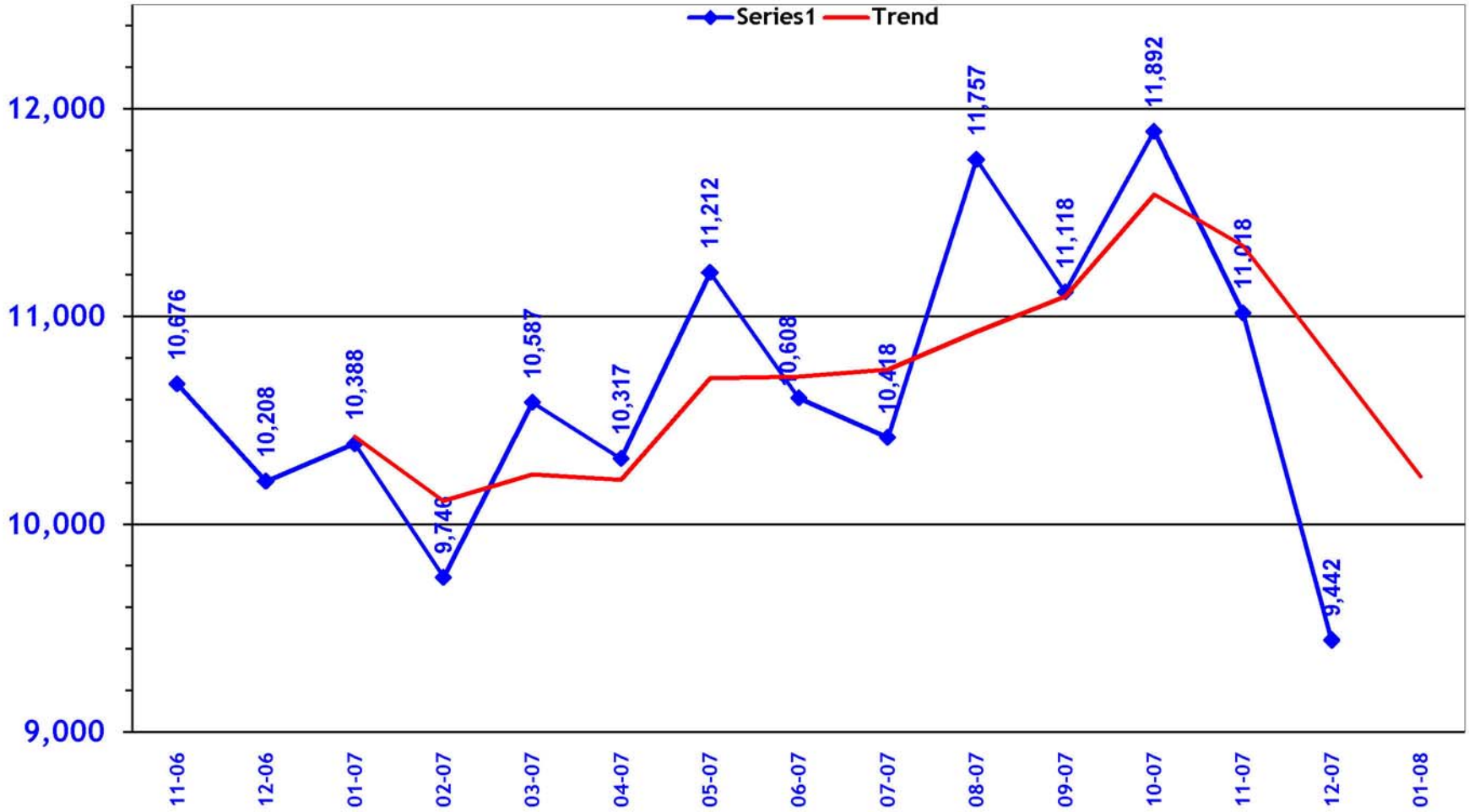
	Average Length of Approvals in Days	Approved	Denied	Total
ACE Inhibitors	127	13	10	23
Angiotensin Receptor Antagonist	331	21	32	53
Antidepressant	284	203	236	439
Antihistamine	105	353	222	575
Antiulcers	12	9	4	13
Anxiolytic	93	2,448	336	2,784
Calcium Channel Blockers	128	6	2	8
Growth Hormones	178	27	3	30
HTN Combos	285	8	13	21
Insomnia	97	28	20	48
Nsaids	306	15	45	60
Plavix	188	137	8	145
Stimulant	194	507	152	659
Others	116	822	555	1,377
Emergency PAs		0	0	0
Total		**4,597**	**1,638**	**6,235**
Overrides				
Brand	278	27	15	42
Dosage Change	15	277	21	298
Lost/Broken Rx	12	83	5	88
Nursing Home Issue	14	26	0	26
Other	29	26	12	38
Quantity vs. Days Supply	216	153	83	236
Stolen	2	3	5	8
Overrides Total		**595**	**141**	**736**

Denial Reasons

Lack required information to process request.	1,454
Unable to verify required trials.	578
Does not meet established criteria.	118
Considered duplicate therapy. Member has a prior authorization for similar medication.	115
Not an FDA approved indication/diagnosis.	100
Requested dose exceeds maximum recommended FDA dose.	68
Member has active PA for requested medication.	24
Medication not covered as pharmacy benefit.	4
Duplicate Requests	284
* Changes to existing	596

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

CALL VOLUME MONTHLY REPORT
November 2006 – December 2007



04-06 thru 03-07: corrected totals

Appendix C

Vote on 2008 DUR Meeting Dates

Oklahoma Health Care Authority
January 2008

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

Appendix D

Vote for Product Based Prior Authorization of Topical Antifungals
Oklahoma Health Care Authority
January 2008

Recommendations

The College of Pharmacy recommends including the Topical Antifungals in the Product Based Prior Authorization (PBPA) program.

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®.

Appendix E

Vote to Prior Authorize Soma® 250mg

Oklahoma Healthcare Authority
January 2008

Manufacturer: **MedPointe Pharmaceuticals**
Classification: **Skeletal Muscle Relaxant, Centrally Acting**

Summary

Soma® 250mg is the same chemical compound and formulation as the carisoprodol 350mg, but at a lower dosage.

Soma® 250mg is currently being marketed with the following points:

- Short term relief of back pain comparable to that of the 350mg dosage.
- Better tolerability, i.e. less drowsiness.

Recommendations

Skeletal Muscle Relaxants+		
Tier-1	***Tier-2***	***Hard PA***
Cyclobenzaprine (Flexeril®)	***Metaxolone (Skelaxin®)**	**Carisoprodol (Soma®)**
Baclofen (Lioresal®)		**Carisoprodol w Aspirin**
Tizanidine (Zanaflex®)		**Carisoprodol, ASA, Codeine**
Methocarbamol (Robaxin®)		**Tizanidine (Zanaflex®) Caps**
Chlorzoxazone (Parafon Forte®, Paraflex®)		**Cyclobenzaprine ER (Amrix®) Caps**
Orphenadrine (Norflex®)		**Cyclobenzaprine 7.5mg (Fexmid®) Tabs**
		Carisoprodol (Soma®) 250mg Tabs

+Brand products are subject to the Brand Name Override where generic is available.
***Tier one due to Supplemental Rebate Participation through 12/31/2007.**

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.

Appendix F

Vote to Prior Authorize Azor™ (amlodipine/olmesartan) and Update Antihypertensive Prior Authorization Criteria

Oklahoma Health Care Authority
January 2008

Manufacturer	Daiichi Sankyo, Inc
FDA Classification	Oral Antihypertensive
Status	Prescription only

Summary

Azor™ is a dihydropyridine calcium channel blocker and angiotensin II receptor blocker (ARB) combination product indicated for once daily treatment of hypertension, alone, or with other antihypertensive agents.

Recommendations

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 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 medications, or
- previous stabilization on the Tier 3 medication, or
- a unique indication for which the lower tiered antihypertensives lack

REFERENCES

1. Azor™ Product information, Daiichi Sankyo, Inc

Appendix G

Annual Review of State Fiscal Year 2007

Oklahoma Health Care Authority

January 2008

Please see appendix F of the December 2007 DUR packet for this information.

Appendix H

Required Annual Review of Amitiza®, Lotronex® and Zelnorm® - Fiscal Year 2007

Oklahoma Health Care Authority
January 2008

Amitiza®

- Locally acting chloride channel activator.
- For treatment of chronic idiopathic constipation in the adult population.

Lotronex®

- Potent and selective antagonist of the serotonin 5-HT3 receptor.
- For women with severe diarrhea-predominant IBS

Zelnorm®

- Partial agonist of the 5-HT4 receptor.
- Short term (12 weeks) treatment of women with IBS whose primary bowel symptom is constipation and for chronic idiopathic constipation in patients less than 65 years of age.

Prior Authorization Category for FY '07

Criteria to Prior Authorize Amitiza®:

Quantity limit of 100/50.

Chronic Idiopathic Constipation in males and females who meet the following criteria:

a. Patient is between 19 and 65 years of age.
b. Have documentation that constipating therapies for other disease states have been discontinued (excluding opioid pain medications for cancer patients).
c. Documented and updated Colon Screening. (>50 years of age)

For both diagnoses, hydration and treatment attempts with a minimum of three alternate products must be documented.

Initial approval for 12 weeks of therapy. An additional year approval may be authorized if physician documents client is responding well to treatment.

Criteria to Prior Authorize Zelnorm® at time of recall.

SALE OF ZELNORM STOPPED MARCH 2007. Still available under restricted access.

Quantity limit of 60/30.

1. Constipation-Predominate IBS in women.
2. Chronic Idiopathic Constipation in males and females who meet the following criteria:
    a. Patient is between 19 and 65 years of age.
    b. Have documentation that constipating therapies for other disease states have been discontinued.
    c. Documented and updated Colon Screening. (>50 years of age)

For both diagnoses, hydration and treatment attempts with a minimum of three alternate products must be documented.

Initial approval for 12 weeks of therapy. An additional year approval may be authorized if physician documents client is responding well to treatment.

Lotronex® - currenty does not require a prior authorization.

Quantity limit of 60/30.

Utilization

From July 1, 2006 to June 30, 2007 a total of 120 members received Amitiza® or Zelnorm® through the SoonerCare program for fiscal year 2007.

Product	# of Claims	Total Units	Total Days	Units/ Day	Total Cost	Total Members	Per Diem
Amitiza 24mcg	47	2,674	1,412	1.89	$7,720.47	25	$5.47
Zelnorm 2mg	41	2,190	1,110	1.97	$6,756.77	8	$6.09
Zelnorm 6mg	314	17,767	9,209	1.93	$54,078.31	91	$5.87
Lotronex 1mg	13	660	390	1.69	$5,295.04	7	$13.58

Total Cost FY '07	**$73,850.59**
Total Cost FY '06	*$619,797.50*
Total Claims FY '07	**415**
Total Claims FY '06	*4,002*
Total Members FY '07	**120***
Total Members FY '06	*1,355*
Per Diem FY '07	**$6.09**
Per Diem FY '06	*$5.25*

*Number of Unduplicated Members

Total petitions submitted for this category during specified time period:

Approved	164
Denied	655*
Incomplete	121*
Supers	4
Therapy Management	6

*Of the 776 petitions that were denied or incomplete, 141 were subsequently approved.

Claims were reviewed to determine the age/gender of the members.

FY '07 all members

Age	Female	Male	Totals
0 to 9	0	0	0
10 to 19	8	2	10
20 to 34	36	3	39
35 to 49	38	6	44
50 to 64	21	2	23
65 to 79	1	2	3
80 to 94	0	1	1
95 and Over	0	0	0
Totals	**104**	**16**	**120**

Recommendations

The College of Pharmacy recommends no changes to the current prior authorization criteria for Amitiza®.

Appendix I

Prior Authorization Annual Review – Fiscal Year 2007
Immunomodulators: Elidel®/Protopic®

Oklahoma Health Care Authority
January 2008

Current Product Based Prior Authorization Criteria

With respect to the immunomodulator topical medications there are two products in this therapeutic category. Both are immunosuppressants classified as topical calcineurin inhibitors.

- The first 90 days of a 12 month period will be covered without a prior authorization if member meets age requirement.
- After the initial period, authorization will be granted with documentation of one trial of a topical corticosteroid for six weeks duration within the past 90 days.
- Therapy will be approved only once each 90 day period to ensure appropriate short-term and intermittent utilization as advised by the FDA.
- Quantities will be limited to 30 grams for use on the face, neck, and groin, and 100 grams for all other areas.
- Authorizations will be restricted to those patients who are not immunocompromised.

Approved Clinical Diagnosis:

- **Elidel®** (Pimecrolimus) for short-term and intermittent treatment for mild to moderate *atopic dermatitis (eczema)*
- **Protopic®** (Tacrolimus) for short-term and intermittent treatment for moderate to severe *atopic dermatitis (eczema)*

Age Restriction:

- **Elidel® 1% Cream** ≥ 2 years of age
- **Protopic® 0.03% Cream** ≥ 2 years of age
- **Protopic® 0.1% Cream** ≥ 15 years of age

Clinical exceptions for topical corticosteroid trials for members meeting age requirement:

- Documented adverse effect, drug interaction, or contraindication to topical corticosteroid products
- Atopic dermatitis on the face, neck, or groin where physician does not want to use topical corticosteroids
- Prescription by allergist or dermatologist *(regardless of age)*

Utilization

During the period between July 2006 and June 2007 a total of 4,024 members had claims for topical immunosuppressant drugs paid through Sooner*Care*.

FY 2007 versus FY 2006*			% Change
Cost FY '07		**$ 803,196.84**	**46.9 ↓**
	Cost FY '06	*$ 1,511,208.17*	
Claims FY '07		**6,512**	**49.4 ↓**
	Claims FY '06	*12,859*	
Per Diem FY '07		**$ 4.39**	**38.0 ↓**
	Per Diem FY '06	*$ 7.08*	
Members FY '07		**4,024**	**43.8 ↓**
	Members FY '06	7,156	

*Totals represent only 6 month utilization of Dual-Eligibles

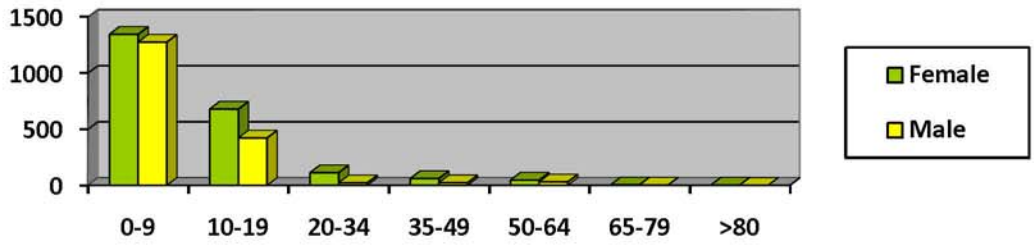
Utilization FY '07

Drugname	Total Claims	Total Units**	Total Days	Members	Total Paid
Elidel Cream 1%	5,643	322,101	157,982	3,631	$ 688,269.65
Protopic Ointment 0.03%	735	39,471	21,097	386	$ 94,705.36
Protopic Ointment 0.1%	134	8,140	3,685	80	$ 20,221.83
TOTAL	**6,512**	**369,712**	**182,764**	**4,024***	**$ 803,196.84**

*Unduplicated members FY '07.

**Average quantity per day for intermittent use is 1.6 grams/day; SoonerCare average in FY '06 = 3.6 grams/day and in FY '07 = 2.0 grams/day. (Novartis safety update February 2005)

Age and Gender FY '07

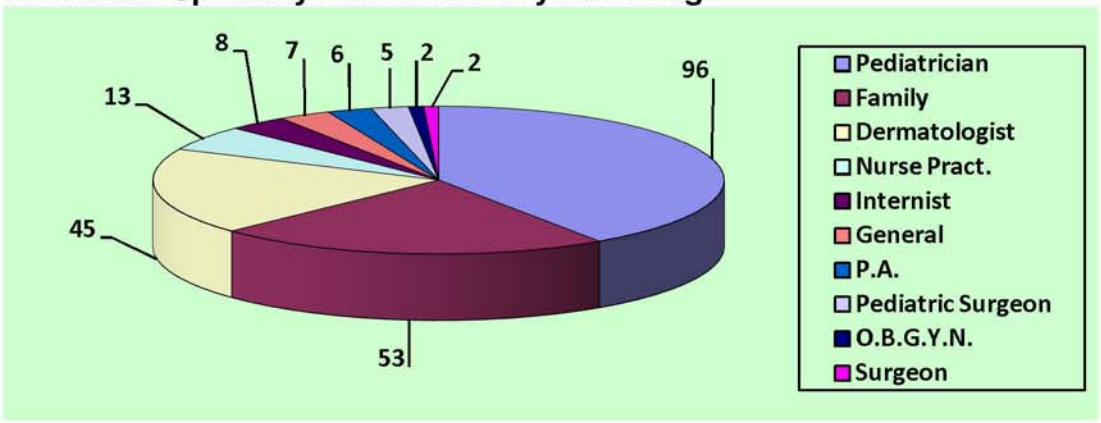


Utilization of Elidel® and Protopic® for children under 2 years of age

Member < 2 years of age	FY 2007*	FY 2006	FY 2005
Female	23	745	908
Male	26	945	1,268
Total	**49**	**1,690**	**2,166**

*44 Members granted approval due to affected area on the face

Prescriber Specialty: Members <2 years of age



Petition Summary FY '07

Total Petitions: 1,298

Approved.....	385
Denied.....	728
Incomplete.....	152

Recommendations

The College of Pharmacy does not recommend any changes at this time and will continue to monitor and evaluate this PBPA category according to current treatment guidelines and FDA approved product labeling.

Topical Corticosteroids A= proven in well-conducted RCTs with adequate # of pts. B=case studies, low # of pts. , non-RCTs, short duration,etc... C=ineffective in well-conducted RCTs with adequate # of pts.	FDA-approved	Non-FDA approved (age,# pts, trial length)	Level of Evidence
Super-High Potency			
Diprolene®, (Betamethasone dipropionate aug.)0.05%	≥ 12 yr		
Olux®, Temovate® (Clobetasol propionate) 0.05%	≥ 12 yr	5 yr, n=30, 5 weeks	B
Psorcon® (Diflorasone diacetate) 0.05%	≥ 12 yr		
Ultravate® (Halobetasol propionate) 0.05%	≥ 12 yr	5-15 yr, n=81,14-day	B
High Potency			
Cyclocort® (Amcinonide) 0.1%	≥ 12 yr		
Topicort® (Desoximetasone) 0.05%	≥ 10 yr		
Diprolene AF® (Betamethasone dipropionate augmented)0.05%	≥ 12 yr		
Psorcon E®, Maxiflor® (Diflorasone diacetate) 0.05%	≥ 12 yr		
Lidex® (Fluocinonide) 0.05%	≥ 12 yr		
Halog E®, Halog® (Halcinonide) 0.1%	≥ 12 yr	5 mos. – 15yr, n=105, 2 weeks	B
Elocon® (Mometasone furoate) 0.1%	≥ 2 yr		
Medium-High Potency			
Aristocort A®, Kenalog®(Triamcinolone acetonide) 0.5,0.1%	> 16 yr	3 mos. – 10yr, n=101, 8-day	B
Betatrex® (Betamethasone valerate) 0.1%	≥ 12 yr		
Cutivate® (Fluticasone propionate) 0.005% ointment	≥ 17 yr		
Cyclocort® (Amcinonide) 0.1% cream, lotion	≥ 12 yr		
Alphatrex® (Betamethasone dipropionate) 0.05%	≥ 12 yr		
Maxiflor® (Diflorasone diacetate) 0.05% cream	≥ 12 yr		
Lidex E® (Fluocinonide) 0.05%	≥ 12 yr		
Medium Potency			
Luxiq® (Betamethasone valerate) 0.12%	> 16 yr		
Synalar® (Fluocinolone acetonide) 0.025%	≥ 2 yr		
Cordran® (Flurandrenolide) 0.025, 0.05%	pediatric		
Westcort® (Hydrocortisone valerate) 0.2%	pediatric		
Elocon® (Mometasone furoate) 0.1% cream, lotion	≥ 2 yr		
Aristocort A®, Kenalog®(Triamcinolone acetonide) 0.1% cream	pediatric		
Medium-Low Potency			
Desowen®, Tridesilon® (Desonide) 0.05%	> 16 yr		
Locoid® or Locoid Lipocream® (Hydrocortisone butyrate) 0.1%	pediatric		
Dermatop® (Prednicarbate) 0.1%	≥ 1 yr	≥ 2mos., n=55, 3 wks	B
Synalar® (Fluocinolone acetonide)0.025%, 0.01% cream, solution	≥ 2 yr		
Cordran SP® (Flurandrenolide) 0.025%, 0.05% cream, lotion	pediatric		
Aclovate® (Alclometasone dipropionate) 0.05%	≥ 1 yr		
Betatrex® (Betamethasone valerate) 0.025% cream	pediatric		
Cloderm® (Clocortolone) 0.1%	pediatric		
Cutivate® (Fluticasone propionate) 0.05% cream	≥ 3 mos.		
Westcort® (Hydrocortisone valerate) 0.2% cream	pediatric		
Kenalog®(Triamcinolone acetonide) 0.025%, 0.1% cream, lotion	pediatric		
Lowest Potency			
Hytone® (Hydrocortisone) 0.5, 1.0, 2.5%	pediatric		

Appendix J

FDA News

FOR IMMEDIATE RELEASE
November 21, 2007

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

FDA Approves Zyrtec for Nonprescription Use in Adults and Children

The U.S. Food and Drug Administration has approved tablet, chewable tablet, and syrup formulations of Zyrtec (cetirizine HCl) for nonprescription use. The nonprescription drug is approved for the temporary relief of symptoms due to hay fever or other respiratory allergies (sneezing; runny nose; itchy, watery eyes; itchy throat or nose) in adults and children 2 years of age and older.

The nonprescription Zyrtec products also are approved for the relief of itching due to hives in people 6 years of age and older, including adults.

"The approval of Zyrtec for nonprescription use offers an additional treatment option for children and adults," said Andrea Leonard-Segal, M.D., director, Division of Nonprescription Clinical Evaluation in the FDA's Center for Drug Evaluation and Research. "As for all nonprescription drugs, consumers and caregivers should read and carefully follow all directions on the labeling."

The tablets and chewable tablets are approved for adults and children 6 years of age and older:

- for the treatment of the symptoms of hay fever and other respiratory allergies, and
- to relieve the itching due to hives.

The syrup is approved for:

- adults and children 2 years of age and older for the treatment of the symptoms of hay fever and other respiratory allergies, and
- adults and children 6 years of age and older to relieve the itching due to hives.

The company will market two distinct Zyrtec products for each dosage form. One will provide directions for treating the symptoms of hay fever and other respiratory allergies. The other will contain directions for use to relieve the itching due to hives.

Zyrtec may cause drowsiness in some people at recommended doses. Other common side effects include fatigue and dry mouth.

On November 9, 2007, the FDA announced that it had approved Zyrtec-D, a product which contains cetirizine HCl and pseudoephedrine HCl, for nonprescription use. Sales of the Zyrtec-D are subject to restrictions in the Combat Methamphetamine Epidemic Act. This law places restrictions on the sale of products containing pseudoephedrine, such as limiting the amount that an individual can purchase, and imposing record keeping requirements on the retail establishments that sell the product and that it be located with the pharmacist. Nonprescription Zyrtec-D was approved for the relief of symptoms due to hay fever or other upper respiratory allergies such as runny nose, sneezing, itchy, watery eyes, itching of the nose or throat, and nasal congestion. Zyrtec-D is also approved for reducing swelling of nasal passages, for relief of sinus congestion and pressure, and for restoring freer breathing through the nose due to hay fever and other upper respiratory allergies. Zyrtec-D is not approved for the relief of itching due to hives.

FDA News

FOR IMMEDIATE RELEASE
November 20, 2007

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

FDA Issues Early Communication for Chantix

Background: The U.S. Food and Drug Administration (FDA) issued an Early Communication about an Ongoing Safety Review of Chantix, a drug approved as an aid to smoking cessation treatment. An Early Communication reflects FDA's current analysis of available data concerning these drugs and does not mean that FDA has concluded that there is a causal relationship between the drug and the emerging safety issue.

FDA is evaluating postmarketing adverse event reports for Chantix (varenicline), a prescription medicine to help adults stop smoking.

Based on FDA's request for information from the manufacturer, Pfizer, Inc., the company recently submitted reports to the agency describing suicidal ideation (thoughts). In the wake of a case report citing erratic behavior in an individual who had used Chantix, FDA has also asked the company for any information on additional cases that may be similar in patients who have taken the drug.

FDA's Center for Drug Evaluation and Research is working to complete an analysis of the available information and data. When this analysis is completed, FDA will communicate the conclusions and recommendations to the public.

In the meantime, FDA recommends that health care providers monitor patients taking Chantix for behavior and mood changes. Patients taking Chantix should contact their doctors if they experience behavior or mood changes.

FDA also advises that, due to reports of drowsiness, patients should use caution when driving or operating machinery until they know how using Chantix may affect them.

Full text of the Early Communication about the Ongoing Safety Review can be found at: http://www.fda.gov/cder/drug/early_comm/varenicline.htm.

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FDA News

FOR IMMEDIATE RELEASE
November 8, 2007

Media Inquiries:
Karen Riley, 301-827-6242
Consumer Inquiries:
888-INFO-FDA

FDA Strengthens Boxed Warnings, Approves Other Safety Labeling Changes for Erythropoiesis-Stimulating Agents (ESAs)

The U.S. Food and Drug Administration today approved revised boxed warnings and other safety-related product labeling changes for erythropoiesis-stimulating agents (ESAs), which treat certain types of anemia. These new statements address the risks that the drugs Aranesp, Epogen and Procrit pose to patients with cancer and patients with chronic kidney failure.

The labeling changes, which incorporate advice from FDA advisory committees and expand upon labeling changes made in March 2007, also include a statement that symptoms of anemia, fatigue and quality of life have not been shown to improve in patients with cancer who are treated with ESAs.

Epogen, Procrit and Aranesp are approved to treat anemia in patients with chronic kidney failure and anemia caused by chemotherapy in certain patients with cancer. Epogen and Procrit are also approved for use in certain patients with anemia who are scheduled to undergo major surgery to reduce blood transfusions during or shortly after surgery and for the treatment of anemia caused by zidovudine (AZT) therapy in HIV patients.

For Patients with Cancer

For patients with cancer, the new boxed warnings emphasize that ESAs caused tumor growth and shortened survival in patients with advanced breast, head and neck, lymphoid and non-small cell lung cancer when they received a dose that attempted to achieve a hemoglobin level of 12 grams per deciliter (g/dL) or greater.

The boxed warnings also emphasize that no clinical data are available to determine whether there is a similar risk of shortened survival or increased tumor growth for patients with cancer who receive an ESA dose that attempts to achieve a hemoglobin level of less than 12 g/dL. This is the hemoglobin level commonly achieved in clinical practice.

Health care providers determine whether a patient is anemic and decide on ESA dosing by measuring how much of the protein known as hemoglobin is present in a patient's red blood cells.

An earlier boxed warning, approved in March, described the results of six studies demonstrating that survival was shorter and tumors progressed faster when ESAs were used to achieve hemoglobin levels of 12 g/dL or greater in cancer patients.

Today's new boxed warning also clarifies that ESAs should only be used in patients with cancer when treating anemia specifically caused by chemotherapy and not for other causes of anemia. Moreover, it states that ESAs should be discontinued once the patient's chemotherapy course has been completed.

"Health care professionals need to consider the risks of increased tumor progression and decreased survival in patients with cancer when prescribing ESAs," said Janet Woodcock, M.D., FDA's deputy commissioner for scientific and medical programs, chief medical officer and acting

director of its Center for Drug Evaluation and Research. "ESAs should be used in patients with cancer only when their anemia is due to chemotherapy and only at the lowest dose necessary to avoid the need for blood transfusions."

The FDA is working with the manufacturer to design and conduct clinical trials of different dosing regimens and tumor types to further characterize potential tumor progression associated with ESAs.

For Patients with Chronic Kidney Failure

For patients with chronic kidney failure, the new boxed warning states that ESAs should be used to maintain a hemoglobin level between 10 g/dL to 12 g/dL. Maintaining higher hemoglobin levels in patients with chronic kidney failure increases the risk for death and for serious cardiovascular reactions such as stroke, heart attack or heart failure, the boxed warning states.

In addition to the boxed warning, the new labeling provides specific instructions for dosage adjustments and hemoglobin monitoring for chronic kidney failure patients who do not respond to ESA treatment with an adequate increase in their hemoglobin levels.

The new labeling also emphasizes that there are no data from controlled trials demonstrating that ESAs improve symptoms of anemia, quality of life, fatigue, or patient well-being for patients with cancer or for patients with HIV undergoing AZT therapy.

In March 2007 the FDA approved labeling changes and issued a public health advisory outlining the new safety information about ESAs. Safety concerns regarding ESAs were discussed during May 2004 and May 2007 meetings of FDA's Oncologic Drug Advisory Committee and a September 2007 joint meeting of FDA's Cardiovascular and Renal Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee. ESA product labeling was previously revised in 1997, 2004 and 2005 to reflect new safety information.

The agency is currently reviewing a proposed Medication Guide that will better communicate the safety and effectiveness of ESAs to patients and will replace the existing patient labeling.

ESAs are a bioengineered version of a natural protein made in the kidney that stimulates the bone marrow to produce more red blood cells. These drugs are manufactured by Amgen Inc., Thousand Oaks, Calif. Procrit is marketed and distributed by Ortho Biotech LP of Bridgewater, N.J, a subsidiary of Johnson & Johnson.

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

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DRUG SAFETY COMMUNICATIONS

Posted by FDA from January 1, 2007, to June 1, 2007 (advisories are available at www.fda.gov/cder/drug/DrugSafety/DrugIndex.htm)

Date	Product(s)	Safety Issue and Web Address
May 23, 2007	Gadolinium-Containing Contrast Agents [Magnevist (gadopentate dimeglumine), Omniscan (gadodiamide), OptiMARK (gadoversetamide), MultiHance (gadobenate dimeglumine), and Prohance (gadoteridol)]	Reports of nephrogenic systemic fibrosis (NSF); *www.fda.gov/cder/drug/infopage/gcca*
May 21, 2007	Avandia, Avandemet, and Avandaryl (rosiglitazone maleate)	Pooled analysis of controlled clinical trials describing increased risks of heart attack and heart-related deaths; *www.fda.gov/cder/drug/infopage/rosiglitazone/default.htm*
March 30, 2007	Zelnorm[1] (tegaserod maleate)	Increased risk of heart attack, stroke, and worsening heart chest pain; *www.fda.gov/cder/drug/advisory/tegaserod.htm*
March 29, 2007	Permax[2] (pergolide mesylate)	Increased risk of heart valve damage; *www.fda.gov/cder/drug/infopage/pergolide/default.htm*
March 16, 2007	Zyvox (linezolid)	Increased risk of death when used for intravascular catheter-related infections where there is a gram negative or no organism at time of study entry; *www.fda.gov/cder/drug/infopage/linezolid/default.htm*
March 9, 2007	Erythropoiesis Stimulating Agents [Aranesp (darbepoetin alfa), Epogen (epoetin alfa), Procrit (epoetin alfa)]	Increased risk of death, non-fatal heart attacks, strokes, heart failure, blood clots, and tumor progression; *www.fda.gov/cder/drug/infopage/RHE*
March 9, 2007	Actimmune (interferon gamma-1b)	Early termination of clinical trial evaluating Actimmune for treatment of idiopathic pulmonary fibrosis (IPF) due to lack of benefit; *www.fda.gov/cder/drug/infopage/interferon_gamma_1b*
February 21, 2007	Xolair (omalizumab)	Reports of delayed anaphylaxis; *www.fda.gov/cder/drug/infopage/omalizumab*
February 9, 2007	Topical Anesthetic Creams	Reports of life-threatening adverse events, such as an irregular heartbeat, seizures, and death; *www.fda.gov/cder/drug/advisory/topical_anesthetics.htm*

NOTES:

1. Withdrawn from marketing March 30, 2007.

2. Withdrawn from marketing March 29, 2007.

U.S. Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
5600 Fishers Lane, Rockville MD 20857-0001
Phone: 1-888-INFO-FDA (1-888-463-6332)

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Acknowledgments:
Office of Surveillance and Epidemiology and Office of New Drugs

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We value your comments. Please let us know by reaching us at www.fda.gov/cder/comment.htm. All text in the articles in the Drug Safety Newsletter is in the public domain and may be used and reprinted without permission; citation as to source, however, is appreciated.

FDA News

FOR IMMEDIATE RELEASE
Dec. 21, 2007

Media Inquiries:
Chris Kelly, 301-827-6242
Consumer Inquiries:
888-INFO-FDA

FDA Issues Second Safety Warning on Fentanyl Skin Patch

Deaths and serious injuries from improper

The Food and Drug Administration today issued its second safety warning about the fentanyl transdermal system, an adhesive patch that delivers a potent pain medicine through the skin. In July 2005, the agency issued a similar warning to the public and to health care providers, saying that the directions on the product label and on the patient package insert should be followed exactly in order to avoid overdose. FDA has continued to receive reports of deaths and life-threatening side effects after doctors have inappropriately prescribed the patch or patients have incorrectly used it.

In addition, the agency is asking manufacturers of all fentanyl patches to update their product information and to develop a medication guide for patients.

The fentanyl skin patch contains the opioid fentanyl, a potent narcotic. The skin patch was approved by FDA in 1990 for use in patients with persistent, moderate-to-severe pain who have become opioid tolerant – meaning that they have been using another strong opioid narcotic pain medicine around-the-clock, and have been using the medicine regularly for a week or longer. The skin patch is most commonly prescribed for patients with cancer.

Recent reports to FDA describe deaths and life-threatening side effects after doctors and other health care professionals inappropriately prescribed the patch to relieve pain after surgery, for headaches, or for occasional or mild pain in patients who were not opioid tolerant. In other cases, patients used the patch incorrectly: The patients replaced it more frequently than directed in the instructions, applied more patches than prescribed, or applied heat to the patch – all resulting in dangerously high fentanyl levels in the blood.

“There is an unmet need to provide patients suffering from chronic pain with safe and effective products that will not only alleviate their pain, but that will also be tolerable when used chronically,” said Bob Rappaport, M.D., FDA’s director of the Division of Anesthesia, Analgesia and Rheumatology Products. "While these products fill an important need, improper use and misuse can be life-threatening. Therefore, it is crucial that doctors prescribe these products appropriately and that patients use them correctly."

In its Public Health Advisory and Health Care Professional Sheet published today, FDA stressed the following safety information:

- Fentanyl patches are only for patients who are opioid-tolerant and have chronic pain that is not well controlled with other pain medicines. The patches are not to be used to treat sudden, occasional or mild pain, or pain after surgery.
- Health care professionals who prescribe the fentanyl patch, and patients who use it, should be aware of the signs of fentanyl overdose: trouble breathing or slow or shallow breathing; slow heartbeat; severe sleepiness; cold, clammy skin; trouble walking or talking; or feeling faint, dizzy, or confused. If these signs occur, patients should get medical attention right away.

- Patients prescribed the fentanyl patch should tell their doctor, pharmacist and other health care professionals about all the medicines that they take. Some medicines may interact with fentanyl, causing dangerously high fentanyl levels in the blood and life-threatening breathing problems.
- Patients and their caregivers should be told how to use fentanyl patches. This important information, including instructions on how often to apply the patch, reapplying a patch that has fallen off, replacing a patch, and disposing of the patch, is provided in the patient information that comes with the fentanyl patch.
- Heat may increase the amount of fentanyl that reaches the blood and can cause life-threatening breathing problems and death. Patients should not use heat sources such as heating pads, electric blankets, saunas, or heated waterbeds or take hot baths or sunbathe while wearing a patch. A patient or caregiver should call the patient's doctor right away if the patient has a temperature higher than 102 degrees while wearing a patch.

This information will be reflected in the updated product information new medication guides for patients that manufacturers are being asked by FDA to develop.

The fentanyl skin patch is marketed under the brand name Duragesic by Johnson and Johnson, and generic versions of the product are sold by other manufacturers.

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Information for Healthcare Professionals
Carbamazepine (marketed as Carbatrol, Equetro, Tegretol, and generics)

FDA ALERT [12/12/2007]: Dangerous or even fatal skin reactions (Stevens Johnson syndrome and toxic epidermal necrolysis), that can be caused by carbamazepine therapy, are significantly more common in patients with a particular human leukocyte antigen (HLA) allele, HLA-B*1502. This allele occurs almost exclusively in patients with ancestry across broad areas of Asia, including South Asian Indians. Genetic tests for HLA-B*1502 are already available. Patients with ancestry from areas in which HLA-B*1502 is present should be screened for the HLA-B*1502 allele before starting treatment with carbamazepine. If they test positive, carbamazepine should not be started unless the expected benefit clearly outweighs the increased risk of serious skin reactions. Patients who have been taking carbamazepine for more than a few months without developing skin reactions are at low risk of these events ever developing from carbamazepine. This is true for patients of any ethnicity or genotype, including patients positive for HLA-B*1502. This new safety information will be reflected in updated product labeling.

This information reflects FDA's current analysis of data available to FDA concerning this drug. FDA intends to update this when additional information or analyses become available.

To report any unexpected adverse or serious events associated with the use of this drug, please contact the FDA MedWatch program and complete a form on line at http://www.fda.gov/medwatch/report/hcp.htm or report by fax to 1-800-FDA-0178, by mail using the postage-paid address form provided on line, or by telephone to 1-800-FDA-1088.

Recommendations

Healthcare professionals who prescribe carbamazepine products, including Carbatrol, Equetro, Tegretol, and generic carbamazepine, should be fully aware of new prescribing information in the product label and in the revised boxed warning. Following are highlights of the important new safety information (see Drugs@FDA for full prescribing information):

- The risk of Stevens Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN) from carbamazepine is significantly increased in patients positive for the HLA-B*1502 allele. This allele is found almost exclusively in patients with ancestry across broad areas of Asia, including South Asian Indians. Due to wide variability in rates of HLA-B*1502 even within ethnic groups, the difficulty in ascertaining ethnic ancestry, and the likelihood of mixed ancestry, screening for HLA-B*1502 should be performed for most patients of Asian ancestry. Prevalence of HLA-B*1502 has not been studied in many regions of Asia. The following figures must therefore be considered no more than a rough guide in deciding which patients to screen:
  - 10-15% or more of patients may carry the allele in parts of China, Thailand, Malaysia, Indonesia, the Philippines, and Taiwan.
  - South Asians, including Indians, appear to have intermediate prevalence of HLA-B*1502, averaging 2 to 4%, but higher in some groups.
  - HLA-B*1502 appears to be present at a low frequency, <1%, in Japan and Korea.

- Patients with ancestry in at-risk populations should be screened for the HLA-B*1502 allele prior to starting carbamazepine. Patients who test positive for HLA-B*1502 should not be treated with carbamazepine unless the expected benefit clearly outweighs the increased risk of SJS/TEN.

- Tested patients who are found to be negative for HLA-B*1502 have a low risk of SJS/TEN from carbamazepine, but SJS/TEN can still rarely occur, so healthcare professionals should still watch for symptoms in these patients.

- Patients who test positive for HLA-B*1502 may be at increased risk of SJS/TEN from other antiepileptic drugs that have been associated with SJS/TEN. Therefore, in HLA-B*1502 positive patients, doctors should consider avoiding use of other antiepileptic drugs associated with SJS/TEN when alternative therapies are equally acceptable.

- Over 90% of carbamazepine treated patients who will experience SJS/TEN have this reaction within the first few months of treatment. Patients of any ethnicity or genotype (including HLA-B*1502 positive) who have been taking carbamazepine for more than a few months are at low risk of SJS/TEN from carbamazepine.

Information for the patient: *Physicians who are prescribing carbamazepine products should ensure that their patients or their caregivers understand the following:*

Patients for whom a genetic test is recommended:

- Different people sometimes respond differently to drugs. Some people with Asian ancestry are at greater risk for dangerous skin reactions when first starting treatment with carbamazepine. We can test for a risk factor for such reactions, which is called HLA-B*1502, before giving carbamazepine.

- Tests for HLA-B*1502 are already used to check for compatibility before tissue transplants.

- Having HLA-B*1502 is not abnormal, and there is no other known risk from having it.

- If you test positive for HLA-B*1502, then your doctor will take that into account for your medical care.

- If you test negative for HLA-B*1502, you are at lower risk of dangerous skin reactions when first starting carbamazepine, but dangerous skin reactions could still occur, and you still should be watchful.

Patients who are prescribed carbamazepine:

- If you and your doctor decide that, in your case, the benefits of starting carbamazepine outweigh possible risks, then you should watch for any sign of a rash. If you see any sign of a rash, then you should contact your doctor immediately.

Data Summary

The overall estimated risk of SJS/TEN associated with carbamazepine is based on countries

with mainly Caucasian populations, and is fairly low, 1- to 6 per 10,000 new users (Tennis and Stern, 1997; Mockenhaupt et al., 2005). Recently, post-marketing adverse events reported to the World Health Organization (WHO) and carbamazepine manufacturers pointed to a much higher rate of SJS/TEN, about 10 times higher, in some Asian countries. Studies from Taiwan (Hung et al., 2006), Europe (Lonjou et al., 2006), and Hong Kong (Man et al., 2007), indicated that this increased risk of SJS/TEN was associated with HLA-B*1502, an inherited allelic variant of the HLA-B gene found almost exclusively in some individuals across broad areas of Asia, including South Asian Indians.

- Hung et al. (2006) in a case control study in Taiwan found that of 59 out of 60 patients with SJS/TEN associated with carbamazepine were positive for HLA-B*1502, far higher than the 4% incidence of HLA-B*1502 in carbamazepine-tolerant controls. These findings, combined with postmarketing data on cases per patient-year exposure, suggest an initial estimate of 5% absolute risk of SJS/TEN in HLA-B*1502 positive patients exposed to carbamazepine.

- Lonjou et al. (2007) in a case series of European patients with SJS/TEN associated with carbamazepine found that patients with Asian ancestry were over-represented considering the small percentage of Asians in the general population. Out of 12 patients, 4 were of Asian ancestry. All four were positive for HLA-B*1502.

- Man et al. (2007) in a case series in patients in Hong Kong found 4 of 4 cases of SJS/TEN associated with carbamazepine in patients positive for HLA-B*1502.

HLA-B*1502 is largely absent in individuals not of Asian origin, and therefore has not been found to be a risk factor for SJS/TEN in Caucasians (Alfirevic et al., 2006).

Background Information

Carbamazepine is FDA-approved for treatment of epilepsy, mania/bipolar disorder, and neuropathic pain. SJS and TEN are serious blistering reactions of the skin and mucous membranes that can be permanently disabling or fatal.

After review of the information from manufacturers as well as published studies and post-marketing adverse event reports, FDA and the manufacturers have agreed that labeling changes are needed for carbamazepine products.

Information on the association of carbamazepine and SJS/TEN, and information to guide testing for the HLAB*1502 allele in at-risk populations, has been added to the existing boxed warning, and to the sections of the labeling covering warnings, laboratory tests, and adverse reactions.

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Date created: December 12, 2007
