Drug Utilization Review Board

Oklahoma Health Care Authority
2401 N.W. 23rd Street, Suite 1A
Oklahoma City, Oklahoma 73107
Ponca Room

Wednesday
March 9, 2011
6:00 p.m.

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

MEMORANDUM

TO: Drug Utilization Review Board Members

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

SUBJECT: Packet Contents for Board Meeting – March 9, 2011

DATE: March 3, 2011

NOTE: THE DUR BOARD WILL MEET AT 6:00 P.M. THE MEETING WILL BE HELD IN THE PONCA ROOM AT THE OKLAHOMA HEALTH CARE AUTHORITY OFFICES IN SHEPHERD MALL. (NORTH ENTRANCE)

Enclosed are the following items related to the March 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 Benign Prostate Hyperplasia (BPH) Medications – See Appendix C.

Action Item – Vote to Prior Authorize Tribenzor®, Tekamlo®, Nexiclon XR®, and Catapres-TTS®– See Appendix D.

Action Item – Vote to Prior Authorize Silenor™ – See Appendix E.

Action Item – Vote to Prior Authorize Kapvay® and Xyrem® – See Appendix F.

Action Item – Annual Review of Osteoporosis Medications and 30 Day Notice to Prior Authorize Prolia™ and Atelvia™ – See Appendix G.

Drug Utilization Review of Topical Steroids – See Appendix H.

Action Item – Annual Review of Lamisil® Granules – See Appendix I.

FDA and DEA Updates – See Appendix J.

Future Business

Adjournment

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Oklahoma Health Care Authority
Drug Utilization Review Board
(DUR Board)
Meeting – March 9, 2011 @ 6:00 p.m.

Oklahoma Health Care Authority
2401 N.W. 23rd Street, Suite 1-A
Oklahoma City, Oklahoma 73107
Ponca Room (North Entrance)

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

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

Items to be presented by Dr. Muchmore, Chairman:

2. Public Comment Forum
- A. Acknowledgment of Speakers and Agenda Items

Items to be presented by Dr. Muchmore, Chairman:

3. Action Item – Approval of DUR Board Meeting Minutes – See Appendix A.
- A. January 12, 2011 DUR Minutes – Vote
- B. January 13, 2011 DUR Recommendation Memorandum

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

4. Update on DUR / Medication Coverage Authorization Unit – See Appendix B.
- A. Retrospective Drug Utilization Review for November 2010
- B. Retrospective Drug Utilization Review Response for October 2010
- C. Medication Coverage Activity Audit for January 2011, February 2011
- D. Pharmacy Help Desk Activity Audit for January 2011, February 2011

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

5. Action Item – Vote to Prior Authorize Benign Prostate Hyperplasia (BPH) Medications – See Appendix C.
- A. COP Recommendations

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

6. Action Item – Vote to Prior Authorize Tribenzor®, Tekamlo®, Nexiclon XR®, and Catapres-TTS® – See Appendix D.
- A. COP Recommendations

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

7. Action Item – Vote to Prior Authorize Silenor™– See Appendix E.
- A. Current Authorization Criteria for Hypnotics Category
- B. COP Recommendations

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

8. Action Item – Vote to Prior Authorize Kapvay® and Xyrem® – See Appendix F.

A. COP Recommendations

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

9. Action Item – Annual Review of Osteoporosis Medications and 30 Day Notice to Prior Authorize Prolia™ and Atelvia™ – See Appendix G.

A. Current Authorization Criteria
B. Utilization Review
C. Prior Authorizations Review
D. Market News and Updates
E. COP Recommendations
F. Utilization Details
G. New Product Details
H. FDA Drug Safety Communication

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

10. Drug Utilization Review of Topical Steroids – See Appendix H.

A. Overview
B. Utilization Review
C. Market News and Updates
D. COP Recommendations
E. Utilization Details

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

11. Action Item – Annual Review of Lamisil® Granules – See Appendix I.

A. Current Authorization Criteria
B. Utilization Review
C. Prior Authorizations Review
D. COP Recommendations
E. Utilization Details

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

12. FDA and DEA Updates – See Appendix J.

13. Future Business

A. Utilization Review of Diabetes Products
B. Annual Review of Plavix® and Effient®
C. Annual Review of Triptans
D. Annual Review of Fibromyalgia Products
E. New Product Reviews

14. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES of MEETING of JANUARY 12, 2011

BOARD MEMBERS:	PRESENT	ABSENT
Brent Bell, D.O., D.Ph.: Vice-Chairman	X	
Mark Feightner, Pharm.D.		X
Anetta Harrell, Pharm.D.	X	
Evelyn Knisely, Pharm.D.	X	
Thomas Kuhls, M.D.	X	
John Muchmore, M.D., Ph.D.: Chairman	X	
Paul Louis Preslar, D.O., MBA	X	
James Rhymer, D.Ph.	X	
Bruna Varalli-Claypool, MHS, PA-C	X	
Eric Winegardener, D.Ph.	X	

COLLEGE of PHARMACY STAFF:	PRESENT	ABSENT
Metha Chonlahan, D.Ph.; Clinical Pharmacist	X	
Karen Egesdal, D.Ph.; SMAC-ProDUR Coordinator/OHCA Liaison	X	
Ronald Graham, D.Ph.; Pharmacy Director	X	
Shellie Keast, Pharm.D, M.S..; DUR Manager	X	
Chris Le, Pharm.D.; Clinical Pharmacist/Coordinator	X	
Carol Moore, Pharm.D.; Clinical Pharmacist	X	
Neeraj Patel, Pharm.D.; Clinical Pharmacist	X	
Lester A. Reinke, Ph.D.; Associate Dean for Graduate Studies & Research	X	
Leslie Robinson, D.Ph.; PA Coordinator	X	
Jennifer Sipols, Pharm.D.; Clinical Pharmacist	X	
Visiting Pharmacy Student(s): Joel Davenport, Stephanie Manning	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
Garth Splinter, M.D., M.B.A.; Director of Medicaid/Medical Services		X
Nancy Nesser, Pharm.D., J.D.; Pharmacy Director	X	
Howard Pallotta, J.D.; Director of Legal Services		X
Lynn Rambo-Jones, J.D.; Deputy General Counsel III	X	
Rodney Ramsey; Drug Reference Coordinator	X	
Jill Ratterman, D.Ph.; Pharmacy Specialist	X	
Kerri Wade, Senior Pharmacy Financial Analyst	X	

OTHERS PRESENT:		
David Williams, Forest	Davilla Williams, Forest	Jim Dunlap, Lilly USA
Vanessa Papion, UCB	Russ Wilson, OMJPI	Warren Tayes, Merck
Tori Magee, Dyax	Charlene Kaiser, Amgen	Janie Huff, Takeda
Brian Maves, Pfizer	Ron Schnare, Shire	

PRESENT FOR PUBLIC COMMENT:

None

AGENDA ITEM NO. 1: CALL TO ORDER

1A: Roll Call

Dr. Muchmore called the meeting to order. Roll call by Dr. Graham established the presence of a quorum.
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: December 8, 2010 DUR Minutes

Dr. Kuhls moved to approve as submitted; seconded by Ms. Varalli-Claypool.
ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: UPDATE ON DUR/MEDICATION COVERAGE AUTHORIZATION UNIT

4A: Retrospective Drug Utilization Review Response: September 2010
4B: Medication Coverage Activity Audit: December 2010
4C: Help Desk Activity Audit: December 2010

Reports included in agenda packet; presented by Dr. Keast.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: VOTE TO PRIOR AUTHORIZE ZYFLO CR®

Materials included in agenda packet; presented by Dr. Le.
Dr. Winegardener moved to approve as submitted; seconded by Dr. Harrell.
ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: VOTE TO PRIOR AUTHORIZE LATUDA™

Materials included in agenda packet; presented by Dr. Keast.
Dr. Kuhls moved to approve as submitted; seconded by Ms. Varalli-Claypool.
ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: 30-DAY NOTICE TO PRIOR AUTHORIZE BENIGN PROSTATE HYPERPLASIA (BPH) PRODUCTS

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

AGENDA ITEM NO. 8: ANNUAL REVIEW OF HYPNOTIC MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE SILENOR®

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

AGENDA ITEM NO. 9: ANNUAL REVIEW OF ANTIHYPERTENSIVES AND 30-DAY NOTICE TO PRIOR AUTHORIZE TRIBENZOR®, TEKAMLO®, NEXICLON SR®, AND CATAPRES-TTS®

Materials included in agenda packet; presented by Dr. Sipols.
Dr. Winegardener moved to approve moving losartan and losartan/HCTZ to Tier 1; seconded by Ms. Varalli-Claypool.
ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: ANNUAL REVIEW OF ADHD MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE KAPVAY® AND XYREM®

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

AGENDA ITEM NO. 11: FDA & DEA UPDATES

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

AGENDA ITEM NO. 12: FUTURE BUSINESS

Materials included in agenda packet; submitted by Dr. Graham.
A: Utilization Review of Diabetes Products
B: Annual Review of Triptans
C: Annual Review of Antiemetics
D: New Product Reviews
ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: ADJOURNMENT

The meeting was adjourned at 7:05 p.m.

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

Memorandum

Date: January 13, 2011

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

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

Subject: DUR Board Recommendations from Meeting of January 12, 2011

Recommendation 1: Vote to Prior Authorize Zyflo (zileuton) CR®

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends prior authorization of Zyflo (zileuton) CR® with the following criteria:

Children age 12 and older and adults:

- Diagnosis of mild or moderate persistent asthma, AND
- Trial of inhaled corticosteroid AND corticosteroid/LAB_2A therapy within the previous 6 months and reason for trial failure, AND
- Recent trial with at least one other available leukotriene modifier that did not yield adequate response.

Recommendation 2: Vote to Prior Authorize Latuda® (lurasidone) and Update Antipsychotic PBPA Criteria

MOTION CARRIED by unanimous approval.

The College of Pharmacy has the following recommendations:

1. Placement of Latuda® (lurasidone) into Tier 3 of the PBPA category.
2. Addition of Symbyax® (olanzapine/fluoxetine) to the following section of criteria: For aripiprazole, quetiapine extended release and olanzapine/fluoxetine: a diagnosis of depression requires current use of an antidepressant, and previous trials with at least two other antidepressants. Tier structure still applies.
3. Perform an additional class review in six months to ensure that the goals of this PBPA category are being met.
4. For 2011 only, change the item 2 of the criteria for Tier 3 to read: A trial of ~~all available~~ two Tier 2 medications, at least 14 days in duration, titrated to recommended dose, that did not yield adequate response or resulted in intolerable adverse effects.

Recommendation 3: Annual Review of Hypnotic Medications

NO ACTION REQUIRED.

Recommendation 4: Utilization Review of Antihypertensive Medications

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following changes to the Antihypertensives PBPA category:

1. Move Cozaar (losartan) and Hyzaar (losartan /HCTZ) into Tier 1 of the ARB category.
2. Changes to the antihypertensive prior authorization criteria as follows :

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

1. documented inadequate response to two Tier 1 medications (trials must include medication from all available classes where applicable), or
2. adverse drug reaction to all Tier 1 class of medications, or
3. previous stabilization on the Tier 2 medication, or
4. a unique indication for which the Tier 1 antihypertensives lack

ARBs (Angiotensin Receptor Blockers) and ARB Combination Products		
Tier-1	**Tier-2**	**Tier-3**
Any Tier-1 ACE Inhibitor:	amlodopine / valsartan (Exforge®)	candesartan (Atacand®)
benazepril (Lotensin®)	amlodopine / valsartan (Exforge® HCT)	candesartan / HCTZ (Atacand® HCT)
captopril (Capoten®)	amlodipine / olmesartan (Azor™)	eprosartan (Teveten®)
enalapril (Vasotec®)	irbesartan (Avapro®)	eprosartan / HCTZ (Teveten® HCT)
enalaprilat (Vasotec® IV)	irbesartan / HCTZ (Avalide®)	telmisartan/amlodipine (Twynsta)
fosinopril (Monopril®)	valsartan (Diovan®)	telmisartan (Micardis®)
lisinopril (Prinivil®, Zestril®)	valsartan / HCTZ (Diovan HCT®)	telmisartan / HCTZ (Micardis® HCT)
moexipril (Univasc®)	olmesartan (Benicar®)	
quinapril (Accupril®)	olmesartan / HCTZ (Benicar HCT®)	
trandolapril (Mavik®)		
ramipril (Altace®)		
losartan (Cozaar®)		
losartan / HCTZ (Hyzaar®)		

Recommendation 5: Annual Review of ADHD/Narcolepsy Medications

NO ACTION REQUIRED.

Appendix B

RETROSPECTIVE DRUG UTILIZATION REVIEW REPORT
November 2010

MODULE	DRUG INTERACTION	DUPLICATION OF THERAPY	DRUG-DISEASE PRECAUTIONS	DOSING & DURATION
Total # of messages	55,470	65,941	1,102,113	31,533
Limits applied	Established, Major, Males and Females, Age 60-150	Duplication in Antidepressants, Age 0-9	Contraindicated, Males and Females, Myocardial Infarction, Age 0-55	High Dose, Low Dose, Incretin Mimetics (Byetta, Victoza), Males & Females, Age 0-150
Total # of messages after limits were applied	52	115	48	5
Total # of members reviewed	52	96	26	5

LETTERS

Category	Prescribers	Pharmacies	Total Letters
Drug Interaction	6	0	6
Duplication of Therapy	87	74	161
Drug-Disease Precautions	28	27	55
Dosing & Duration	2	1	3
Total Letters Sent	123	102	225

Retrospective Drug Utilization Review Report

Claims Reviewed for October 2010

Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
Limits which were applied	Established, Major, Males and Females, Age 51-59	Narcotics, Males and Females, Age 21-25	Contraindicated, Leukemia, Males and Females, Age 0-150	High & Low Dose, Duration, Vitamin K (Mephyton®) Males and Females, Age 0-150

Response Summary (Prescriber)
Letters Sent: 135
Response Forms Returned: 78

The response forms returned yielded the following results:

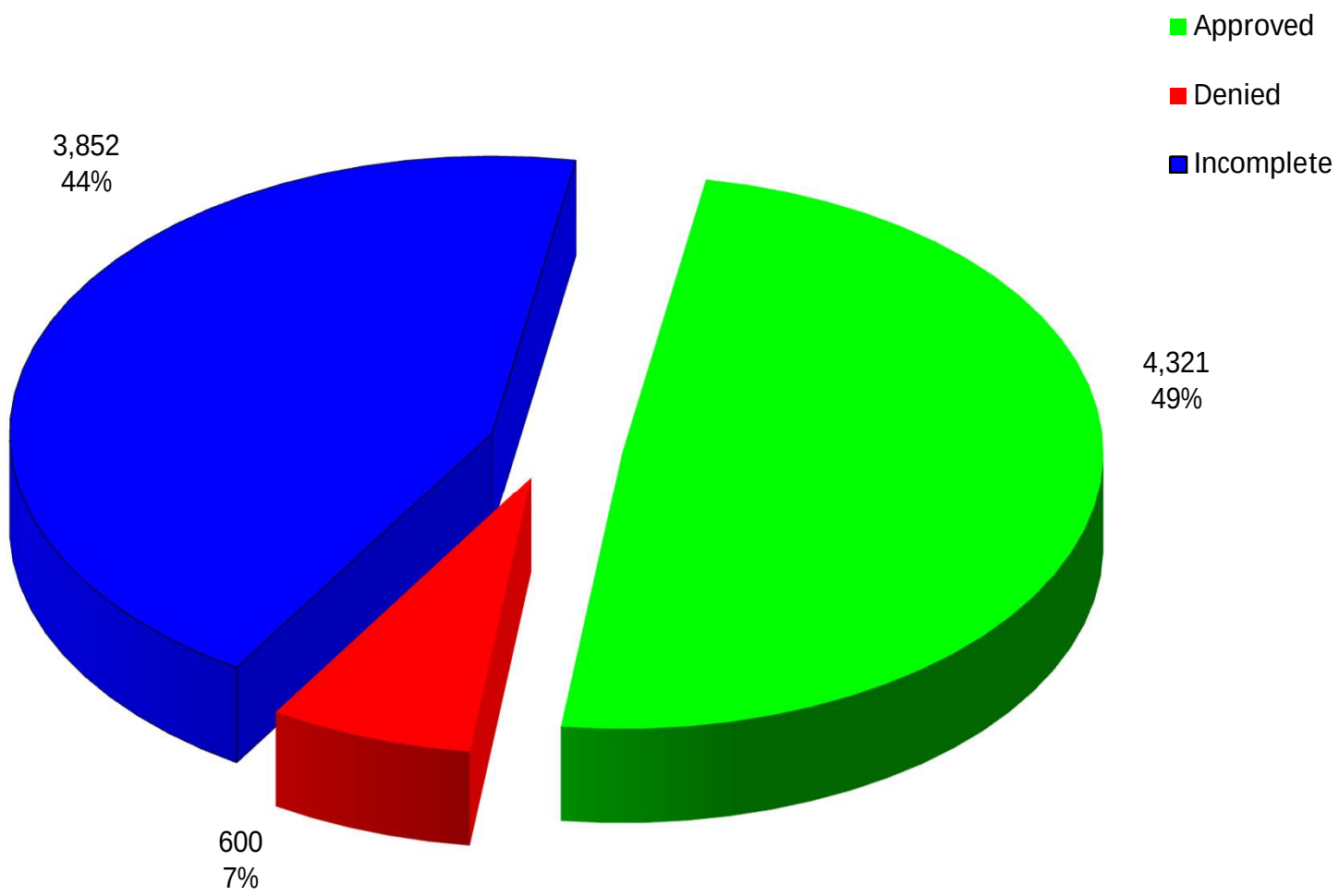
9 (12%)	*Record Error—Not my patient.*
12 (15%)	*No longer my patient.*
4 (5%)	*Medication has been changed prior to date of review letter.*
18 (23%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
18 (23%)	*I am aware of this situation and will plan to continue monitoring therapy.*
17 (22%)	*Other*

Response Summary (Pharmacy)
Letters Sent: 75
Response Forms Returned: 46

The response forms returned yielded the following results:

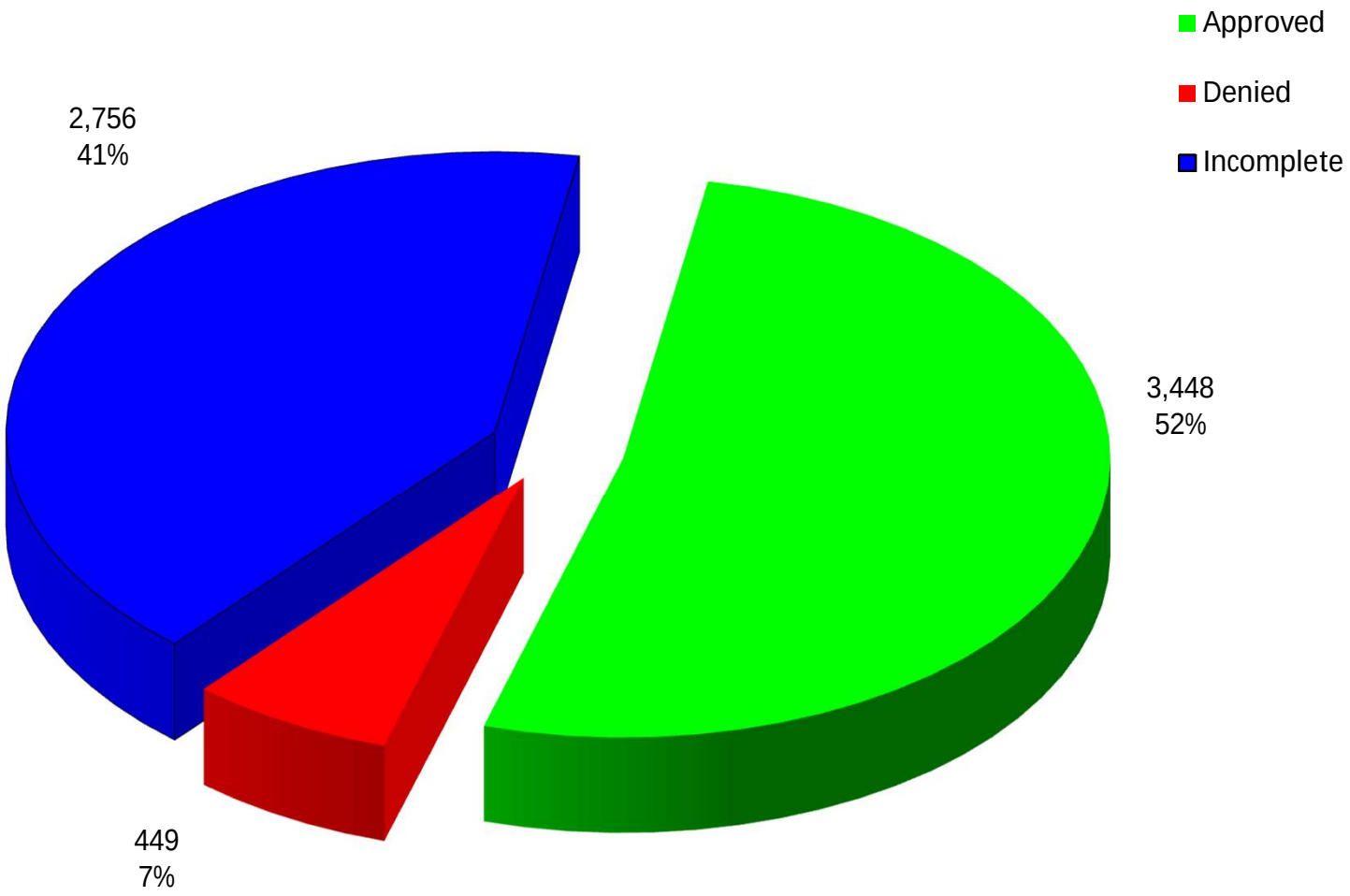
2 (4%)	*Record Error—Not my patient.*
3 (7%)	*No longer my patient.*
2 (4%)	*Medication has been changed prior to date of review letter.*
11 (24%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
14 (30%)	*I am aware of this situation and will plan to continue monitoring therapy.*
14 (30%)	*Other*

PRIOR AUTHORIZATION ACTIVITY REPORT: January 2011



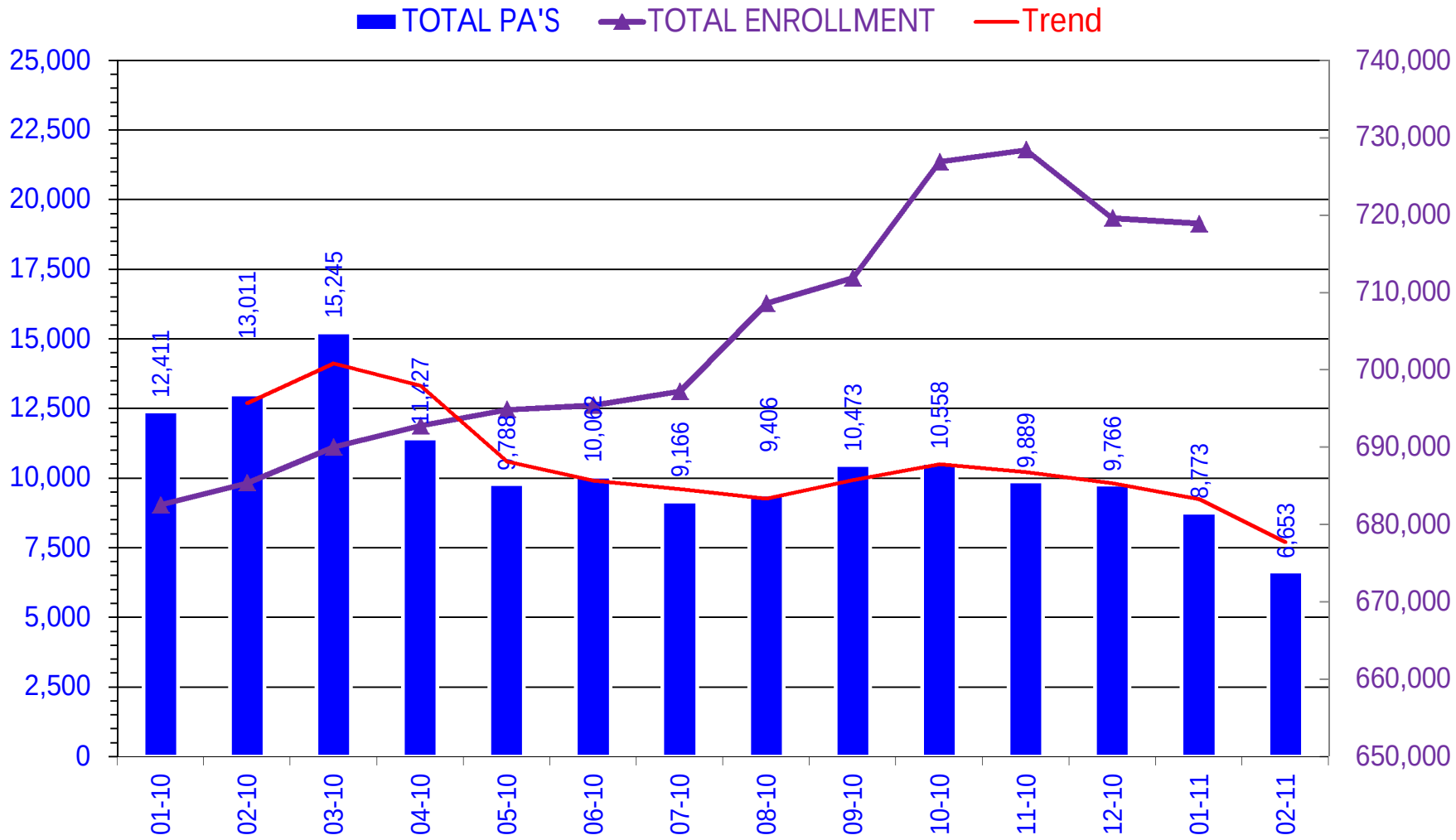
PA totals include overrides

PRIOR AUTHORIZATION ACTIVITY REPORT: February 2011



PA totals include overrides

PRIOR AUTHORIZATION REPORT: January 2010 – February 2011



PA totals include overrides

Prior Authorization Activity

1/1/2011 Through 1/31/2011

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort	378	164	11	203	359
Amitiza	16	5	1	10	251
Anti-Ulcer	445	133	37	275	100
Antidepressant	395	149	12	234	345
Antihistamine	352	229	8	115	340
Antihypertensives	117	40	11	66	360
Antimigraine	75	33	3	39	270
Atypical Antipsychotics	661	309	24	328	349
Benzodiazepines	86	31	5	50	244
Bladder Control	58	7	7	44	320
Brovana (Arformoterol)	1	0	0	1	0
Byetta	28	6	5	17	330
Elidel/Protopic	42	21	5	16	87
ESA	99	80	2	17	83
Fibric Acid Derivatives	9	1	0	8	365
Fibromyalgia	118	29	19	70	334
Forteo	5	2	0	3	362
Glaucoma	31	9	1	21	363
Growth Hormones	30	22	0	8	132
HFA Rescue Inhalers	74	28	6	40	309
Insomnia	64	15	11	38	232
Misc Analgesics	45	5	31	9	184
Muscle Relaxant	153	58	58	37	49
Nasal Allergy	217	72	15	130	122
NSAIDS	172	30	15	127	267
Ocular Allergy	117	16	6	95	184
Ocular Antibiotics	43	9	5	29	25
Opioid Analgesic	452	206	24	222	227
Other	522	126	98	298	142
Otic Antibiotic	113	68	5	40	19
Pediculicides	108	50	11	47	17
Plavix	150	98	5	47	321
Qualaquin (Quinine)	3	0	2	1	0
Singulair	727	395	22	310	252
Smoking Cessation	66	17	2	47	40
Statins	127	22	17	88	361
Stimulant	869	477	37	355	248
Symlin	1	0	0	1	0
Synagis	202	152	17	33	68
Topical Antibiotics	12	3	1	8	18
Topical Antifungals	17	4	2	11	37
Ultram ER and ODT	9	1	2	6	178
Xolair	11	5	2	4	281
Xopenex Nebs	33	15	4	14	250
Zetia (Ezetimibe)	20	10	1	9	361
Emergency PAs	1	1	0	0	
Regular PAs Total	**7,274**	**3,153**	**550**	**3,571**	

Overrides					
Brand	54	31	4	19	244
Dosage Change	500	480	2	18	12
High Dose	5	5	0	0	253
IHS-Brand	32	30	0	2	108
Ingredient Duplication	5	4	0	1	11
Lost/Broken Rx	85	80	1	4	13
NDC vs Age	33	32	0	1	143
Nursing Home Issue	93	90	0	3	7
Other	33	31	0	2	34
Quantity vs. Days Supply	648	375	43	230	266
Stolen	10	10	0	0	4
Wrong D.S. on Previous Rx	1	0	0	1	0
Overrides Total	**1,499**	**1,168**	**50**	**281**	
Total Regular PAs+Overrides	**8,773**	**4,321**	**600**	**3,852**	

Denial Reasons	
Unable to verify required trials.	2,833
Lack required information to process request.	1,025
Does not meet established criteria.	565

Duplicate Requests: 691

Letters: 1,284

No Process: 431

Changes to existing PAs: 395

Activity Audit for

2/1/2011 Through 2/28/2011

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort	276	140	8	128	358
Amitiza	21	8	1	12	298
Anti-Ulcer	273	81	26	166	94
Antidepressant	288	110	7	171	353
Antihistamine	301	162	14	125	329
Antihypertensives	65	22	1	42	336
Antimigraine	51	27	1	23	344
Atypical Antipsychotics	531	274	17	240	351
Benzodiazepines	61	22	3	36	168
Bladder Control	47	6	5	36	362
Byetta	7	3	0	4	361
Elidel/Protopic	35	16	1	18	86
ESA	96	72	3	21	87
Fibric Acid Derivatives	2	0	0	2	0
Fibromyalgia	103	29	17	57	338
Fortamet/Glumetza	1	0	0	1	0
Forteo	2	1	1	0	364
Glaucoma	17	4	0	13	364
Growth Hormones	46	31	3	12	122
HFA Rescue Inhalers	51	21	2	28	306
Insomnia	70	15	3	52	156
Misc Analgesics	30	8	15	7	263
Muscle Relaxant	119	42	46	31	68
Nasal Allergy	169	43	24	102	104
NSAIDS	136	25	20	91	324
Ocular Allergy	90	15	5	70	77
Ocular Antibiotics	45	12	1	32	20
Opioid Analgesic	214	110	7	97	231
Other	394	101	79	214	144
Otic Antibiotic	78	52	1	25	19
Pediculicides	79	31	6	42	15
Plavix	157	116	3	38	320
Singulair	508	301	16	191	259
Smoking Cessation	57	15	4	38	35
Statins	100	30	6	64	362
Stimulant	698	441	33	224	240
Symlin	1	0	0	1	0
Synagis	101	80	9	12	40
Topical Antibiotics	22	7	1	14	75
Topical Antifungals	18	3	1	14	43
Ultram ER and ODT	5	1	1	3	176
Xolair	2	2	0	0	358
Xopenex Nebs	45	17	3	25	286
Zetia (Ezetimibe)	21	12	1	8	361
Emergency PAs	7	7	0	0	
Total	**5,440**	**2,515**	**395**	**2,530**	

Overrides					
Brand	44	21	1	22	178
Dosage Change	384	360	5	19	11
High Dose	3	1	0	2	28
IHS-Brand	1	0	0	1	0
Ingredient Duplication	6	6	0	0	20
Lost/Broken Rx	78	72	4	2	6
NDC vs Age	51	47	0	4	227
Nursing Home Issue	87	78	1	8	8
Other	25	22	0	3	6
Quantity vs. Days Supply	532	324	43	165	275
Stolen	2	2	0	0	14
Overrides Total	**1,213**	**933**	**54**	**226**	
Total Regular PAs + Overrides	**6,653**	**3,448**	**449**	**2,756**	

Denial Reasons

Unable to verify required trials.	2,137
Lack required information to process request.	639
Does not meet established criteria.	424

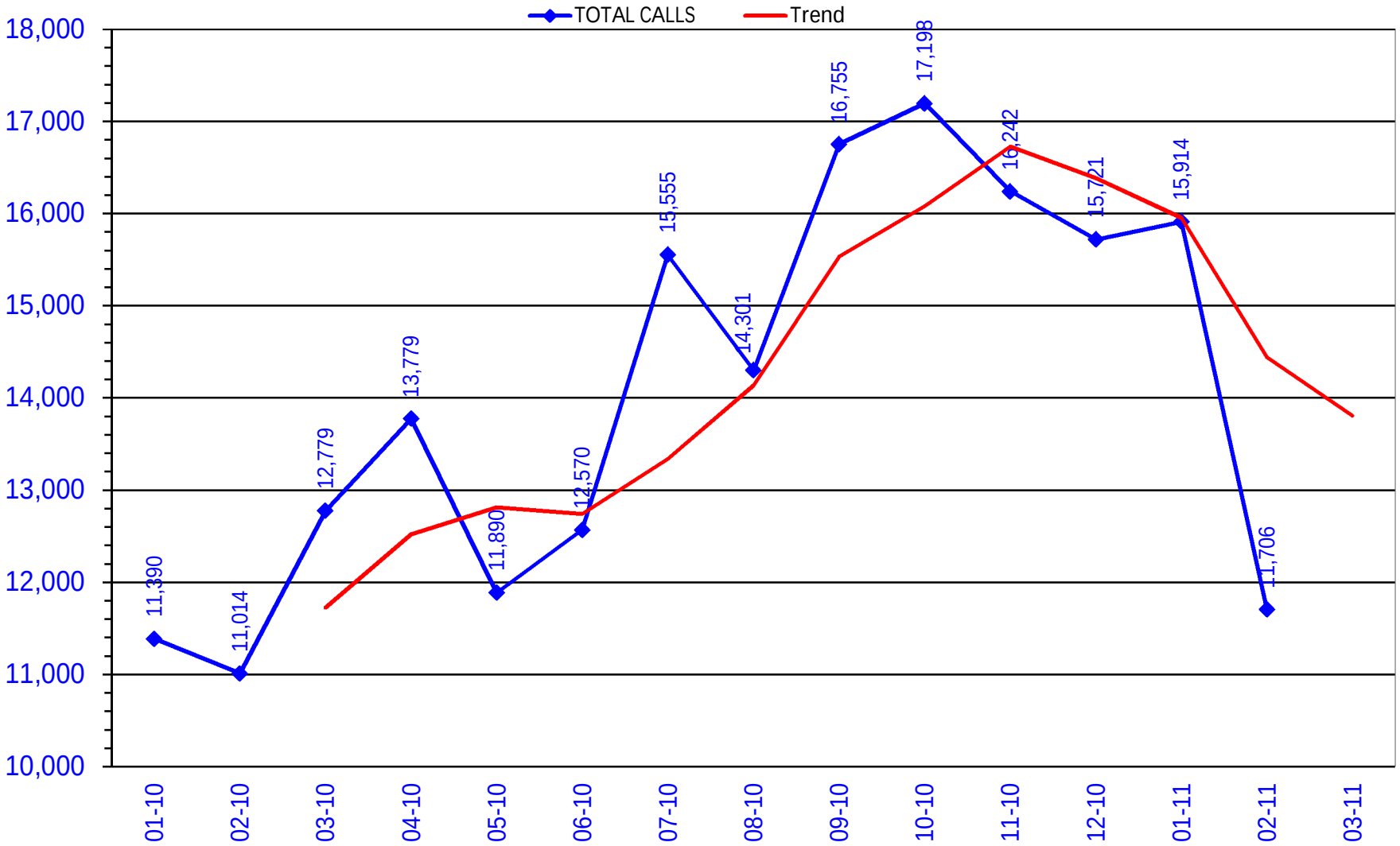
Duplicate Requests: 509

Letters: 1,123

No Process: 374

Changes to existing PAs: 400

CALL VOLUME MONTHLY REPORT:
January 2010 – February 2011



Appendix C

Vote to Prior Authorize
Benign Prostate Hyperplasia Medications
Oklahoma HealthCare Authority
March 2011

This category was introduced for possible inclusion in the Product Based Prior Authorization program in November 2010. See the November, December 2010, and January 2011 DUR packets 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.

Recommendations

The College of Pharmacy recommends the addition of the BPH class of medications to the Product Based Prior Authorization program. The 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
Hytrin® (Terazosin)	Uroxatrol® (Alfuzosin)
Cardura® (Doxazosin)	Rapaflo® (Silodosin)
Flomax® (Tamsulosin)	Cardura XL® (Doxazosin)
Proscar® (Finasteride)	Avodart® (Dutasteride)
	Jalyn® (Dutasteride/Tamsulosin)

Prior Authorization Criteria:

1. FDA approved diagnosis.
2. Recent 4-week trial of at least two Tier 1 medications from different pharmacological classes within the last 90 days.
3. Documented adverse effect, drug interaction, or contraindication to all available Tier 1 products.

Appendix D

Vote to Prior Authorize Tribenzor® (olmesartan/amlodipine/HCTZ), Tekamlo® (aliskiren/amlodipine), Nexiclon XR® (clonidine extended-release), and Catapres-TTS® (clonidine transdermal patch)

Oklahoma Health Care Authority, March 2011

Recommendations:

The College of Pharmacy recommends the following changes to the Antihypertensives PBPA category:

1. Placement of Tribenzor® (olmesartan/amlodipine/HCTZ) in Tier 3 of the ARB category.
2. Placement of Tekamlo® (aliskiren/amlodipine) into Tier 3 of the DRI category.
3. Prior Authorization of Nexiclon XR® (clonidine extended release) and Catapres TTS® Patch (clonidine) with the following criteria:
    a. FDA-approved indication of hypertension in adults.
    b. Must provide a clinically significant reason why the member cannot take clonidine immediate release tablets.

ARBs (Angiotensin Receptor Blockers) and ARB Combination Products		
Tier-1	Tier-2	Tier-3
benazepril (Lotensin®)	amlodopine / valsartan (Exforge®)	amlodipine / olmesartan (Azor™)
captopril (Capoten®)	amlodopine / valsartan (Exforge® HCT)	candesartan (Atacand®)
enalapril (Vasotec®)	irbesartan (Avapro®)	candesartan / HCTZ (Atacand® HCT)
enalaprilat (Vasotec® IV)	irbesartan / HCTZ (Avalide®)	eprosartan (Teveten®)
fosinopril (Monopril®)	valsartan (Diovan®)	eprosartan / HCTZ (Teveten® HCT)
lisinopril (Prinivil®, Zestril®)	valsartan / HCTZ (Diovan® HCT)	telmisartan/amlodipine (Twynsta®)
moexipril (Univasc®)	olmesartan (Benicar®)	olmesartan/amlodipine/HCTZ (Tribenzor®)
quinapril (Accupril®)	olmesartan / HCTZ (Benicar® HCT)	
trandolapril (Mavik®)	telmisartan (Micardis®)	
ramipril (Altace®)	telmisartan / HCTZ (Micardis® HCT)	
losartan (Cozaar®)		
losartan / HCTZ (Hyzaar®)		

Direct Renin inhibitors		
Tier-1	Tier-2	Tier-3
Tier-1 ACE Inhibitor + Diuretic	ARB + Diuretic	aliskiren (Tekturna®)
		aliskiren/HCTZ (Tekturna HCT®)
		aliskiren/valsartan (Valturna®)
		aliskiren/amlodipine (Tekamlo®)

Appendix E

Vote to Prior Authorize Silenor™ (doxepin)

Oklahoma Health Care Authority
March 2011

Current Prior Authorization Criteria for Hypnotics Medication PBPA Category

1. In order to receive a Tier 2 product (or a Tier 3 product if no Tier 2 products exists) a minimum trial of 30 days with at least two Tier 1 products (including zolpidem) should be attempted. Also, clinical documentation of attempts to correct any primary cause for insomnia should be provided.
2. In order to receive a Tier 3 product, all available Tier 2 products should be attempted for a minimum of 30 days each. All other applicable criteria should also be met.
3. FDA approved diagnosis.
4. No concurrent anxiolytic benzodiazepine therapy greater than TID dosing and no concurrent ADHD medications.
5. Approvals granted for 6 months.

All members under the age of 18 will require a petition for use of hypnotic medications.
Quantity limit of #30 per 30 apply for all medications in this category.

Recommendations

The College of Pharmacy recommends the placement of generic Ambien CR® in Tier 2 and Silenor™ in Tier 3 of the Hypnotics Medications PBPA Category.

Tier 1	Tier 2	Tier 3
Estazolam **(ProSom®)**	Zolpidem **(Ambien CR®)**	Eszopiclone **(Lunesta®)**
Temazepam **(Restoril®)**15 & 30 mg		Temazepam **(Restoril®)** 7.5 mg & 22.5mg
Flurazepam **(Dalmane®)**		Ramelteon **(Rozerem®)**
Triazolam **(Halcion®)**		Zolpidem† Oral Spray **(Zolpimist™)**
Zolpidem **(Ambien®)**		Zolpidem† SL Tabs **(Edular®)**
Saleplon **(Sonata®)**		Zolpidem† SL Tabs **(Intermezzo®)**
		Doxepin **(Silenor™)**

Mandatory generic plan applies.
+Requires special reason for use.

Appendix F

VOTE TO PRIOR AUTHORIZE XYREM® (SODIUM OXYBATE) AND KAPVAY® (CLONIDINE EXTENDED RELEASE)

Oklahoma HealthCare Authority
March 2011

RECOMMENDATIONS

The College recommends the addition of Kapvay® in Tier 2 and Xyrem® in Tier 3 of the ADHD/Narcolepsy PBPA category with a hard edit. In addition the College recommends changes to the current criteria in blue.

Tier 1	Tier 2	Tier 3
Amphetamine	Amphetamine	Amphetamine
Adderall®	Vyvanse®	Desoxyn®
Adderall XR®	Methylphenidate	Dexedrine®
Methylphenidate	Metadate ER®	Dexedrine Spansules®
Ritalin®	Metadate CD®	ProCentra™ Oral Solution
Methylin®	Ritalin LA®	Methylphenidate
Ritalin SR®	Non-Stimulant	Daytrana™ Patch
Concerta®	Intuniv®	Non-Stimulant
Focalin®	Kapvay®	Provigil®
Focalin XR®		Nuvigil®
Non-Stimulant		Xyrem®
Strattera®		

2011 Tiers based on Net Cost after Supplemental Rebates.
Mandatory Generic Plan Applies.
Current Tiers based on Supplemental Rebate Participation

For Tier 2 Products:

1. FDA approved diagnosis.
2. Trials of long acting medications from both the amphetamine and methylphenidate category, or a non-stimulant medication if a Tier 2 non-stimulant medication is requested, that did not yield adequate response.
   a. Trials should have been within the last 30-60 days.
   b. Dosed up to maximum recommended dose or provide information regarding side effects at higher dose.
   c. If trials are not in member's claim history, the pharmacy profile should be submitted or detailed information regarding dates and doses should be included along with the signature from the physician.
3. Concomitant use of stimulant and nonstimulant medicatons is approved only for members with severe disease who have tried multiple stimulant medications alone, titrated to maximum recommended dose, AND the non-stimulant medication alone, titrated to maximum recommended dose, that did not yield adequate response.

For Tier 3 Products:

1. FDA approved diagnosis
2. Trials with at least three lower tiered medications, each from different chemical categories, unless contraindicated, that did not yield adequate response.
   a. Trials should have been within the last 60-90 days.
   b. Dosed up to maximum recommended dose or provide information regarding side effects at higher dose.
   c. If trials are not in member's claim history, the pharmacy profile should be submitted or detailed information regarding dates and doses should be included along with the signature from the physician.
3. Concomitant use of stimulant and nonstimulant medicatons is approved only for members with severe disease who have tried multiple stimulant medications alone, titrated to maximum recommended dose, AND the non-stimulant medication alone, titrated to maximum recommended dose, that did not yield adequate response.

Additional Criteria:

1. Dose exceeding 1.5 times the FDA maximum is not covered.
2. Prior Authorization is required for all tiers for members greater than 20 years of age.
3. Use of Xyrem® requires recent trials with Tier 1 and Tier 2 stimulants from different chemical categories, and trials with both Provigil® and Nuvigil® within the past 6 months, unless contraindicated, that did not yield adequate results.
4. The diagnosis of obstructive sleep apnea requires concurrent treatment for the obstructive sleep apnea.
5. The diagnosis of shift work sleep disorder requires the member's work schedule to be included with the petition.

Appendix G

Annual Review of Osteoporosis Medications - Fiscal Year 2010 and 30 Day Notice to Prior Authorize Prolia ™ (Denosumab) and Atelvia™ (Risedronate sodium) Delayed Release

Oklahoma HealthCare Authority
March 2011

Current Prior Authorization Criteria

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

Mandatory Generic Plan Applies.
***Calcitonin and raloxifene are not included as Tier 1 trials.**
†Must be used at recommended doses in conjunction with Tier 1 bisphosphonate for trial to be accepted unless member has a rece nt laboratory result showing adequate Vitamin D or member is unable to tolerate calcium. OTC Calcium and Vitamin D are only covered for members with osteoporosis.

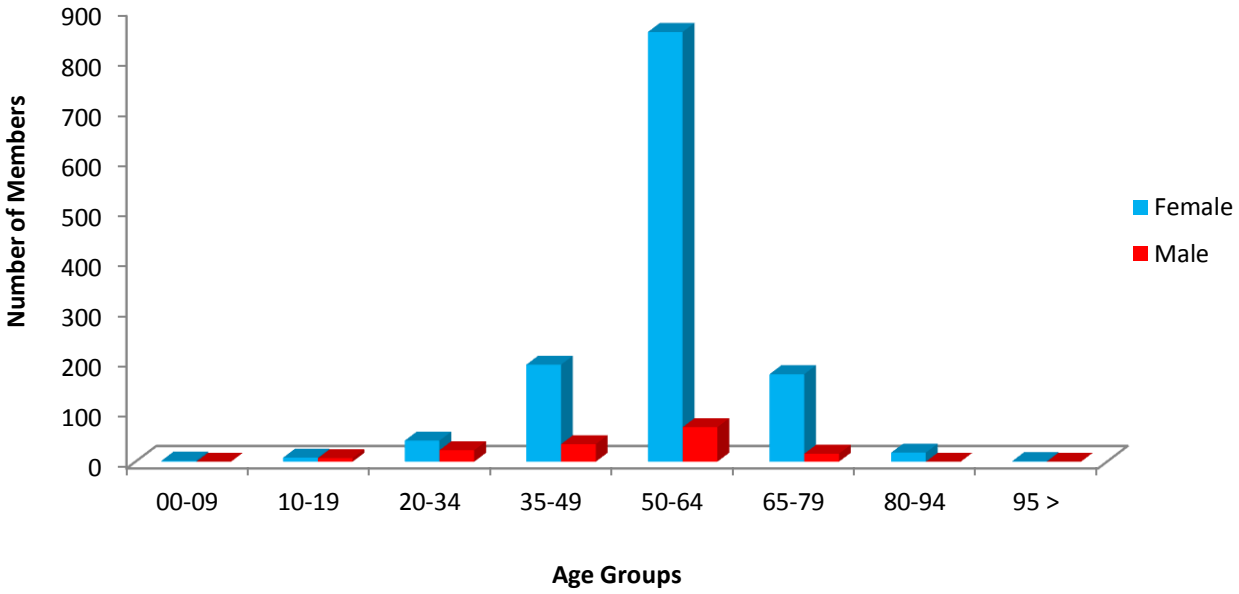
1. **Treatment failure with all lower tiered products, or**
2. **Contraindication to all lower tiered products, or**
3. **Allergic reaction to all lowered tiered products, or**
4. **Specific indication not covered by a lower tiered product.**
5. **No concomitant use of bisphosphonate therapy will be approved. No additional bisphosphonate may be approved for 365 days following zoledronic acid infusion.**
6. **Clinical Exceptions:**
   a. **Risedronate** may be approved for members with high risk for gastric side effects.
   b. **Zoledronic acid** may be approved for members with a diagnosis of Paget's disease or for osteoporosis if secondary diagnosis meets criteria below:
      i. Severe esophageal disease (e.g., ulcerations, strictures)
      ii. Inability to take anything by mouth
      iii. Inability to sit or stand for prolonged periods
      iv. Inability to take an oral bisphosphonate for other special medical circumstances that justify the method of administration
   c. **Teriparatide** may be used after a minimum 12 month trial with a bisphosphonate plus adequate calcium and vitamin D (unless contraindicated, intolerant, or allergic) and a BMD (T-score at or below -2.5) test within the last month.
7. **Quantity Limits apply based on FDA maximum doses.**

Utilization of Osteoporosis Medications

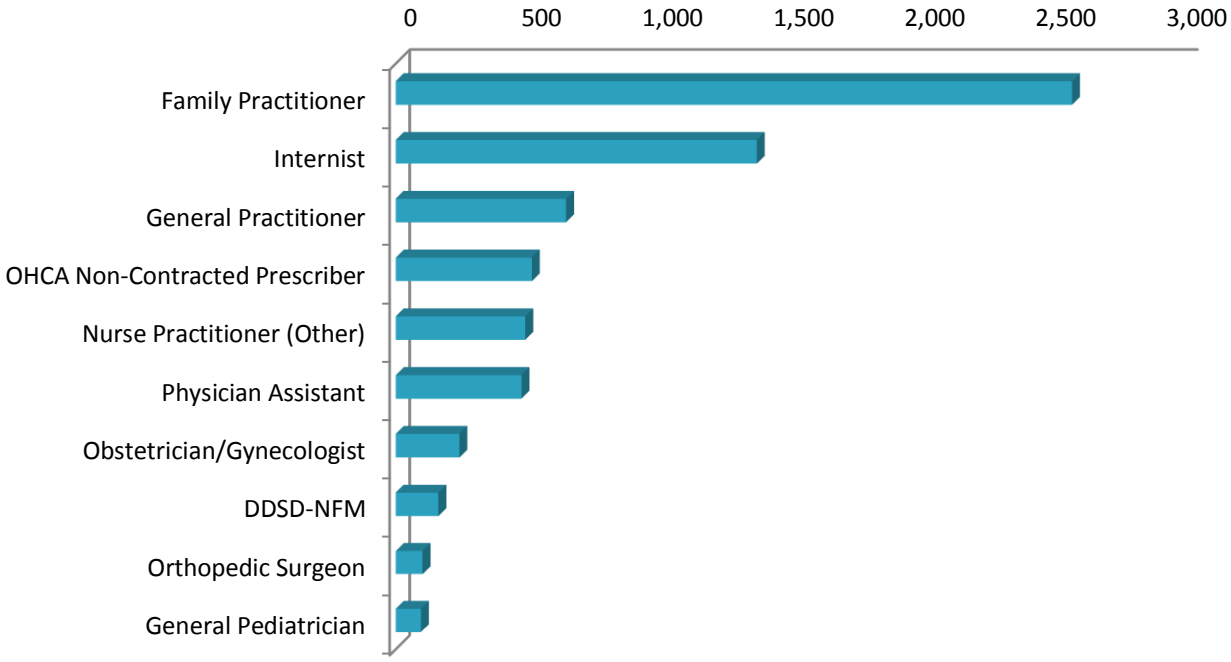
Comparison of Fiscal Years

Fiscal Year	Members	Claims	Cost	Cost/Claim	Perdiem	Units
2009	1,394	7,412	$614,097.08	$82.85	$2.66	78,208
2010	1,445	7,184	$451,940.60	$62.91	$2.03	87,402
% Change	**3.70%**	**-3.10%**	**-26.40%**	**-24.10%**	**-23.70%**	**11.80%**
Change	**51**	**-228**	**-$162,156.48**	**-$19.94**	**-$0.63**	**9,194**

Demographics of Members Utilizing Osteoporosis Medications: FY 2010



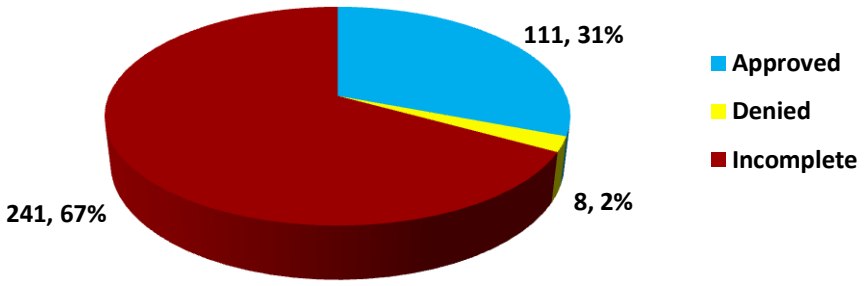
Top 10 Prescribers of Osteoporosis Medications by Number of Claims: FY 2010



Prior Authorization of Osteoporosis Medications

There were a total of 360 petitions submitted for this PBPA category during Fiscal Year 2010. The following chart shows the status of the submitted petitions.

Status of Petitions for Osteoporosis Medications: FY 2010



Market News and Update

- Prolia ™ (denosumab)- Approved by the FDA in June 2010 for the treatment of postmenopausal women with osteoporosis at high risk for fracture, defined as a history of osteoporotic facture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy.
  - Available in 60mg/ml single use prefilled syringes and 60mg/ml single use vials. Administered via subcutaneous injection in the upper arm, upper thigh, or the abdomen
  - Should be administered by a healthcare professional
  - All patients should receive calcium 1,000mg daily and at least 400IU vitamin D daily

- Atelvia™ (risedronate delayed release) - Approved by the FDA in October 2011 for the prevention and treatment of postmenopausal osteoporosis and glucocorticoid-induced osteoporosis (men & women), to increase bone mass in men with osteoporosis and the treatment of Paget's disease of bone.
  - It is a bisphosphonate and is a delayed release formulation of Actonel® (made by Warner Chilcott Company, LLC- who is also the maker of Actonel®)
  - Available in 35mg delayed-release tablets that can be taken immediately after breakfast, once a week
  - Patients should not lie down for 30 minutes after taking Atelvia™
  - EAC- $26.79, same as Actonel®
- Patent Expiration- patent for Actonel® (risedronate) is expected to expire around May 2012

- October 2010- The following information was added to the *Warnings and Precaution* section of the labels of all bisphosphonate drugs approved for the prevention or treatment of osteoporosis:- "Atypical subtrochanteric femur fractures are fractures in the bone just below the hip joint. Diaphyseal femur fractures occur in the long part of the thigh bone. These fractures are very uncommon and appear to account for less than 1% of all hip and femur fractures overall. Although it is not clear if

bisphosphonates are the cause, these unusual femur fractures have been predominantly reported in patients taking bisphosphonates." (See Attachment A for complete information regarding the FDA update).

Conclusion and Recommendations

The College of Pharmacy recommends continuing the current criteria for the Osteoporosis medications with the following additions :

1. Place Atelvia™ (risedronate sodium) delayed-release into tier-2 category and
2. Place Prolia™ (denosumab) into the tier-3 category of the Osteoporosis medication tier list.

Tier 1*	Tier 2	Tier 3
Alendronate (Fosamax®) Calcium + Vitamin D†	Alendronate + D (Fosamax®+D) Ibandronate (Boniva®) Risedronate (Actonel®) **Risedronate delayed release (Atelvia™)**	Zoledronic acid (Reclast®) Teriparatide (Forteo®) **Prolia ™ (Denosumab)**

***Branded products will require a brand name override. Calcitonin and raloxifene are not included as Tier 1 trials.**
†Must be used at recommended doses in conjunction with Tier 1 bisphosphonate for trial to be accepted unless member has a recent laboratory result showing adequate Vitamin D or member is unable to tolerate calcium. OTC Calcium and Vitamin D are only covered for members with osteoporosis.

Utilization Details of Osteoporosis Medications: Fiscal Year 2010

BRAND NAME	CLAIMS	MEMBERS	COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ DAY	% COST
ACTONEL TAB 150MG	182	42	$18,850.36	0.03	4.33	$3.45	4.17%
ACTONEL TAB 30MG	8	4	$2,843.73	0.27	2	$6.61	0.63%
ACTONEL TAB 35MG	785	109	$76,777.48	0.14	7.2	$3.46	16.99%
ACTONEL TAB 5MG	49	8	$3,530.11	0.68	6.13	$2.43	0.78%
ACTONEL WITH TAB CALCIUM	7	2	$678.17	0.99	3.5	$3.43	0.15%
ALENDRONATE TAB 10MG	154	34	$1,742.63	0.97	4.53	$0.38	0.39%
ALENDRONATE TAB 35MG	388	98	$2,493.47	0.14	3.96	$0.23	0.55%
ALENDRONATE TAB 40MG	7	3	$571.62	0.77	2.33	$2.77	0.13%
ALENDRONATE TAB 5MG	55	13	$612.54	1	4.23	$0.38	0.14%
ALENDRONATE TAB 70MG	3,960	916	$29,514.68	0.14	4.32	$0.26	6.53%
FOSAMAX + D TAB 70-2800	48	20	$4,171.16	0.14	2.4	$3.08	0.92%
FOSAMAX + D TAB 70-5600	13	6	$1,148.00	0.14	2.17	$3.15	0.25%
FOSAMAX SOL	191	24	$17,428.32	10.54	7.96	$3.24	3.86%
BONIVA KIT 3MG/3ML	4	1	$1,480.28	0.01	4	$4.11	0.33%
BONIVA TAB 150MG	1,217	243	$187,347.82	0.03	5.01	$3.66	41.45%
FORTEO SOL 600/2.4	115	22	$101,565.67	0.08	5.23	$30.61	22.47%
RECLAST INJ 5/100ML	1	1	$1,184.56	0.27	1	$3.25	0.26%
TOTAL	**7,184**	**1,445***	**$451,940.60**	**0.39**	**4.97**	**$2.03**	**100.00**

***Total number of unduplicated members**

PRODUCT DETAILS OF PROLIA™ (DENOSUMAB)

FDA-APPROVED IN JUNE 2010

INDICATIONS : For the treatment of postmenopausal women with osteoporosis at high risk for fracture, defined as a history of osteoporotic facture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy. In postmenopausal women with osteoporosis, Prolia™ reduces the incidence of vertebral, nonvertebral, and hip fractures.

DOSAGE FORMS :

- 1 mL of 60 mg/mL solution in a single-use prefilled syringe
- 1 mL of 60 mg/mL solution in a single-use vial

ADMINISTRATION:

- Administer Prolia™ via subcutaneous injection in the upper arm, the upper thigh, or the abdomen
- Prolia™ should be administered by a healthcare professional
- All patient should receive calcium 1000 mg daily and at least 400 IU vitamin D daily

CONTRAINDICATIONS:

- Hypocalcemia: Pre-existing hypocalcemia must be corrected prior to initiating therapy with Prolia™

SPECIAL POPULATIONS:

- **Pregnancy Category C**: Based on animal data, may cause fetal harm.
- **Nursing Mothers:** It is not known whether Prolia™ is excreted into human milk
- **Pediatric Use:** Not recommended. Safety and effectiveness have not been evaluated.
- **Geriatric Use:** No overall differences in safety or efficacy were observed in patients over the age of 65 and younger patients, but greater sensitivity of some older individuals cannot be ruled out.
- **Renal Impairment:** No dosage adjustment needed
- **Hepatic Impairment:** No clinical studies have been conducted to evaluate the effect of hepatic impairment on the pharmacokinetics of Prolia™

WARNINGS & PRECAUTIONS:

- **Hypocalcemia and Mineral Metabolism:** Hypocalcemia may be exacerbated by the use of Prolia™. Pre-existing hypocalcemia must be corrected before starting Prolia™ therapy. In patients predisposed to hypocalcemia and disturbances of mineral metabolism, clinical monitoring of calcium and mineral levels is highly recommended. Hypocalcemia following Prolia™ administration is a significant risk in patients with severe renal impairment or receiving dialysis. Instruct all patients with severe renal impairment about the symptoms of hypocalcemia and the importance of maintaining calcium levels with adequate calcium and vitamin D supplementation.
- **Serious Infections**: Serious skin infections, as well as infections of the abdomen, urinary tract, and ear were more frequent in patients treated with Prolia™. Endocarditis was also reported more frequently. Advise patients to seek prompt medical attention if they develop signs or symptoms of severe infection, including cellulitis
- **Dermatologic Adverse Reactions:** Epidermal and dermal adverse events such as dermatitis, exzema, and rashes occurred at a significantly higher rate in the Prolia™ group compared to placebo. Most of these events were not specific to the injection site.
- **Osteonecrosis of the Jaw:** Generally associated with tooth extraction and/or local infection with delayed healing. A routine oral exam should be performed by the prescriber prior to initiation of Prolia™ treatment. For patients requiring invasive dental procedures, clinical judgment of the treating physician

and/or oral surgeon should guide the management plan of each patient based on individual benefit-risk assessment

- **Suppression of Bone Turnover:** Treatment with Prolia™ resulted in significant suppression of bone remodeling as evidenced by marker of bone turnover and bone histomorphometry. The significance of these findings and effect of long-term treatment with Prolia™ are unknown.

ADVERSE REACTIONS (reported in ≥ 2% of patients treated):

- Anemia
- Angina pectoris
- Atrial fibrillation
- Vertigo
- Abdmonal pain upper
- Flatulence
- Gastroesophageal reflux disease
- Injection site reaction
- Infections
- Hypercholesterolemia
- Back pain
- Myalgia
- Musckoskeletal pain
- Pain in extremity
- Insomnia
- Sciatica
- Rash
- Pruritus

DRUG INTERACTIONS:

- No drug-drug interaction studies have been conducted with Prolia™

PATIENT INFORMATION:

The side effects and precautions of Prolia™ should be discussed with each patient. These side effects include hypocalcemia, serious infections, dermatologic reactions, and osteonecrosis of the jaw. The shot should be given 6 months from the date of the last injection.

REFERENCES

Prolia™ Label Information. Amgen, Inc. Available online at: http://pi.amgen.com/united_states/prolia/prolia_pi.pdf Last revised January 2011.

PRODUCT DETAILS OF ATELVIA™ (RISEDRONATE)

FDA-APPROVED IN OCTOBER 2010

INDICATIONS : the treatment of osteoporosis in postmenopausal women.

DOSAGE FORMS :

- 35 mg delayed release tablet

ADMINISTRATION:

- Should be taken in the morning immediately following breakfast
- Should be swallowed whole while the patient is in an upright position and with at least 4 ounces of plain water.
- Tablets should not be chewed, cut, or crushed.
- Patients should not lie down for 30 minutes after taking the medication
- Patients should receive supplemental calcium and vitamin D

CONTRAINDICATIONS:

- Abnormalities of the esophagus which delay esophageal emptying such as stricture or achalasia
- Inability to stand or sit upright for at least 30 minutes
- Hypocalcemia
- Known hypersensitivity to any component of this product

SPECIAL POPULATIONS:

- **Pregnancy Category C**
- **Nursing Mothers:** It is not known whether Atelvia™ is excreted into human milk
- **Pediatric Use:** Not indicated for pediatric use.
- **Geriatric Use:** No overall differences in safety or efficacy were observed in patients over the age of 65 and younger patients, but greater sensitivity of some older individuals cannot be ruled out.
- **Renal Impairment:** Atelvia™ is not recommended for use in patients with severe renal impairment (creatinine clearance <30 mL/min) because of lack of clinical experience. No dosage adjustment is necessary in patients with a creatinine clearance ≥30 mL/min.
- **Hepatic Impairment:** No clinical studies have been conducted to evaluate the effect of hepatic impairment on the pharmacokinetics of Atelvia™. However, it is unlikely dose adjustments are needed for hepatic dysfunction

WARNINGS & PRECAUTIONS:

- **Drug Products with the Same Ingredient:** Atelvia™ contains the same active ingredient found in Actonel®. A patient being treated with Actonel® should not receive Atelvia™.
- **Upper Gastrointestinal Adverse Effects:** Atelvia™, like other bisphosphonates administered orally, may cause local irritation of the upper gastrointestinal mucosa. Because of these possible irritant effects and a potential for worsening of the underlying disease, caution should be used when Atelvia™ is given to patients with active upper gastrointestinal problems.
- **Mineral Metabolism:** Hypocalcemia and other disturbances of bone and mineral metabolism should be effectively treated before starting Atelvia™ therapy. Adequate intake of calcium and vitamin D is important in all patients.
- **Ostenonecrosis of the Jaw:** Generally associated with tooth extraction and/or local infection with delayed healing. A routine oral exam should be performed by the prescriber prior to initiation of Prolia™

treatment. For patients requiring invasive dental procedures, clinical judgment of the treating physician and/or oral surgeon should guide the management plan of each patient based on individual benefit-risk assessment

- **Musculoskeletal Pain:** In postmarketing experience, there have been reports of severe and occasionally incapacitating bone, joint, and/or muscle pain in patients taking bisphosphonates.
- **Renal Impairment:** Atelvia™ is not recommended for use in patients with severe renal impairment (creatinine clearance <30 mL/min) because of lack of clinical experience.
- **Laboratory Test Interactions:** Bisphosphonates are known to interfere with the use of bone-imaging agents. Specific studies with Atelvia™ have not been performed.

ADVERSE REACTIONS (reported in ≥ 2% of patients treated):

- Gastrointestinal Disorders
- Influenza
- Bronchitis
- Upper respiratory tract infection
- Arthralgia
- Back Pain
- Pain in extremity
- Musculoskeletal pain
- Dizziness
- Headache

DRUG INTERACTIONS:

- Calcium Supplements/Antacids
- Hormone therapy
- Asprin/Nonsteroidal Anti-Inflammatory Drugs
- Histamine 2 (H_2) Blockers, Proton Pump Inhibitors

PATIENT INFORMATION:

- Patients should not take Atelvia™ if they have abnormalities of the esophagus which delay esophageal emptying such as stricture or achalasia, inability to stand or sit upright for at least 30 minutes, hypocalcemia, or known hypersensitivity to any component of this product.
- Atelvia™ and Actonel® contain the same active ingredient. Patients receiving Actonel® should not receive Atelvia ™
- To facilitate delivery to the stomach, and thus reduce the potential for esophageal irritation, patients should take Atelvia™ in the morning, while in an upright position (sitting or standing) with at least 4 ounces of plain water immediately following breakfast. Atelvia ™should not be taken before breakfast. Patients must swallow Atelvia™ tablets whole. Patients should not chew, cut, or crush the tablet because of a potential for oropharyngeal irritation, and because the tablet coating is an important part of the delayed-release formulation. Patients should not lie down for 30 minutes after taking the medication.
- Severe irritation of the upper gastrointestinal (GI) mucosa can occur. Caution should be used in patients with active upper GI disease. Patients should be instructed that if they develop symptoms of esophageal disease (such as difficulty or pain upon swallowing, retrosternal pain or severe persistent or worsening heartburn) they should consult their physician before continuing Atelvia™.
- Patients should receive supplemental calcium and vitamin D.
- Osteonecrosis of the jaw has been reported rarely. Severe bone, joint, or muscle pain may occur. Consider discontinuing use if severe symptoms develop. Atelvia™ is not recommended for use in

patients with severe renal impairment because of lack of clinical experience.

- Most common adverse reactions while taking Atelvia™ include diarrhea, influenza, arthralgia, back pain, and abdominal pain. Hypersensitivity reactions (angioedema, generalized rash, bullous skin reactions), and eye inflammation (iritis, uveitis) have been reported rarely.
- Weight-bearing exercise should be considered along with the modification of certain behavioral factors, such as excessive cigarette smoking, and/or alcohol consumption, if these factors exist.
- Patients should be instructed that if they miss a dose of Atelvia™ 35 mg once-a-week, they should take 1 tablet on the morning after they remember and return to taking 1 tablet once-a-week, as originally scheduled on their chosen day. Patients should not take 2 tablets on the same day.
- Patients should be reminded to give all of their healthcare providers an accurate medication history. Instruct patients to tell all of their healthcare providers that they are taking Atelvia™.

REFERENCES

Atelvia™ Label Information. Norwich Pharmaceuticals, Inc. Available online at: http://www.wcrx.com/pdfs/pi/pi_atelvia.pdf Last revised January 2011.

Attachment A

FDA Drug Safety Communication: Safety update for osteoporosis drugs, bisphosphonates, and atypical fractures

Safety Announcement

[10-13-2010] The U.S. Food and Drug Administration (FDA) is updating the public regarding information previously communicated describing the risk of atypical fractures of the thigh, known as subtrochanteric and diaphyseal femur fractures, in patients who take bisphosphonates for osteoporosis. This information will be added to the *Warnings and Precautions* section of the labels of all bisphosphonate drugs approved for the prevention or treatment of osteoporosis.

Bisphosphonates are a class of medicines that can be effective at preventing or slowing the loss of bone mass (osteoporosis) in postmenopausal women, thus reducing the risk of common osteoporotic bone fracture. Osteoporotic fractures can result in pain, hospitalization, and surgery.

Atypical subtrochanteric femur fractures are fractures in the bone just below the hip joint. Diaphyseal femur fractures occur in the long part of the thigh bone. These fractures are very uncommon and appear to account for less than 1% of all hip and femur fractures overall. Although it is not clear if bisphosphonates are the cause, these unusual femur fractures have been predominantly reported in patients taking bisphosphonates.

The bisphosphonates affected by this notice are only those approved to treat osteoporosis, including Fosamax, Fosamax Plus D, Actonel, Actonel with Calcium, Boniva, Atelvia, and Reclast[1] (and their generic products).

This notice does not affect bisphosphonate drugs that only are used to treat Paget's disease or high blood calcium levels due to cancer (i.e., Didronel, Zometa, Skelid, and their generic products).

Although the optimal duration of bisphosphonate use for osteoporosis is unknown, these atypical fractures may be related to long-term term bisphosphonate use. FDA will require a new Limitations of Use statement in the *Indications and Usage* section of the labels for these drugs. This statement will describe the uncertainty of the optimal duration of use of bisphosphonates for the treatment and/or prevention of osteoporosis.

A Medication Guide will also be required to be given to patients when they pick up their bisphosphonate prescription. This Medication Guide will describe the symptoms of atypical femur fracture and recommend that patients notify their healthcare professional if they develop symptoms.

These actions are part of an ongoing safety review of bisphosphonate use and the occurrence of atypical subtrochanteric and diaphyseal femur fractures, as previously announced in a Drug Safety Communication on March 10, 2010[2].

Additional Information for Patients

If you currently take a bisphosphonate, you should:

- Continue to take your medication unless you are told to stop by your healthcare professional.
- Talk to your healthcare professional if you develop new hip or thigh pain (commonly described as dull or aching pain), or have any concerns with your medications.
- Report any side effects with your bisphosphonate medication to FDA's MedWatch program using the information at the bottom of the page in the "Contact Us" box.

Additional Information for Healthcare Professionals

FDA recommends that healthcare professionals should:

- Be aware of the possible risk of atypical subtrochanteric and diaphyseal femur fractures in patients taking bisphosphonates.
- Continue to follow the recommendations in the drug label when prescribing bisphosphonates.
- Discuss the known benefits and potential risks of using bisphosphonates with patients.
- Evaluate any patient who presents with new thigh or groin pain to rule out a femoral fracture.
- Discontinue potent antiresorptive medications (including bisphosphonates) in patients who have evidence of a femoral shaft fracture.
- Consider periodic reevaluation of the need for continued bisphosphonate therapy, particularly in patients who have been treated for over 5 years.
- Report any adverse events with the use of bisphosphonates to FDA's MedWatch program using the information at the bottom of the page in the "Contact Us" box.

Any information provided to MedWatch should be as detailed as possible and include information concerning fracture location/configuration, magnitude of trauma, fracture details (complete or incomplete, bilateral, or comminuted), presence and duration of prodromal thigh or groin pain, duration of bisphosphonate use, relevant medical history, and concomitant use of other medications.

Data Summary

FDA has reviewed all available data, including data summarized in the American Society for Bone and Mineral Research (ASBMR) Task Force report regarding bisphosphonates and atypical subtrochanteric and diaphyseal femur fractures[1], released on September 14, 2010. These atypical femur fractures can occur anywhere in the femoral shaft, from just below the lesser trochanter to above the supracondylar flare, and are transverse or short oblique in orientation without evidence of comminution. The fractures can be complete (involving both cortices) or incomplete (involving the lateral cortex only), and may be bilateral. Many patients report prodromal pain in the affected area, usually presenting as dull, aching thigh pain, weeks to months before a complete fracture occurs. The exact incidence of atypical femoral fractures is unknown but appears to account for less than one percent of hip and femoral fractures overall. Therefore, atypical fractures are very uncommon. Although atypical femoral fractures have been predominantly reported in patients taking bisphosphonates, they have also been reported in patients who have not taken bisphosphonates.

The optimal duration of bisphosphonate treatment for osteoporosis is unknown. Bisphosphonate medications approved for the prevention and/or treatment of osteoporosis have clinical trial data supporting fracture reduction efficacy through at least 3 years of treatment and, in some cases, through 5 years. The FDA is continuing its evaluation of data supporting the safety and effectiveness of long term use (greater than 3 to 5 years) of bisphosphonates for the treatment and prevention of osteoporosis and will provide additional guidance at the completion of our review.

In summary, FDA is continuing its ongoing safety review of bisphosphonate use and the occurrence of atypical femur fractures. As of this notice, the FDA is notifying patients and healthcare professionals of new *Warnings and Precautions* information that is being added regarding this risk to the labels of all bisphosphonate products approved for the prevention or treatment of osteoporosis. A new Limitations of Use statement will describe the uncertainty of the optimal duration of use of bisphosphonates for the treatment and/or prevention of osteoporosis. In addition, the FDA will require that a Medication Guide be included with all bisphosphonate medications approved for osteoporosis indications to better inform patients of the risk for atypical femur fracture.

References:

1. Shane E, Burr D, Ebeling PR, et al. Atypical subtrochanteric and diaphyseal femoral fractures: Report of a task force of the American Society for Bone and Mineral Research [published online ahead of print]. *Journal of Bone and Mineral Research*. 2010; http://onlinelibrary.wiley.com/doi/10.1002/jbmr.253/pdf[3]. Accessed September 17, 2010.

Appendix H

Drug Utilization Review of Topical Steroids

Oklahoma HealthCare Authority

March 2011

Review of Topical Steroids

Many different topical steroid products are currently on the market in varying potencies and formulations. When utilizing these products, it is important to consider the diagnosis as well as steroid potency, delivery vehicle, frequency of administration, duration of treatment, and adverse effects. Topical steroids are generally used for their anti-inflammatory properties, although no single agent has been proven to have the best benefit-to-risk ratio.

Many conditions are commonly treated with topical steroids, summarized in the chart below:

High potency-steroids	Medium-potency steroids	Low-potency steroids
Alopecia areata	Anal inflammation (severe)	Dermatitis (diaper)
Atopic dermatitis (resistant)	Asteatotic eczema	Dermatitis (eyelids)
Discoid lupus	Atopic dermatitis	Dermatitis (face)
Hyperkeratotic eczema	Lichen sclerosus (vulva)	Intertrigo
Lichen planus	Nummular eczema	Perianal inflammation
Lichen sclerosus (skin)	Scabies (after scabicide)	
Lichen simplex chronicus	Seborrheic dermatitis	
Nummular eczema	Severe dermatitis	
Poison ivy (severe)	Severe intertrigo (short-term)	
Psoriasis	Stasis dermatitis	
Severe hand eczema		

Steroids may differ in potency based on the vehicle in which they are formulated. Ointments provide more lubrication and occlusion than other preparations, and therefore are useful for dry or thick hyperkeratotic lesions. Their occlusive nature improves steroid absorption, but their greasiness may result in poor patient satisfaction and compliance. Ointments should not be used in hairy areas, and may cause maceration and folliculitis if used on intertriginous areas such as the groin, gluteal cleft, and axilla.

Creams are mixes of water suspended in oil, which provides good lubricating qualities along with the ability to vanish into the skin. Creams are generally less potent than ointments of the same medication, and they often contain preservatives which can cause irritation, stinging, and allergic reaction. They can be used in intertriginous areas, but do not provide the occlusive effects of the ointments.

Lotions and gels are the least greasy and occlusive of all topical steroid vehicles. Lotions contain alcohol for a drying effect, and are useful for hairy areas, with fast penetration and little residue. Gels have a jelly-like consistency and are beneficial for exudative types of inflammation like poison ivy. Gels dry quickly and can be applied on the scalp or other hairy areas and do not cause matting.

Foams, mousses, and shampoos are also effective vehicles for application to the scalp. They are easy to apply and spread, but are usually more expensive.

There are seven groups of topical steroid potency, ranging from ultra high (group I) to low (group VII). Low potency steroids are the safest for long-term use, on the face or areas of the body with thinner

skin, and on children. High and ultra-high potency steroids should not be used on the face, groin, axilla, or under occlusion, except in rare situations and for short durations.

Topical Steroid Potency					
Ultra high (I)	High (II)	Med/high (III)	Medium (IV,V)	Low (VII)	Least (VII)
Augmented betamethasone dipropionate 0.05% (G, O)	Amcinonide 0.1% (O)	Amcinonide 0.1% (C)	Betamethasone valerate (C, L, F)	Alclometasone dipropionate 0.05%	Hydrocortisone 1%, 2.5%
Clobetasol propionate 0.05%	Augmented betamethasone dipropionate 0.05% (L, C)	Betamethasone dipropionate 0.05% (C)	Desoximetasone 0.05% (C)	Desonide 0.05%	
Diflorasone diacetate 0.05% (O)	Betamethasone dipropionate 0.05% (O)	Fluticasone propionate 0.005% (O)	Fluocinolone acetonide 0.025% (C, O)	Fluocinolone 0.01%	
Fluocinonide 0.1%	Desoximetasone 0.25% (C, O, G-0.05%)	Triamcinolone acetonide 0.5%	Fluticasone propionate 0.05% (C)	Hydrocortisone butyrate 0.1%	
Flurandrenolide 4 mcg per m2	Diflorasone diacetate 0.05% (C)		Hydrocortisone butyrate 0.1%		
Halobetasol propionate 0.05%	Fluocinonide 0.05%		Hydrocortisone probutate 0.1%		
	Halcinonide 0.1%		Hydrocortisone valerate 0.2%		
			Mometasone furoate 0.1%		
			Triamcinolone acetonide 0.025%		
			Triamcinolone acetonide 0.1%		
O=ointment, C=cream, G=gel, F=foam. If not specified, includes all formulations.					

Once or twice daily application is recommended for most topical steroid products. More frequent administration does not provide better results. Chronic application of these medications can induce tolerance and tachyphylaxis. Ultra-high potency steroids should not be used for more than three weeks continuously. If longer durations are required, the steroid should be gradually tapered to avoid rebound symptoms, and treatment may be resumed after a week of no steroid use. The amount of steroid product applied to a particular area may be quantified by using the fingertip unit method. A fingertip unit is the amount that can be squeezed from the fingertip to the first crease of the finger. The following chart shows approximate amounts required:

Area of the body	Fingertip units for one application	Product weight for one application (g)	Product weight required to treat BID for 1 week (g)
Face and neck	2.5	1.25	17.5
Trunk (front OR back)	7	3.5	49
One arm	3	1.5	21
One hand (one side)	0.5	0.25	3.5
One leg	6	3	42
One foot	2	1	14
*One fingertip unit = approximately 0.5 g			

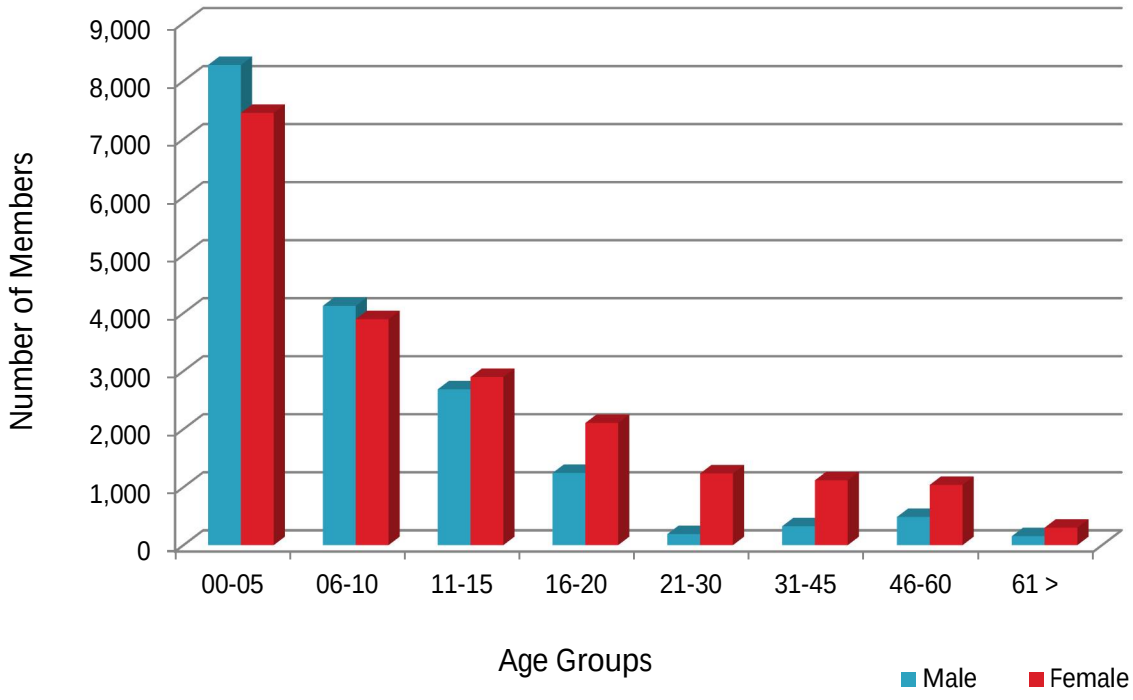
The use of topical steroid products may cause adverse effects. All topical steroids can commonly induce skin atrophy, but use of higher potency steroids, occlusion, thinner skin, and older age may increase the risk. Resolution often occurs after discontinuing use, but it may take months and the effects are sometimes permanent. Other side effects include telangiectasia, striae, rosacea, skin infections, hypopigmentation, and contact dermatitis. The ultra high- and high- potency steroids can be absorbed enough to cause systemic side effects such as hypothalamic-pituitary-adrenal suppression, glaucoma, septic necrosis of the femoral head, hyperglycemia, and hypertension.

Utilization of Topical Steroids

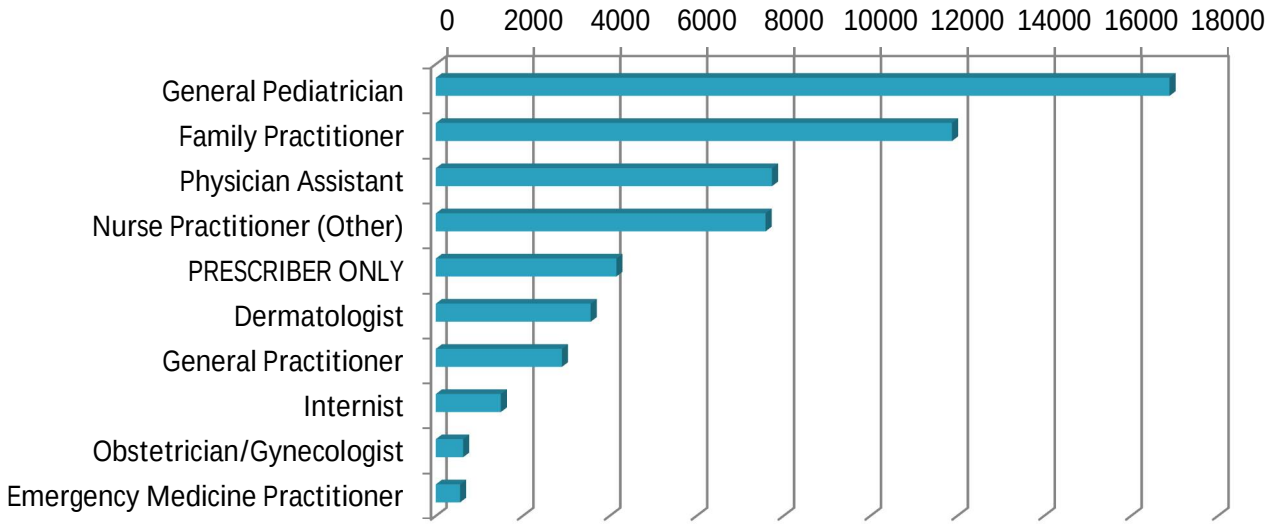
Comparison of Fiscal Years

Fiscal Year	Members	Claims	Cost	Cost/Claim	Perdiem	Units	Days
2009	33,711	53,860	$1,718,898.03	$31.91	$2.27	3,557,849	756,151
2010	37,623	59,933	$1,878,407.37	$31.34	$2.14	4,232,420	878,346
Percent Change	11.6%	11.3%	9.3%	-1.8%	-5.7%	19.0%	16.2%
Change	3,912	6,073	$159,509.34	-$0.57	-$0.13	674,571	122,195

Demographics of Members Utilizing Topical Steroids: FY 2010



Prescribers of Topical Steroids by Number of Claims: FY 2010



Market News and Updates

- Patent Expirations:
  - Locoid Lipocream®- June 2014
  - Luxiq®- May 2017
  - Clobex®- September 2017
  - Cutivate®- October 2019
  - Verdeso®- September 2019
  - Desonate® gel- August 2020

- The American Academy of Dermatology published evidence-based guidelines in 2009 for the management of psoriasis and psoriatic arthritis.

Conclusion and Recommendations

The College of Pharmacy recommends a Product Based Prior Authorization for the category of Topical Steroids with the following criteria:

1. Tier 1 products are covered with no authorization necessary.
2. Tier 2 authorization requires:
   a. Documented trials of at least two Tier 1 topical steroids in the past 30 days.
   b. In addition, when the same medication is available in Tier 1, a clinical reason must be provided for using a special dosage form in Tier 2 (foams, shampoos, sprays, kits, etc.).

Topical Steroids	
Tier 1	Tier 2
Ultra high to high potency	
Amcinonide (O,L)	Augmented betamethasone dipropionate (Diprolene® O, L)
Augmented betamethasone dipropionate (Diprolene AF® G,C)	Clobetasol propionate (Clobex® L,Sh,Spr; Olux® F)
Betamethasone dipropionate (Diprosone® O)	Desoximetasone (Topicort® C,O,G)
Clobetasol propionate (Temovate® C,G,O,So)	Diflorasone diacetate (Apexicon® O, Apexicon E® C)
Fluocinonide (Lidex® G,C,O)	Flurandrenolide tape (Cordran®)
Halobetasol dipropionate (Ultravate® C,O)	Halcinonide (Halog® C,O)
Med/high to medium potency	
Betamethasone dipropionate (Betanate® C)	Amcinonide (Cyclocort® C)
Betamethasone valerate (Beta-Val® C,O,L)	Betamethasone dipropionate/calcipotriene (Taclonex® O, Sus, Spr)
Fluocinolone acetonide (Synalar® C,O)	Betamethasone valerate (Luxiq® F)
Fluocinonide emollient (Lidex E® C)	Desoximetasone (Topicort LP ® O,G)
Fluticasone propionate (Cutivate® C,O)	Fluticasone propionate (Cutivate® L)
Hydrocortisone valerate 0.2% C	Hydrocortisone butyrate (Locoid® O,C, L; Locoid Lipo C)
Mometasone furoate (Elocon® O,C,L)	Hydrocortisone probutate (Pandel® C)
Triamcinolone acetonide (Kenalog® C,O,L)	Hydrocortisone valerate (Westcort® C,O)
	Prednicarbate (Dermatop® O,C)
	Triamcinolone acetonide (Kenalog® Spr)
Low potency	
Desonide (LoKara® C,O,L)	Alclometasone dipropionate (Aclovate® C,O)
Fluocinolone acetonide (So, C; Derma-Smooth®; Derma-Smooth FS® oil)	Coclortolone pivalate (Cloderm®, Vanos® C)
Hydrocortisone acetate 2.5% (C,O,L)	Desonide (Desonate® G, Verdeso® F)
	Desonide/emollient (Desowyn® kit C,O)
	Fluocinolone acetonide (Capex® Sh)
	Hydrocortisone acetate 2%/aloe (Nucort®, L)
	Hydrocortisone/lidocaine (LidaMantle HC® C)
	Hydrocortisone/urea (U-Cort® C)
C=cream, O=ointment, L=lotion, G=gel, F=foam, So=solution, Sh=shampoo, Spr=Spray, Sus=suspension	

Utilization Details of Topical Steroids: Fiscal Year 2010

BRAND NAME	CLAIMS	UNITS	DAYS	MEMBERS	COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ CLAIM	PERCENT COST
ALCLOMETASON CRE 0.05%	168	6,810	2,330	133	$5,833.10	2.92	1.26	$34.72	0.31%
ALCLOMETASON OIN 0.05%	58	2,160	767	35	$1,667.38	2.82	1.66	$28.75	0.09%
AMCINONIDE CRE 0.1%	26	1,710	401	18	$1,180.74	4.26	1.44	$45.41	0.06%
AMCINONIDE LOT 0.1%	1	60	30	1	$35.33	2	1	$35.33	0.00%
AMCINONIDE OIN 0.1%	15	960	370	12	$625.95	2.59	1.25	$41.73	0.03%
BETAMETH DIP CRE 0.05%	778	35,045	11,398	607	$6,758.01	3.07	1.28	$8.69	0.36%
BETAMETH DIP LOT 0.05%	56	3,360	735	37	$620.40	4.57	1.51	$11.08	0.03%
BETAMETH DIP OIN 0.05%	486	22,315	6,950	293	$5,822.59	3.21	1.66	$11.98	0.31%
AUG BETAMET CRE 0.05%	411	16,980	6,710	333	$8,789.69	2.53	1.23	$21.39	0.47%
AUG BETAMET GEL 0.05%	10	245	160	9	$229.85	1.53	1.11	$22.99	0.01%
AUG BETAMET LOT 0.05%	35	2,370	713	27	$2,135.24	3.32	1.3	$61.01	0.11%
AUG BETAMET OIN 0.05%	249	10,620	3,114	159	$8,712.45	3.41	1.57	$34.99	0.46%
BETAMETH VAL CRE 0.1%	766	29,859	11,963	564	$5,453.25	2.5	1.36	$7.12	0.29%
BETA-VAL CRE 0.1%	158	6,877	2,068	122	$1,462.17	3.33	1.3	$9.25	0.08%
LUXIQ AER 0.12%	243	20,500	5,128	159	$54,898.25	4	1.53	$225.92	2.92%
BETAMETH VAL LOT 0.1%	67	4,140	1,172	59	$629.62	3.53	1.14	$9.40	0.03%
BETA-VAL LOT 0.1%	18	1,080	324	15	$211.41	3.33	1.2	$11.75	0.01%
BETAMETH VAL OIN 0.1%	234	8,371	3,733	185	$1,793.62	2.24	1.26	$7.67	0.10%
CLOBEX SPR 0.05%	37	3,759	708	22	$12,529.15	5.31	1.68	$338.63	0.67%
CLOBETASOL SOL 0.05%	355	19,775	6,184	183	$5,712.17	3.2	1.94	$16.09	0.30%
CLOBETASOL CRE 0.05%	577	29,149	8,465	399	$7,246.56	3.44	1.45	$12.56	0.39%
CLOBETASOL AER 0.05%	6	550	119	3	$864.85	4.62	2	$144.14	0.05%
CLOBETASOL GEL 0.05%	20	1,395	438	15	$603.47	3.18	1.33	$30.17	0.03%
CLOBEX LOT 0.05%	60	5,026	1,212	28	$16,791.63	4.15	2.14	$279.86	0.89%
CLOBETASOL OIN 0.05%	520	23,775	8,121	334	$6,282.22	2.93	1.56	$12.08	0.33%
CLOBEX SHA 0.05%	66	7,788	1,312	39	$19,249.96	5.94	1.69	$291.67	1.02%
CLOBETASOL E CRE 0.05%	60	3,510	945	42	$1,641.17	3.71	1.43	$27.35	0.09%
CLODERM CRE 0.1%	22	1,305	393	16	$2,974.46	3.32	1.38	$135.20	0.16%
CLODERM CRE 0.1% PMP	16	1,050	330	13	$2,937.69	3.18	1.23	$183.61	0.16%
DESONIDE CRE 0.05%	1,605	73,912	23,922	1,128	$23,254.85	3.09	1.42	$14.49	1.24%
VERDESO AER 0.05%	917	77,200	17,979	729	$213,824.51	4.29	1.26	$233.18	11.38%
DESONATE GEL 0.05%	197	12,240	3,468	152	$41,188.95	3.53	1.3	$209.08	2.19%
DESONIDE LOT 0.05%	554	50,935	10,126	367	$17,875.04	5.03	1.51	$32.27	0.95%
DESONIDE OIN 0.05%	1,194	64,562	18,005	721	$19,815.39	3.59	1.66	$16.60	1.05%
DESOWEN CRM KIT 0.05%	6	6	120	5	$1,114.58	0.05	1.2	$185.76	0.06%
DESOXIMETAS CRE 0.05%	349	13,840	4,790	294	$25,268.12	2.89	1.19	$72.40	1.35%
DESOXIMETAS CRE 0.25%	733	33,633	11,023	573	$58,018.86	3.05	1.28	$79.15	3.09%
DESOXIMETAS GEL 0.05%	91	4,995	1,707	72	$6,683.05	2.93	1.26	$73.44	0.36%
DESOXIMETAS OIN 0.25%	82	3,515	1,212	71	$7,326.90	2.9	1.15	$89.35	0.39%

BRAND NAME	CLAIMS	UNITS	DAYS	MEMBERS	COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/CLAIM	PERCENT COST
DIFLORASONE CRE 0.05%	15	630	282	8	$600.13	2.23	1.88	$40.01	0.03%
DIFLORASONE OIN 0.05%	10	570	185	8	$502.18	3.08	1.25	$50.22	0.03%
APEXICON E CRE 0.05%	9	330	119	4	$364.58	2.77	2.25	$40.51	0.02%
DERMA-SMOOTH OIL /FS SCLP	480	61,412	10,224	293	$20,303.76	6.01	1.64	$42.30	1.08%
DERMA-SMOOTH OIL /FS BODY	293	37,154	6,152	178	$12,092.84	6.04	1.65	$41.27	0.64%
FLUOCIN ACET SOL 0.01%	113	7,620	2,199	88	$1,297.97	3.47	1.28	$11.49	0.07%
FLUOCIN ACET CRE 0.01%	22	1,005	303	18	$331.04	3.32	1.22	$15.05	0.02%
FLUOCIN ACET CRE 0.025%	282	11,850	3,732	208	$4,714.00	3.18	1.36	$16.72	0.25%
FLUOCIN ACET OIN 0.025%	85	7,680	1,469	52	$1,635.67	5.23	1.63	$19.24	0.09%
CAPEX SHA 0.01%	30	3,598	555	22	$4,777.14	6.48	1.36	$159.24	0.25%
FLUOCINONIDE SOL 0.05%	252	15,305	4,786	166	$3,285.10	3.2	1.52	$13.04	0.17%
FLUOCINONIDE POW MICRONIZ	1	121	30	1	$63.59	4.03	1	$63.59	0.00%
FLUOCINONIDE CRE 0.05%	370	19,590	5,202	241	$3,310.87	3.77	1.54	$8.95	0.18%
VANOS CRE 0.1%	18	780	329	13	$2,952.30	2.37	1.38	$164.02	0.16%
FLUOCINONIDE GEL 0.05%	90	2,285	913	79	$1,282.42	2.5	1.14	$14.25	0.07%
FLUOCINONIDE OIN 0.05%	140	8,535	2,536	85	$2,907.31	3.37	1.65	$20.77	0.15%
FLUOCINONIDE CRE -E 0.05%	26	2,190	551	16	$515.74	3.97	1.63	$19.84	0.03%
FLUOCINONIDE CRE 0.05%	11	870	256	5	$208.76	3.4	2.2	$18.98	0.01%
CORDRAN 80X3 TAP 4MCG/CM	12	12	235	7	$1,050.96	0.05	1.71	$87.58	0.06%
CORDRAN 24X3 TAP 4MCG/CM	6	7	83	6	$290.45	0.08	1	$48.41	0.02%
FLUTICASONE CRE 0.05%	696	29,344	10,321	511	$13,528.50	2.84	1.36	$19.44	0.72%
CUTIVATE LOT 0.05%	1,961	235,582	41,842	1,466	$664,122.35	5.63	1.34	$338.67	35.36%
FLUTICASONE OIN 0.005%	200	10,470	3,328	127	$4,105.64	3.15	1.57	$20.53	0.22%
HALOG CRE 0.1%	49	2,070	683	36	$4,467.61	3.03	1.36	$91.18	0.24%
HALOG OIN 0.1%	16	750	296	14	$1,588.16	2.53	1.14	$99.26	0.08%
HALOBETASOL CRE 0.05%	41	1,520	561	33	$784.17	2.71	1.24	$19.13	0.04%
HALOBETASOL OIN 0.05%	57	2,535	833	31	$1,431.79	3.04	1.84	$25.12	0.08%
HYDROCORT CRE 1%	761	25,030	8,877	654	$4,389.06	2.82	1.16	$5.77	0.23%
HYDROCORT CRE 2.5%	2,962	111,509	36,285	2,333	$23,636.74	3.07	1.27	$7.98	1.26%
HYDROCORT LOT 1%	3	354	57	3	$32.70	6.21	1	$10.90	0.00%
HYDROCORT LOT 2.5%	394	40,196	6,453	297	$9,328.50	6.23	1.33	$23.68	0.50%
HYDROCORT OIN 1%	99	4,388	1,141	87	$628.79	3.85	1.14	$6.35	0.03%
HYDROCORT OIN 2.5%	747	34,106	9,403	531	$7,042.32	3.63	1.41	$9.43	0.37%
HYDROCORT POW	23	4,935	479	14	$221.21	10.3	1.64	$9.62	0.01%
HYDROCORT AC POW	4	996	70	4	$55.73	14.23	1	$13.93	0.00%
HYDROCORT AC POW MICRO	1	0	6	1	$3.17	0.03	1	$3.17	0.00%
NUCORT LOT 2%	212	13,142	3,521	168	$13,982.70	3.73	1.26	$65.96	0.74%
HC VALERATE CRE 0.2%	1,467	56,909	19,399	1,131	$23,387.57	2.93	1.3	$15.94	1.25%
HC VALERATE OIN 0.2%	270	9,990	3,399	226	$8,999.28	2.94	1.19	$33.33	0.48%

BRAND NAME	CLAIMS	UNITS	DAYS	MEMBERS	COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/CLAIM	PERCENT COST
PANDEL CRE 0.1%	12	405	146	6	$1,330.51	2.77	2	$110.88	0.07%
HC BUTYRATE SOL 0.1%	31	1,780	517	22	$505.34	3.44	1.41	$16.30	0.03%
HC BUTYRATE CRE 0.1%	312	11,851	4,316	225	$12,185.65	2.75	1.39	$39.06	0.65%
LOCOID CRE 0.1%	7	450	65	5	$454.99	6.92	1.4	$65.00	0.02%
LOCOID LOT 0.1%	7	531	130	5	$1,715.68	4.08	1.4	$245.10	0.09%
HC BUTYRATE OIN 0.1%	74	2,385	998	52	$1,260.57	2.39	1.42	$17.03	0.07%
LOCOID LIPO CRE 0.1%	377	17,326	5,859	288	$73,714.93	2.96	1.31	$195.53	3.92%
PEDIADERM HC KIT	4	4	90	2	$449.30	0.04	2	$112.33	0.02%
MOMETASONE SOL 0.1%	93	5,565	1,737	75	$1,808.41	3.2	1.24	$19.45	0.10%
MOMETASONE CRE 0.1%	2,253	83,466	32,052	1,603	$45,933.56	2.6	1.41	$20.39	2.45%
MOMETASONE OIN 0.1%	475	18,541	6,841	330	$11,736.42	2.71	1.44	$24.71	0.62%
PREDNICARBAT CRE 0.1%	147	7,395	2,358	96	$6,702.31	3.14	1.53	$45.59	0.36%
PREDNICARBAT OIN 0.1%	38	1,935	478	27	$1,711.26	4.05	1.41	$45.03	0.09%
TRIAMCINOLON POW ACETONID	50	12,223	1,316	35	$973.03	9.29	1.43	$19.46	0.05%
KENALOG AER SPRAY	74	5,552	1,209	58	$9,171.46	4.59	1.28	$123.94	0.49%
TRIAMCINOLON CRE 0.025%	5,196	325,834	70,702	3,990	$29,923.51	4.61	1.3	$5.76	1.59%
TRIAMCINOLON CRE 0.1%	18,368	1,596,642	253,488	13,537	$125,484.44	6.3	1.36	$6.83	6.68%
TRIAMCINOLON CRE 0.5%	2,182	71,758	27,263	1,638	$19,271.87	2.63	1.33	$8.83	1.03%
TRIAMCINOLON LOT 0.025%	341	22,260	5,140	275	$9,648.22	4.33	1.24	$28.29	0.51%
TRIAMCINOLON LOT 0.1%	491	32,371	7,352	378	$12,461.62	4.4	1.3	$25.38	0.66%
TRIAMCINOLON OIN 0.025%	1,077	85,691	15,650	801	$9,267.86	5.48	1.34	$8.61	0.49%
TRIAMCINOLON OIN 0.05%	8	1,948	185	7	$142.02	10.53	1.14	$17.75	0.01%
TRIAMCINOLON OIN 0.1%	4,442	539,375	68,983	3,090	$37,407.19	7.82	1.44	$8.42	1.99%
TRIAMCINOLON OIN 0.5%	309	11,385	4,249	239	$3,355.73	2.68	1.29	$10.86	0.18%
LIDOCAINE/HC CRE 3%-0.5%	6	283	67	4	$315.28	4.23	1.5	$52.55	0.02%
LIDAMANTLE CRE HC3-0.5%	4	340	72	3	$632.59	4.72	1.33	$158.15	0.03%
LIDOCAINE/HC LOT 3%-0.5%	1	177	5	1	$115.45	35.4	1	$115.45	0.01%
TACLONEX SUS SCALP	6	360	119	5	$2,610.12	3.03	1.2	$435.02	0.14%
TACLONEX OIN	36	2,200	706	20	$14,672.66	3.12	1.8	$407.57	0.78%
HC AC/ALOE GEL 2%	36	1,548	479	29	$1,081.73	3.23	1.24	$30.05	0.06%
U-CORT CRE 1%	2	85	34	2	$78.23	2.5	1	$39.12	0.00%
TOTALS:	59,933	4,232,418	878,346	37,623*	$1,878,407.37	4.82	1.59	$66.78	100.00%

*Total unduplicated number of members

Appendix I

Annual Review of Lamisil® Granules - Fiscal Year 2010

Oklahoma HealthCare Authority

March 2011

Current Prior Authorization Criteria

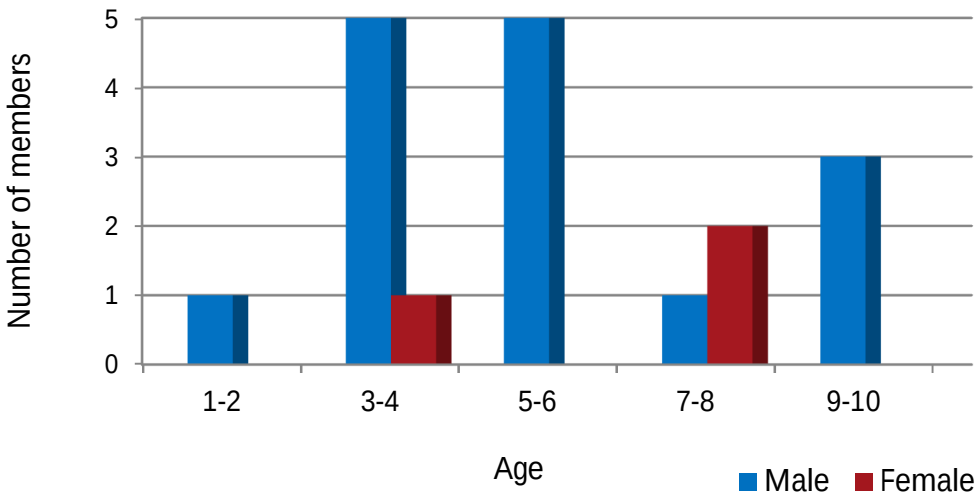
1. FDA approved indication of tinea capitis
2. No improvement after at least 3 weeks of therapy with griseofulvin
3. Intolerance or hypersensitivity to griseofulvin or penicillin
4. Member unable to swallow tablets

Utilization of Lamisil Granules

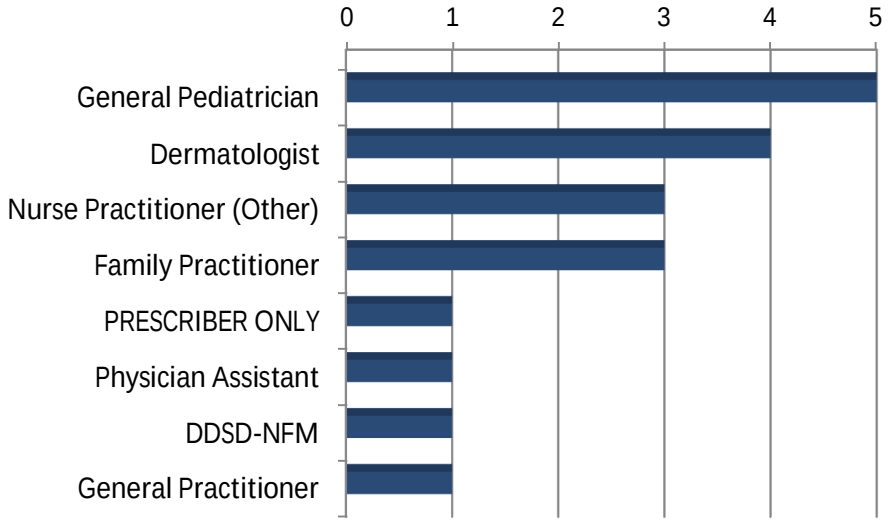
Comparison of Fiscal Years

Fiscal Year	Members	Claims	Cost	Cost/Claim	Perdiem	Units	Days
2009	49	72	$19,938.27	$276.92	$8.05	2,427	2,477
2010	18	19	$5,796.22	$305.06	$8.60	713	674
% Change	-63.30%	-73.60%	-70.90%	10.20%	6.80%	-70.60%	-72.80%
Change	-31	-53	-$14,142.05	$28.14	$0.55	-1,714	-1,803

Demographics of Members Utilizing Lamisil® Granules: FY 2010



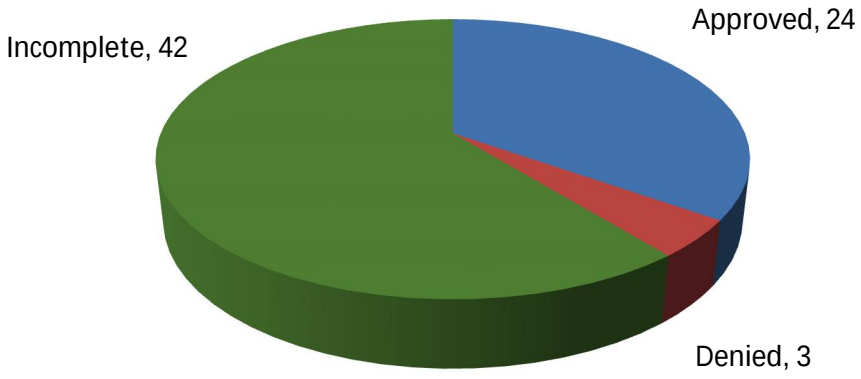
Prescribers of Lamisil® Granules by Number of Claims: FY 2010



Prior Authorization of Lamisil® Granules

There were a total of 69 petitions submitted for this drug during fiscal year 2010. The following chart shows the status of the submitted petitions.

Status of Petitions for Lamisil® Granules: FY 2010



Conclusion and Recommendations

The College of Pharmacy recommends the continuation of the Lamisil® granules prior authorization program.

Utilization Details of Lamisil® Granules: Fiscal Year 2010

Medication	Claims	Members	Units	Days	Units/ Day	Claims/ Member	% Cost
LAMISIL GRANULES 125MG	17	16	641	612	1.05	1.06	85.25%
LAMISIL GRANULES 187.5MG	2	2	72	62	1.16	1	14.75%
TOTALS	19	18*	713	674	1.06	1.06	100%

*Total number of unduplicated members

Appendix J

U.S. Food and Drug Administration

Drugs

FDA Drug Safety Communication: Prescription Acetaminophen Products to be Limited to 325 mg Per Dosage Unit; Boxed Warning Will Highlight Potential for Severe Liver Failure

Safety Announcement

[1-13-2011] The U.S. Food and Drug Administration (FDA) is asking drug manufacturers to limit the strength of acetaminophen in prescription drug products, which are predominantly combinations of acetaminophen and opioids. This action will limit the amount of acetaminophen in these products t 325 mg per tablet, capsule, or other dosage unit, making these products safer for patients.

In addition, a Boxed Warning highlighting the potential for severe liver injury and a Warning highlighting the potential for allergic reactions (e.g., swelling of the face, mouth, and throat, difficulty breathing, itching, or rash) are being added to the label of all prescription drug products that contain acetaminophen.

These actions will help to reduce the risk of severe liver injury and allergic reactions associated with acetaminophen.

Acetaminophen is widely and effectively used in both prescription and over-the-counter (OTC) products to reduce pain and fever. It is one of the most commonly-used drugs in the United States. Examples of prescription products that contain acetaminophen include hydrocodone with acetaminophen (Vicodin, Lortab), and oxycodone with acetaminophen (Tylox, Percocet).

OTC products containing acetaminophen (e.g., Tylenol) are not affected by this action. Information about the potential for liver injury is already required on the label for OTC products containing acetaminophen. FDA is continuing to evaluate ways to reduce the risk of acetaminophen related liver injury from OTC products. Additional safety measures relating to OTC acetaminophen products will be taken through separate action, such as a rulemaking as part of the ongoing OTC monograph proceeding for internal analgesic drug products.

Additional Information for Patients

- Acetaminophen-containing prescription products are safe and effective when used as directed, though all medications carry some risks.
- Do not stop taking your prescription pain medicine unless told to do so by your healthcare professional.
- Carefully read all labels for prescription and OTC medicines and ask the pharmacist if your prescription pain medicine contains acetaminophen.
- Do not take more than one product that contains acetaminophen at any given time.
- Do not take more of an acetaminophen-containing medicine than directed.
- Do not drink alcohol when taking medicines that contain acetaminophen.
- Stop taking your medication and seek medical help immediately if you:
  - Think you have taken more acetaminophen than directed or
  - Experience allergic reactions such as swelling of the face, mouth, and throat, difficulty breathing, itching, or rash.
- Report side effects to FDA's MedWatch program using the information in the "Contact Us" box at the bottom of the page.

Additional Information for Healthcare Professionals

The maximum amount of acetaminophen in a prescription tablet, capsule, or other dosage unit will be limited to 325 mg. However, the total number o tablets or capsules that may be prescribed and the time intervals at which they may be prescribed will not change as a result of the lower amount of acetaminophen. For example, for a product that previously contained 500 mg of acetaminophen with an opioid and was prescribed as 1-2 tablets every 4-6 hours, once reformulated to contain 325 mg of acetaminophen, the dosing instructions can remain unchanged.

- Advise patients not to exceed the acetaminophen maximum total daily dose (4 grams/day).
- Severe liver injury, including cases of acute liver failure resulting in liver transplant and death, has been reported with the use of acetaminophen.
- Educate patients about the importance of reading all prescription and OTC labels to ensure they are not taking multiple acetaminophen-containing products.
- Advise patients not to drink alcohol while taking acetaminophen-containing medications.
- Rare cases of anaphylaxis and other hypersensitivity reactions have occurred with the use of acetaminophen.
- Advise patients to seek medical help immediately if they have taken more acetaminophen than directed or experience swelling of the face, mouth, and throat, difficulty breathing, itching, and rash.
- Report adverse events to FDA's MedWatch program using the information in the "Contact Us" box at the bottom of the page.

Data Summary and Discussion

A number of studies have tried to answer the question of how common liver injury is in relation to the use of acetaminophen. Although many questions remain about the full scope of the problem, the following examples indicate what is known about the extent of liver failure cases reported in the medical literature and clearly indicates a reason for concern:

- From 1998 to 2003, acetaminophen was the leading cause of acute liver failure in the United States, with 48% of acetaminophen-related cases (131 of 275) associated with accidental overdose.[1]

- A 2007 Centers for Disease Control and Prevention (CDC) population-based report estimates that, nationally, there are 1600 cases of acute liver failure (ALF) each year (all causes). Acetaminophen-related ALF was the most common etiology.[2]
- Summarizing data from three different surveillance systems, there were an estimated 56,000 emergency room visits, 26,000 hospitalizations, and 458 deaths related to acetaminophen-associated overdoses per year during the 1990-1998 period.[3]
- In a study that combined data from 22 specialty medical centers in the United States, acetaminophen-related liver injury was the leading cause of ALF for the years 1998 through 2003.[1] This study also found that a high percentage of cases of liver injury due to acetaminophen were related to unintentional overdose, in which the patient mistakenly took too much acetaminophen. This finding was confirmed in a later study (2007).[2] Many other cases of acute liver injury are caused by intentional overdoses of acetaminophen (i.e., associated with self-harm).
- Across various studies, consumers were found to have taken more than the recommended dose when using an OTC product, a prescription product, or both. The Toxic Exposure Surveillance System (TESS), now named the National Poison Data System (NPDS), which captures data from calls to 61 poison control centers, provides additional data on acetaminophen overdose and serious injury. In 2005, TESS showed that calls about poisoning cases that resulted in major injury numbered 1,187 for OTC single-ingredient products, 653 for OTC combination products, and 1,470 for prescription-opioid combination products.[4]

The risk of liver injury associated with the use of acetaminophen was discussed at the Joint Meeting of the FDA Drug Safety and Risk Management Advisory Committee, Nonprescription Drugs Advisory Committee, and Anesthetic and Life Support Drugs Advisory Committee, held on June 29-30, 2009 (for complete safety reviews and background information[1] discussed at this meeting).

The Advisory Committee recommended a range of additional regulatory actions such as adding a boxed warning to prescription acetaminophen products, withdrawing prescription combination products from the market, or reducing the amount of acetaminophen in each dosage unit. FDA considered the Committee's advice for OTC products when deciding to limit the amount of acetaminophen per dosage unit in prescription products.

By limiting the maximum amount of acetaminophen in prescription products to 325 mg per dosage unit, patients will be less likely to overdose on acetaminophen if they mistakenly take too many doses of acetaminophen-containing products.

For more information on safety considerations for acetaminophen, visit the following link on the FDA web site: Acetaminophen Information[2]

List of Marketed Acetaminophen-Containing Prescription Products (products affected by the new dosage unit limits are in italics)

The label may not spell out the whole word or may have an abbreviation, such as "APAP, AC, Acetaminophn, Acetaminoph, Acetaminop, Acetamin or Acetam "

Brand Name	Generic Name	Dosage Form	Strength
No Current Brand Name	Acetaminophen; Aspirin; Codeine Phosphate	Capsule; Oral	150mg; 180mg; 30mg
No Current Brand Name	Acetaminophen; Caffeine; Dihydrocodeine Bitartrate	Capsule; Oral	356.4mg; 30mg; 16mg
No Current Brand Name	Acetaminophen; Caffeine; Dihydrocodeine Bitartrate	Tablet; Oral	712.8mg; 60mg; 32mg
No Current Brand Name	Acetaminophen; Codeine Phosphate	Solution; Oral	120mg/ 5mL; 12mg/ 5mL
No Current Brand Name	Acetaminophen; Codeine Phosphate	Tablet; Oral	300mg; 15mg
No Current Brand Name	Acetaminophen; Codeine Phosphate	Tablet; Oral	650mg; 30mg
No Current Brand Name	Acetaminophen; Codeine Phosphate	Tablet; Oral	650mg; 60mg
Capital and Codeine	Acetaminophen; Codeine Phosphate	Suspension; Oral	120mg/ 5mL; 12mg/ 5mL
Tylenol W/ Codeine No. 3	Acetaminophen; Codeine Phosphate	Tablet; Oral	300mg; 30mg
Tylenol W/ Codeine No. 4	Acetaminophen; Codeine Phosphate	Tablet; Oral	300mg; 60mg
No Current Brand Name	Acetaminophen; Butalbital; Caffeine	Tablet; Oral	500mg; 50mg; 40mg
Esgic-Plus	Acetaminophen; Butalbital; Caffeine	Tablet; Oral	500mg; 50mg; 40mg
No Current Brand Name	Acetaminophen; Butalbital; Caffeine	Capsule; Oral	500mg; 50mg; 40mg
Esgic-Plus	Acetaminophen; Butalbital; Caffeine	Capsule; Oral	500mg; 50mg; 40mg
No Current Brand Name	Acetaminophen; Butalbital; Caffeine	Tablet; Oral	325mg; 50mg; 40mg
Fioricet	Acetaminophen; Butalbital; Caffeine	Tablet; Oral	325mg; 50mg; 40mg
No Current Brand Name	Acetaminophen; Butalbital; Caffeine; Codeine Phosphate	Capsule; Oral	325mg; 50mg; 40mg; 30mg
Fioricet w/ codeine	Acetaminophen; Butalbital; Caffeine; Codeine Phosphate	Capsule; Oral	325mg; 50mg; 40mg; 30mg
Phrenilin with Caffeine and Codeine	Acetaminophen; Butalbital; Caffeine; Codeine Phosphate	Capsule; Oral	325mg; 50mg; 40mg; 30mg
Anexsia	Acetaminophen; Hydrocodone Bitartrate	Tablet; Oral	500mg; 5mg
Anexsia	Acetaminophen; Hydrocodone Bitartrate	Tablet; Oral	750mg; 10mg
Anexsia 5/ 325	Acetaminophen; Hydrocodone Bitartrate	Tablet; Oral	325mg; 5mg
Anexsia 7.5/ 325	Acetaminophen; Hydrocodone Bitartrate	Tablet; Oral	325mg; 7.5mg
Anexsia 7.5/ 650	Acetaminophen; Hydrocodone Bitartrate	Tablet; Oral	650mg; 7.5mg
Co-Gesic	Acetaminophen; Hydrocodone Bitartrate	Tablet; Oral	500mg; 5mg
No Current Brand Name	Acetaminophen; Hydrocodone Bitartrate	Capsule; Oral	500mg; 5mg
No Current Brand Name	Acetaminophen; Hydrocodone Bitartrate	Solution; Oral	325mg/ 15mL; 10mg/ 15mL
No Current Brand Name	Acetaminophen; Hydrocodone Bitartrate	Solution; Oral	325mg/ 15mL; 7.5mg/ 15mL
No Current Brand Name	Acetaminophen; Hydrocodone Bitartrate	Solution; Oral	500mg/ 15mL; 10mg/ 15mL
No Current Brand Name	Acetaminophen; Hydrocodone Bitartrate	Solution; Oral	500mg/ 15mL; 7.5mg/ 15mL
No Current Brand Name	Acetaminophen; Hydrocodone Bitartrate	Tablet; Oral	300mg; 10mg
No Current Brand Name	Acetaminophen; Hydrocodone Bitartrate	Tablet; Oral	300mg; 5mg
No Current Brand Name	Acetaminophen; Hydrocodone Bitartrate	Tablet; Oral	300mg; 7.5mg
No Current Brand Name	Acetaminophen; Hydrocodone Bitartrate	Tablet; Oral	500mg; 2.5mg
No Current Brand Name	Acetaminophen; Hydrocodone Bitartrate	Tablet; Oral	500mg; 7.5mg
No Current Brand Name	Acetaminophen; Hydrocodone Bitartrate	Tablet; Oral	650mg; 10mg
Lortab	Acetaminophen; Hydrocodone Bitartrate	Tablet; Oral	500mg; 10mg
Lortab	Acetaminophen; Hydrocodone Bitartrate	Tablet; Oral	500mg; 5mg
Norco	Acetaminophen; Hydrocodone Bitartrate	Tablet; Oral	325mg; 10mg
Norco	Acetaminophen; Hydrocodone Bitartrate	Tablet; Oral	325mg; 5mg
Norco	Acetaminophen; Hydrocodone Bitartrate	Tablet; Oral	325mg; 7.5mg
Vicodin	Acetaminophen; Hydrocodone Bitartrate	Tablet; Oral	500mg; 5mg
Vicodin Es	Acetaminophen; Hydrocodone Bitartrate	Tablet; Oral	750mg; 7.5mg

Vicodin Hp	Acetaminophen; Hydrocodone Bitartrate	Tablet; Oral	660mg; 10mg
Zydone	Acetaminophen; Hydrocodone Bitartrate	Tablet; Oral	400mg; 10mg
Zydone	Acetaminophen; Hydrocodone Bitartrate	Tablet; Oral	400mg; 5mg
Zydone	Acetaminophen; Hydrocodone Bitartrate	Tablet; Oral	400mg; 7.5mg
Oxycet	Acetaminophen; Oxycodone Hydrochloride	Tablet; Oral	325mg; 5mg
No Current Brand Name	Acetaminophen; Oxycodone Hydrochloride	Tablet; Oral	300mg; 10mg
No Current Brand Name	Acetaminophen; Oxycodone Hydrochloride	Tablet; Oral	300mg; 2.5mg
No Current Brand Name	Acetaminophen; Oxycodone Hydrochloride	Tablet; Oral	300mg; 5mg
No Current Brand Name	Acetaminophen; Oxycodone Hydrochloride	Tablet; Oral	300mg; 7.5mg
No Current Brand Name	Acetaminophen; Oxycodone Hydrochloride	Tablet; Oral	400mg; 10mg
No Current Brand Name	Acetaminophen; Oxycodone Hydrochloride	Tablet; Oral	400mg; 2.5mg
No Current Brand Name	Acetaminophen; Oxycodone Hydrochloride	Tablet; Oral	400mg; 5mg
No Current Brand Name	Acetaminophen; Oxycodone Hydrochloride	Tablet; Oral	400mg; 7.5mg
No Current Brand Name	Acetaminophen; Oxycodone Hydrochloride	Tablet; Oral	500mg; 10mg
Percocet	Acetaminophen; Oxycodone Hydrochloride	Tablet; Oral	325mg; 10mg
Percocet	Acetaminophen; Oxycodone Hydrochloride	Tablet; Oral	325mg; 2.5mg
Percocet	Acetaminophen; Oxycodone Hydrochloride	Tablet; Oral	325mg; 5mg
Percocet	Acetaminophen; Oxycodone Hydrochloride	Tablet; Oral	325mg; 7.5mg
Percocet	Acetaminophen; Oxycodone Hydrochloride	Tablet; Oral	500mg; 7.5mg
Percocet	Acetaminophen; Oxycodone Hydrochloride	Tablet; Oral	650mg; 10mg
Roxicet	Acetaminophen; Oxycodone Hydrochloride	Solution; Oral	325mg/ 5mL; 5mg/ 5mL
Roxicet	Acetaminophen; Oxycodone Hydrochloride	Tablet; Oral	325mg; 5mg
Roxicet 5/ 500	Acetaminophen; Oxycodone Hydrochloride	Tablet; Oral	500mg; 5mg
Roxilox	Acetaminophen; Oxycodone Hydrochloride	Capsule; Oral	500mg; 5mg
Tylox	Acetaminophen; Oxycodone Hydrochloride	Capsule; Oral	500mg; 5mg
Talacen	Acetaminophen; Pentazocine Hydrochloride	Tablet; Oral	650mg; EQ 25mg BASE
Ultracet	Acetaminophen; Tramadol Hydrochloride	Tablet; Oral	325mg; 37.5mg

References

1. Larson AM, Polson J, Fontana RJ, Davern TJ, Lalani E, Hynan LS, et al. Acute Liver Failure Study Group (ALFSG). Acetaminophen-induced acute liver failure: results of a United States multicenter, prospective study. Hepatology. 2005; 42:1364-72.
2. Bower WA, Johns M, Margolis HS, Williams IT, Bell BP. Population-based surveillance for acute liver failure. Am J Gastroenterol. 2007;102:2459-63.
3. Nourjah P, Ahmad SR, Karwoski C, Willy M. Estimates of acetaminophen (Paracetamol)-associated overdoses in the United States. Pharmacoepidemiol Drug Saf. 2006;15:398-405.
4. Lai MW, Klein-Schwartz W, Rodgers GC, Abrams JY, Haber DA, Bronstein AC, Wruk KM. 2005 Annual Report of the American Association of Poison Control Centers' national poisoning and exposure database. Clin Toxicol. 2006;44:803-932.

Related Information

- Acetaminophen Information [3]
- FDA limits acetaminophen in prescription combination products; requires liver toxicity warnings [4]
  Press Release - 1/13/2011
- Questions and Answers about Prescription Acetaminophen Products to be Limited to 325 mg Per Dosage Unit [5]
  1/13/2011
- List of Marketed Acetaminophen-Containing Prescription Products [6]
- 2009 Meeting Materials, Drug Safety and Risk Management Advisory Committee [7]
- FDA Drug Safety Podcast for Healthcare Professionals: Prescription Acetaminophen Products to be Limited to 325 mg Per Dosage Unit; Boxed Warning Will Highlight Potential for Severe Liver Failure [8]

Contact Us

- **Report a Serious Problem**
- 1-800-332-1088
- 1-800-FDA-0178 Fax

MedWatch Online [9]

Regular Mail: Use postage-paid FDA Form 3500 [10]

Mail to: MedWatch 5600 Fishers Lane

Rockville , MD 20857

Links on this page:

1. /AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DrugSafetyandRiskManagementAdvisoryCommittee/ucm126014.htm
2. /Drugs/DrugSafety/InformationbyDrugClass/ucm165107.htm
3. /Drugs/DrugSafety/InformationbyDrugClass/ucm165107.htm
4. /NewsEvents/Newsroom/PressAnnouncements/ucm239894.htm

5. /Drugs/DrugSafety/InformationbyDrugClass/ucm239871.htm
6. /Drugs/DrugSafety/InformationbyDrugClass/ucm239874.htm
7. /AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DrugSafetyandRiskManagementAdvisoryCommittee/ucm126014.htm
8. /Drugs/DrugSafety/DrugSafetyPodcasts/ucm240513.htm
9. https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm
10. http://www.fda.gov/downloads/Safety/MedWatch/DownloadForms/UCM082725.pdf

U.S. Food and Drug Administration

Drugs

Questions and Answers about Prescription Acetaminophen Products to be Limited to 325 mg Per Dosage Unit

On January 13, 2011, FDA announced that it is asking manufacturers of prescription acetaminophen combination products to limit the maximum amount of acetaminophen in these products to 325 mg per tablet, capsule, or other dosage unit. FDA believes that limiting the amount of acetaminophen per tablet, capsule, or other dosage unit in prescription products will reduce the risk of severe liver injury from acetaminophen overdosing, an adverse event that can lead to liver failure, liver transplant, and death.

Q1. What is acetaminophen?

Acetaminophen is a pain medication and fever reducer that is widely available and used in both prescription and over-the-counter (OTC) products. Acetaminophen is generally considered safe and effective when used as directed.

Acetaminophen in prescription products is always found in combination with other active ingredients, including opioid pain relievers. These are known as prescription acetaminophen combination products. Examples of prescription acetaminophen combination products include hydrocodone with acetaminophen (Vicodin, Lortab), and oxycodone with acetaminophen (Tylox, Percocet). Examples of other prescription acetaminophen combination products may be found in the List of Marketed Acetaminophen-Containing Prescription Products[1].

Q2. Why is FDA limiting the maximum strength of acetaminophen in prescription products?

FDA continues to receive reports of severe liver injury associated with the use of acetaminophen-containing products. The greatest risk for severe liver injury happens when people take more than the prescribed dose of acetaminophen, take more than one acetaminophen-containing product at the same time, or drink alcohol while taking acetaminophen. Severe liver injury can lead to liver failure, liver transplant, and death.

By limiting the maximum amount of acetaminophen in prescription products to 325 mg per tablet, capsule, or other dosage unit, patients will be less likely to overdose on acetaminophen if they mistakenly take too many doses of acetaminophen-containing products.

Q3. Will limiting the maximum amount of acetaminophen in prescription products alter the pain reducing effects of these drugs?

All prescription products containing acetaminophen also contain an additional pain medicine (usually an opioid). There are no data that indicate that taking more than 325 mg of acetaminophen per dosage unit provides more pain relief.

Under the new dosage limit, healthcare professionals can direct patients to take 1 or 2 tablets, capsules or other dosage units of a prescription product containing 325 mg of acetaminophen up to 6 times a day (12 dosage units) and still not exceed the maximum daily dose of acetaminophen (4000 mg).

Q4. Will the new dosage limit affect the dosing directions for prescription acetaminophen combination products?

The new dosage limit will not affect other aspects of prescribing of prescription acetaminophen combination products. The total number of tablets, capsules, or other dosage units that may be prescribed and the time intervals at which they may be prescribed need not change as a result of the lower amount of acetaminophen per dosage unit.

For example, if a healthcare professional previously prescribed 1 or 2 tablets of a prescription acetaminophen combination product every 4 to 6 hours, these dosing instructions will not change. A prescription drug containing 325 mg of acetaminophen prescribed at a maximum dosage of 2 tablets every 4 hours will add up to a total daily dose of 3900 mg (3.9 grams), which is less than the 4000 mg recommended maximum daily dose of acetaminophen.

Q5. How else is FDA communicating the risk of severe liver injury associated with acetaminophen to healthcare professionals?

To communicate the risk of severe liver injury associated with acetaminophen to healthcare professionals, FDA is requiring a new Boxed Warning to be added to the label of all prescription drug products that contain acetaminophen. This Boxed Warning will describe the risk of severe liver injury. A Boxed Warning is FDA's strongest warning in drug labels.

The Agency will also continue to work with healthcare professional organizations to help ensure that healthcare professionals are aware of the risk of severe liver injury associated with the use of acetaminophen.

Q6. When will the new limit on the amount of acetaminophen per dosage unit in prescription drug products take effect?

Drug companies will have three years from the date of publication of the Federal Register Notice (January 14, 2011) to limit the amount of acetaminophen in their prescription drug products to 325 mg per dosage unit (see the Federal Register Notice[2] Docket number FDA-2011-N-0021-0001).

Q7. How will the new limit on the amount of acetaminophen per dosage unit affect availability of prescription acetaminophen combination products?

Many prescription combination acetaminophen products are currently available in multiple strengths, including 325 mg, in the United States. Some of these products contain up to 750 mg of acetaminophen per tablet, capsule, or other dosage unit. To comply with the new requirement, companies that market drug products containing higher strengths of acetaminophen will need to limit the amount of acetaminophen to 325 mg per dosage unit or they may choose to withdraw the drug products.

FDA does not predict that this regulatory action will affect patient healthcare or the options available to patients for the management of their pain.

Q8. Are there other safety issues regarding prescription acetaminophen that FDA is communicating at this time?

FDA is also aware of rare cases of severe allergic reactions (e.g., swelling of the face, mouth, and throat, difficulty breathing, itching, or rash) that have occurred with the use of acetaminophen. FDA has asked companies to add a new Warning about the risk of allergic reactions, including anaphylaxis, to the label of all prescription acetaminophen-containing products.

Q9. Is there any additional information that healthcare professionals need to tell their patients?

Healthcare professionals should advise patients to continue taking their prescription pain medicine as directed. There is no immediate danger to patients who take prescription acetaminophen combination products. The risk of liver injury primarily occurs when patients take multiple products containing acetaminophen at one time and exceed the current maximum dose of 4000 mg within a 24-hour period.

Healthcare professionals should educate patients about how to properly use acetaminophen to avoid liver injury:

- Advise patients not to take more than the prescribed dose of an acetaminophen-containing medication.
- Advise patients not to take more than one product that contains acetaminophen.

- Advise patients to read all prescription and OTC labels to ensure they are not taking multiple acetaminophen-containing products accidentally. A commonly used OTC acetaminophen pain reliever is the brand-name Tylenol. Acetaminophen is also found in many other OTC medicines, such as cough and cold medicines, and sinus medicines. Examples of these OTC medicines include NyQuil, Vicks, Coricidin, etc.
- Advise patients not to drink alcohol while taking acetaminophen-containing medications.

Healthcare professionals should also advise patients to seek medical help immediately if they have taken more acetaminophen than directed or experience swelling of the face, mouth, and throat, difficulty breathing, itching, and rash after taking acetaminophen.

Q10. Has FDA consulted with outside experts about the safety of acetaminophen products?

The risk of liver injury associated with the use of acetaminophen was discussed at the Joint Meeting of the FDA Drug Safety and Risk Management Advisory Committee, Nonprescription Drugs Advisory Committee, and Anesthetic and Life Support Drugs Advisory Committee, held on June 29-30, 2009 (for complete safety reviews and background information[3] discussed at this meeting).

The Advisory Committee recommended a range of additional regulatory actions such as adding a boxed warning to prescription acetaminophen products, withdrawing prescription combination products from the market, or reducing the amount of acetaminophen in each dosage unit. FDA considered the Committee's advice for OTC products when deciding to limit the amount of acetaminophen per dosage unit in prescription products.

Q11. Does this action limit the amount of acetaminophen in OTC acetaminophen products such as Tylenol?

No. OTC acetaminophen products such as Tylenol are not affected by the new 325 mg limit at this time.

Q12. Will there be changes to the dosing of acetaminophen products marketed OTC?

No, not at this time.

FDA is currently working to address the recommendations of the Advisory Committee with regard to OTC acetaminophen products. Additional safety measures relating to OTC monograph products will be taken through separate action, such as a rulemaking as part of the ongoing OTC monograph proceeding for internal analgesic drug products.

Related Information

- FDA Drug Safety Communication: Prescription Acetaminophen Products to be Limited to 325 mg Per Dosage Unit; Boxed Warning Will Highlight Potential for Severe Liver Failure[4]
  1/13/2011
- List of Marketed Acetaminophen-Containing Prescription Products[5]
- FDA limits acetaminophen in prescription combination products; requires liver toxicity warnings[6]
  Press Release - 1/13/2011
- 2009 Meeting Materials, Drug Safety and Risk Management Advisory Committee[7]
- Acetaminophen Information[8]

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2. /RegulatoryInformation/Dockets/FR/default.htm
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4. /Drugs/DrugSafety/ucm239821.htm
5. /Drugs/DrugSafety/InformationbyDrugClass/ucm239874.htm
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7. /AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DrugSafetyandRiskManagementAdvisoryCommittee/ucm126014.htm
8. /Drugs/DrugSafety/InformationbyDrugClass/ucm165107.htm

U.S. Food and Drug Administration

News & Events

FDA PRESS RELEASE

For Immediate Release: Jan 7, 2011
Media Inquiries: Shelly Burgess, 301-796-4651, shelly.burgess@fda.hhs.gov
Consumer Inquiries: 888-INFO-FDA

FDA approves opioid analgesic to help cancer patients manage pain
Enrollment in REMS program required for health care professionals

The U.S. Food and Drug Administration today approved Abstral (fentanyl) transmucosal tablets to manage breakthrough pain for adults with cancer. Fentanyl immediate-release transmucosal medications are administered on the soft surfaces of the mouth (inside of the cheek, gums, tongue), or the nasal passages or throat where they dissolve and are absorbed.

"This is an important step for patients with cancer pain to have options for the treatment of their breakthrough pain," said John Jenkins, M.D., director of FDA's Office of New Drugs in the Center for Drug Evaluation and Research.

Abstral is indicated for the management of breakthrough pain in patients with cancer, ages 18 years and older, who already use opioid pain medication around the clock and who need and are able to safely use high doses of an additional opioid medicine. Breakthrough pain is pain that comes on suddenly for short periods of time and is not alleviated by a patient's normal pain management plan. These patients are considered opioid tolerant because of their current opioid medication use. Only health care professionals skilled in the use of Schedule II opioids to treat pain should prescribe this drug product.

Abstral is available only through a Risk Evaluation and Mitigation Strategy (REMS) program, which is intended to minimize the risk of misuse, abuse, addiction and overdose. Under this program, pharmacies, distributors, and health care professionals who prescribe to outpatients are required to enroll in the program to prescribe, dispense and distribute this product. FDA has standardized key components of the REMS program to facilitate the adoption of a single shared system. These components include the REMS document, the Patient-Prescriber Agreement, and the enrollment form. These components can be used by all sponsors of immediate release transmucosal fentanyl products to develop individual REMS programs such as the program approved for Abstral. FDA has also directed the sponsors of this class of products to work together on a single shared system to implement the REMS.

"This approval is also a significant step toward reducing the burden on the health care system of implementing REMS programs," added Dr. Jenkins. "When fully implemented, FDA expects that prescribers, pharmacies, and distributors of all immediate release transmucosal fentanyl products will be able to use standardized materials and a single shared system to implement the REMS."

The safety of Abstral was evaluated in 311 opioid-tolerant cancer patients with breakthrough pain. Two hundred and seventy of these patients were treated in multiple-dose studies. The duration of therapy for patients in multiple-dose studies ranged from 1-405 days with an average duration of 131 days and with 44 patients treated for at least 12 months.

Common adverse reactions include nausea, constipation, drowsiness and headache. Serious adverse events, including deaths, have been reported in patients with other immediate-release transmucosal fentanyl products. The deaths occurred as a result of improper patient selection and/or improper dosing.

Consumers and health care professionals are encouraged to report adverse side effects or medication errors from the use of Abstral to the FDA's MedWatch Adverse Event Reporting program at www.fda.gov/MedWatch[1] or by calling 800-332-1088.

Abstral is manufactured by ProStraken Inc., based in Bedminster, N.J.

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U.S. Food and Drug Administration

News & Events

FDA NEWS RELEASE

For Immediate Release: March 1, 2011
Media Inquiries: Morgan Liscinsky, 301-796-0397, morgan.liscinsky@fda.hhs.gov
Consumer Inquiries: 888-INFO-FDA

FDA approves new drug to treat chronic obstructive pulmonary disease

Editor's note: Daliresp has been approved as the trade name for roflumilast.

The U.S. Food and Drug Administration approved roflumilast, a pill taken daily to decrease the frequency of flare-ups (exacerbations) or worsening of symptoms from severe chronic obstructive pulmonary disease (COPD).

COPD is a serious lung disease that makes breathing difficult. Symptoms can include breathlessness, chronic cough and excessive phlegm. An exacerbation can last up to several weeks and result in lung function decline, increased risk of death, and may be associated with severe anxiety.

Cigarette smoking is the leading cause of COPD, according to the National Heart, Lung, and Blood Institute. COPD is the fourth leading cause of death in the United States.

Roflumilast, a new drug class for the treatment of COPD, is an inhibitor of an enzyme called phosphodiesterase type 4 (PDE-4). It is indicated for people with severe COPD to treat the symptoms of cough and excess mucus linked to bronchitis. Roflumilast is not intended to treat another form of COPD which involves primary emphysema.

"COPD is a serious disease that gets worse over time," said Curtis Rosebraugh, M.D., M.P.H., director of the Office of Drug Evaluation II in the FDA's Center for Drug Evaluation and Research. "New treatment options that reduce frequency of flare-ups or exacerbations are important in helping patient with COPD associated with chronic bronchitis and a history of exacerbations in managing this debilitating disease."

The safety and effectiveness of roflumilast was demonstrated in two Phase 3 clinical studies that included more than 1,500 patients ages 40 and older who received roflumilast. Those treated had a history of COPD associated with chronic bronchitis and had experienced an exacerbation of the disease during the 12 months prior to beginning treatment.

The FDA approved roflumilast with a medication guide informing patients of the potential risks of mental health problems, including changes in mood, thinking, or behavior, as well as unexplained weight loss.

Roflumilast should not be used to treat sudden breathing problems (acute bronchospam), and is not recommended for people younger than 18 years. The most common side effects reported by those receiving roflumilast included diarrhea, nausea, headache, insomnia, back pain, decreased appetite, and dizziness.

Roflumilast is marketed by St. Louis-based Forest Pharmaceuticals, a subsidiary of Forest Laboratories.

For more information:

- National Heart, Lung, and Blood Institute: Chronic Obstructive Pulmonary Disease [1]

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U.S. Food and Drug Administration

News & Events

FDA NEWS RELEASE

For Immediate Release: February 25, 2011
Media Inquiries: Sandy Walsh, 301-796-4669, sandy.walsh@fda.hhs.gov
Consumer Inquiries: 888-INFO-FDA

FDA approves Edarbi to treat high blood pressure

The U.S. Food and Drug Administration today approved Edarbi tablets (azilsartan medoxomil) to treat high blood pressure (hypertension) in adults.

Data from clinical studies showed Edarbi to be more effective in lowering 24-hour blood pressure compared with two other FDA-approved hypertension drugs, Diovan (valsartan) and Benicar (olmesartan).

"High blood pressure is often called the 'silent killer' because it usually has no symptoms until it causes damage to the body, "said Norman Stockbridge, M.D., Ph.D., director of the Division of Cardiovascular and Renal Drug Products in the FDA's Center for Drug Evaluation and Research. "High blood pressure remains inadequately controlled in many people diagnosed with the condition, so having a variety of treatment options is important. "

Edarbi will be available in 80 milligram and 40 mg doses, with the recommended dose set at 80 mg once daily. The 40 mg dose will be available for patients who are treated with high-dose diuretics taken to reduce salt in the body.

Blood pressure is the force of blood pushing against the walls of the arteries as the heart pumps. If blood pressure rises and stays high over time, it can damage the body in many ways. Nearly 1 in 3 adults in the United States has high blood pressure, which increases the risks of stroke, heart failure, heart attack, kidney failure, and death.

Edarbi is an angiotensin II receptor blocker (ARB) that lowers blood pressure by blocking the action of angiotensin II, a vasopressor hormone.

Adverse reactions reported by patients taking Edarbi in clinical trials were similar to those reported by those taking an inactive drug (placebo).

Edarbi has a boxed warning that says the use of the drug should be avoided in pregnant women because use of the drug during the second or third trimester can cause injury and even death in the developing fetus. If a woman becomes pregnant while using the drug, it should be discontinued as soon as possible.

Edarbi is made by Takeda Pharmaceutical North America of Deerfield, Ill.

For information:

- Approved Drugs: Questions and Answers[1]

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Links on this page:

1. /Drugs/ResourcesForYou/Consumers/ucm054420.htm

U.S. Food and Drug Administration

Drugs

FDA Drug Safety Communication: Safety Review update of Abacavir and possible increased risk of heart attack

Safety Announcement

[03-01-2011] The U.S. Food and Drug Administration (FDA) is updating the public about its ongoing safety review of abacavir and a possible increased risk of heart attack. Abacavir is an antiviral medication used in combination with other antiretroviral drugs for the treatment of HIV-1 infection. Available medications that contain abacavir include Ziagen, Trizivir, and Epzicom.

There has been conflicting information on the potential increased risk of heart attack with abacavir treatment. An increased risk of heart attack (myocardial infarction or MI) has been seen in several observational studies and one randomized controlled trial (RCT) with abacavir. However, an increased risk of heart attack has not been seen in other RCTs and the safety database maintained by the drug manufacturer.

FDA conducted a meta-analysis of 26 randomized clinical trials that evaluated abacavir. This meta-analysis di not show an increased risk of MI associated with the use of abacavir. Healthcare professionals should continue to prescribe abacavir according to the professional label. Patients should not stop taking their abacavir without first talking to their healthcare professional.

FDA will continue to communicate any new safety information to the public as it becomes available.

Additional Information for Patients

- Do not stop taking abacavir without talking to your healthcare professional.
- Discuss any questions or concerns about abacavir with your healthcare professional.
- Report any side effects you experience to the FDA MedWatch program using the information in the "Contact Us" box at the bottom of the page.

Additional Information for Healthcare Professionals

- Continue to prescribe abacavir according to the professional label.
- Be aware there are conflicting data on whether abacavir treatment increases the risk of MI. However, the FDA's recent meta-analysis of 26 RCTs found no statistically significant difference in MI events between patients who received abacavir and those who did not.
- Report adverse events involving abacavir to the FDA MedWatch program, using the information in the "Contact Us" box at the bottom of the page.

Data Summary

FDA's primary objective was to explore the association of abacavir with MI. A literature search was conducte among four databases (International Pharmaceutical Abstracts [IPA], Intelos, Embase and Scopus) for all clinical trials that included a randomized abacavir treatment arm. The FDA manually reviewed the results of the search to identify RCTs that met the following criteria: conducted in adults, sample size greater than 50 subjects, trial status completed, not a pharmacokinetic trial, and not conducted in Africa. The Mantel-Haensze method, with risk difference, odds ratio (OR), and a 95% confidence interval (CI), was used for the primary analysis based on trial-level summaries; the unit of analysis was the subject, and the stratification factor was the trial. For trials with more than two arms, abacavir versus non-abacavir arms were compared.

U.S. Food and Drug Administration

Drugs

FDA Drug Safety Communication: Antipsychotic drug labels updated on use during pregnancy and risk of abnormal muscle movements and withdrawal symptoms in newborns

Safety Announcement

[2-22-2011] The U.S. Food and Drug Administration (FDA) is informing healthcare professionals that it has updated the Pregnancy section of drug labels for the entire class of antipsychotic drugs. The new drug labels now contain more and consistent information about the potential risk for abnormal muscle movements (extrapyramidal signs or EPS) and withdrawal symptoms in newborns whose mothers were treated with these drugs during the third trimester of pregnancy.

Antipsychotic drugs are used to treat symptoms of psychiatric disorders such as schizophrenia and bipolar disorder, and have been shown to improve daily functioning in individuals with these disorders. Common brand names for antipsychotic drugs include Haldol, Clozaril, Risperdal, Zyprexa, Seroquel, Abilify, Geodon, and Invega (see List of Antipsychotic Drugs below).

Healthcare professionals should be aware of the effects of antipsychotic medications on newborns when the medications are used during pregnancy. Patients should not stop taking these medications if they become pregnant without talking to their healthcare professional, as abruptly stopping antipsychotic medications can cause significant complications for treatment.

The symptoms of EPS and withdrawal in newborns may include agitation, abnormally increased or decreased muscle tone, tremor, sleepiness, severe difficulty breathing, and difficulty in feeding. In some newborns, the symptoms subside within hours or days and do not require specific treatment; other newborns may require longer hospital stays.

Additional Information for Patients

- Notify your healthcare professional if you become pregnant or intend to become pregnant while taking an antipsychotic medication.
- Do not stop taking your antipsychotic medication if you become pregnant without first talking to your healthcare professional. Abruptly stoppin antipsychotic medication can cause significant complications in your treatment.
- Talk to your healthcare professional if you have concerns about any treatment you are receiving during pregnancy.
- Report serious side effects from the use of antipsychotic drugs to the FDA MedWatch program, using the information in the "Contact Us" box at the bottom of the page.

Additional Information for Healthcare Professionals

- Know that antipsychotic medications cross the placenta.
- Be aware that neonates exposed to antipsychotic medications during the third trimester of pregnancy are at risk for EPS and/or withdrawal symptoms following delivery.
- Counsel patients about the benefits and risks of taking antipsychotic drugs during pregnancy.
- Monitor neonates exhibiting EPS or withdrawal symptoms. Some neonates recover within hours or days without specific treatment; others may require prolonged hospitalization.
- Report adverse events involving antipsychotic drugs to the FDA MedWatch program using the information in the "Contact Us" box at the botton of this page.

Data Summary

A search of the FDA's Adverse Event Reporting System (AERS) database through October 29, 2008 identified 69 cases of neonatal EPS or withdrawal with all antipsychotic drugs.

Symptoms reported included agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress and feeding disorder. Blood levels were not provided, making it not possible to determine whether the events resulted from antipsychotic drug toxicity or withdrawal. Some cases described the time at which the onset of symptoms occurred, and they ranged from birth to one month after birth. The symptoms varied in severity; some neonates recovered within hours or days without specific treatment, while others required intensive care unit support and prolonged hospitalization. Medications used to treat a suspected withdrawal reaction in the neonates included phenobarbital and benzodiazepines.

A majority of the cases were confounded by other factors, including concomitant use of other drugs known to be associated with withdrawal symptoms (antidepressants, benzodiazepines, non-benzodiazepine hypnotics and opioids), prematurity, congenital malformations, and obstetrical and perinatal complications (placental problems, pre-eclampsia). However, there were some cases which suggest that neonatal EPS and withdrawal may occur with antipsychotics alone.

Based on this information, FDA has updated the Pregnancy section of drug labels for the entire class of antipsychotic drugs to include consistent information about the potential risk for EPS and/or withdrawal symptoms in newborns whose mothers were treated with these drugs during the third trimester of pregnancy.

List of Antipsychotic Drugs

Brand Name	Generic Name
Abilify	aripiprazole
Clozaril	clozapine

FazaClo ODT	clozapine
Fanapt	iloperidone
Geodon	ziprasidone
Haldol	haloperidol
Invega	paliperidone
Invega Sustenna	paliperidone
Loxitane	loxapine
Moban	molindone
Navane	thiothixene
Orap	pimozide
Risperdal	risperidone
Risperdal Consta	risperidone
Saphris	asenapine
Seroquel	quetiapine
Seroquel XR	quetiapine
Stelazine	trifluoperazine
Thorazine	chlorpromazine
Zyprexa	olanzapine
Zyprexa Relprevv	olanzapine
Zyprexa Zydis	olanzapine
Symbyax	olanzapine and fluoxetine
No Current Brand Name	fluphenazine
No Current Brand Name	perphenazine
No Current Brand Name	perphenazine and amitriptyline
No Current Brand Name	prochlorperazine
No Current Brand Name	thioridazine

Related Information

- Atypical Antipsychotic Drugs Information[1]

Contact Us

- **Report a Serious Problem**
- 1-800-332-1088
- 1-800-FDA-0178 Fax

MedWatch Online[2]

Regular Mail: Use postage-paid FDA Form 3500[3]
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Rockville , MD 20857

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1. /Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm094303.htm
2. https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm
3. http://www.fda.gov/downloads/Safety/MedWatch/DownloadForms/UCM082725.pdf

U.S. Food and Drug Administration

Drugs

FDA Drug Safety Communication: New warnings against use of terbutaline to treat preterm labor

Safety Announcement

[02-17-2011] The U.S. Food and Drug Administration (FDA) is warning the public that injectable terbutaline should not be used in pregnant women for prevention or prolonged treatment (beyond 48-72 hours) of preterm labor in either the hospital or outpatient setting because of the potential for serious maternal heart problems and death. The agency is requiring the addition of a Boxed Warning and Contraindication to the terbutaline injection label to warn against this use. In addition, oral terbutaline should not be used for prevention or any treatment of preterm labor because it has not bee shown to be effective and has similar safety concerns. The agency is requiring the addition of a Boxed Warning and Contraindication to the terbutaline tablet label to warn against this use.

Terbutaline is approved to prevent and treat bronchospasm (narrowing of airways) associated with asthma, bronchitis, and emphysema. The drug is sometimes used off-label (an unapproved use) for acute obstetric uses, including treating preterm labor and treating uterine hyperstimulation. Terbutaline has also been used off-label over longer periods of time in an attempt to prevent recurrent preterm labor.

Although it may be clinically deemed appropriate based on the healthcare professional's judgment to administer terbutaline by injection in urgent and individual obstetrical situations in a hospital setting, the prolonged use of this drug to prevent recurrent preterm labor can result in maternal heart problems and death. Terbutaline should not be used in the outpatient or home setting.

The decision to require the addition of a Boxed Warning and Contraindication is based on new safety information received and reviewed by the FDA. Specifically, FDA has reviewed postmarketing safety reports of terbutaline used for obstetrical indications (see Data Summary below), as well as data from the medical literature.[1-6] These label changes are consistent with statements from the American College of Obstetricians and Gynecologists (ACOG).[6]

Additional Information for Patients

- Be aware that serious side effects, including maternal heart problems and death, have been reported after prolonged use of terbutaline to manage preterm labor.
- There are serious situations where a healthcare professional may decide that the short-term use of injectable terbutaline in the hospital setting may benefit a pregnant woman.
- Oral terbutaline should not be used either to treat preterm labor or prevent recurrent preterm labor.
- If you are taking terbutaline for another medical condition (e.g., asthma), talk to your healthcare professional if you are pregnant or become pregnant to determine whether terbutaline is still right for you.
- FDA encourages patients to talk to their healthcare professional if they have concerns about any treatment they are receiving.
- Report any side effects from the use of oral or injectable terbutaline to the FDA MedWatch program, using the information in the "Contact Us" box at the bottom of the page.

Additional Information for Healthcare Professionals

- Be aware that death and serious adverse reactions, including increased heart rate, transient hyperglycemia, hypokalemia, cardiac arrhythmias, pulmonary edema, and myocardial ischemia have been reported after prolonged administration of oral or injectable terbutaline to pregnant women.
- Treatment with terbutaline administered by injection or by continuous infusion pump should not be used beyond 48 to 72 hours. In particular, injectable terbutaline should not be used in the outpatient or home setting.
- There are certain obstetrical conditions where the healthcare professional may decide that the benefit of terbutaline injection for an individual patient in a hospital setting clearly outweighs the risk.
- Oral terbutaline is contraindicated for the treatment or prevention of preterm labor.
- Report adverse events involving terbutaline to the FDA MedWatch program using the information in the "Contact Us" box at the bottom of this page.

Data Summary

In November 1997, FDA issued a Dear Colleague letter to notify healthcare professionals about concerns regarding the safety of long-term subcutaneous administration of terbutaline. The Precautions section of the labeling was revised to warn about serious adverse reactions, including cardiovascular adverse events that may occur after administration of terbutaline to women in labor.

Publications in the medical literature have reported a lack of safety and efficacy of terbutaline for the treatment of recurrent preterm labor.[2-5] Despite labeling changes, FDA's communication to the public, and professional association recommendations, prolonged use of terbutaline continues, with serious and sometimes fatal consequences.

FDA reviewed postmarketing reports of maternal death and serious cardiovascular adverse events submitted to the Adverse Event Reporting System (AERS) associated with obstetric use of terbutaline.

A search of AERS identified 16 maternal deaths that were reported since initial marketing of the drug in 1976 until 2009. Three of the 16 cases reported outpatient use of terbutaline administered by a subcutaneous pump, while nine cases reported use of oral terbutaline alone or in addition to subcutaneous or intravenous terbutaline. Of these nine cases, two reported use of oral terbutaline on an outpatient basis and seven cases involved inpatient use of oral terbutaline. The routes of administration in the remaining four cases were subcutaneous, intravenous, or unknown.

FDA identified 12 maternal cases of serious cardiovascular events associated with use of terbutaline that were reported to AERS between January 1, 1998 (after FDA issued the Dear Colleague letter) and July 2009. These events included cardiac arrhythmias, myocardial infarction, pulmonary edema, hypertension, and tachycardia. Three of the 12 cases reported use of the terbutaline administered by subcutaneous pump. Five cases involved use of oral terbutaline alone or in addition to subcutaneous terbutaline. Of these five cases, three cases involved use of oral terbutaline on an outpatient basis and two cases involved inpatient use of oral terbutaline.

In summary, based on this information, FDA has concluded that the risk of serious adverse events outweighs any potential benefit to pregnant women receiving prolonged treatment with terbutaline injection (beyond 48-72 hours), or acute or prolonged treatment with oral terbutaline. FDA is requiring the addition of a new Boxed Warning and Contraindication to the terbutaline drug labels to warn healthcare professionals about these risks.

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Related Information

- FDA Response to Citizen Petition on Terbutaline (PDF - 151KB)[2]
  2/17/2011
- FDA warns against certain uses of asthma drug terbutaline for preterm labor[3]
  Press Release - 2/17/2011
- Terbutaline Information[4]
- NDA Terbutaline Safety Labeling Change Letter (Injection) (PDF - 75KB)[5]
- NDA Terbutaline Safety Labeling Change Letter (Oral) (PDF - 72KB)[6]
- ANDA Terbutaline Safety Labeling Change Letter (Oral) (PDF - 50KB)[7]
- ANDA Terbutaline Safety Labeling Change Letter (Injection) (PDF - 41KB)[8]
- FDA Drug Safety Podcast for Healthcare Professionals: New warnings against use of terbutaline to treat preterm labor[9]

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- 1-800-FDA-0178 Fax

  MedWatch Online[10]

  Regular Mail: Use postage-paid FDA Form 3500[11]

  Mail to: MedWatch 5600 Fishers Lane

  Rockville , MD 20857

Links on this page:

1. http://www.nhlbi.nih.gov/health/prof/lung/asthma/astpreg/astpreg_full.pdf
2. /downloads/Drugs/DrugSafety/UCM243797.pdf
3. /NewsEvents/Newsroom/PressAnnouncements/ucm243840.htm
4. /Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm243551.htm
5. /downloads/Drugs/DrugSafety/UCM243681.pdf
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7. /downloads/Drugs/DrugSafety/UCM243687.pdf
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U.S. Food and Drug Administration

News & Events

FDA NEWS RELEASE
For Immediate Release: Feb. 16, 2011
Media Inquiries: Christopher Kelly, 301-796-4676, christopher.kelly@fda.hhs.gov
Consumer Inquiries: 888-INFO-FDA

U.S. Marshals seize Auralgan Otic Solution
Product is not FDA-approved

U.S. Marshals, at the request of the U.S. Food and Drug Administration yesterday, seized all lots of Auralgan Otic Solution, a prescription drug used to treat pain and inflammation associated with ear infections, from Integrated Commercialization Solutions Inc. (ICS) in Brooks, Ky. Auralgan is manufactured for Deston Therapeutics, located in Chapel Hill, N.C., and is warehoused at ICS.

Deston s sale of the product in the United States violates federal law because the product does not have FDA approval and its labeling does not include adequate directions for use. The value of the products seized is estimated to be $16.5 million.

"The FDA is committed to taking enforcement action against companies marketing drugs that do not meet federal standards for safety, effectiveness, and quality, "said Deborah M. Autor, director of the Office of Compliance in the FDA s Center for Drug Evaluation and Research. "We will remain vigilant in our efforts to protect consumers from unapproved products. "

On Feb. 5, 2010, the FDA issued a Warning Letter to Deston, citing the company for distributing unapproved new drugs and misbranded drugs. The FDA also warned Deston that Auralgan was an unapproved new drug in April, June, and September 2010, and the company continued distributing the drug in violation of the Federal Food, Drug, and Cosmetic Act.

Today s action is part of the FDA s Unapproved Drugs Initiative, established in 2006 to get unapproved drugs either approved or off the market.

For more information:

February 5, 2010 Warning Letter to Deston Therapeutics, LLC [1]

Unapproved Drugs: Drugs Marketed in the United States That Do Not Have Required FDA Approval [2]

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Links on this page:

1. http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/ucm203037.htm
2. http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/SelectedEnforcementActionsonUnapprovedDrugs/default.htm
3. http://www.facebook.com/FDA
4. http://www.fda.gov/AboutFDA/ContactFDA/StayInformed/RSSFeeds/PressReleases/rss.xml

U.S. Food and Drug Administration

News & Events

FDA NEWS RELEASE

For Immediate Release: Feb. 1, 2011
Media Inquiries: Christopher Kelly, 301-796-4676, christopher.kelly@fda.hhs.gov
Consumer Inquiries: 888-INFO-FDA

FDA reminds health care professionals about safe use of non-sterile alcohol prep pads

Following a recent recall of potentially contaminated non-sterile alcohol prep pads, the U.S. Food and Drug Administration today reminded health care professionals about the safe use of non-sterile alcohol prep pads t clean and disinfect the surface of the skin.

On Jan. 5, 2011 The Triad Group of Hartland, Wis., recalled all lots of its alcohol prep pads and swabs citing concerns about the product s potential contamination with Bacillus cereus, a bacterium that can be harmful to humans.

"Health care professionals should always check the labeling on a prep pad to determine if it is sterile or non-sterile," said Karen Weiss, M.D., director of the Safe Use Initiative in the FDA s Center for Drug Evaluation and Research. "Non-sterile pads are not intended to prep patients prior to procedures requiring strict sterility measures and should not be used on patients with a depressed immune system, to prep patients for catheter insertion, or to prep patients prior to surgery."

Weiss said many patients in hospitals are particularly susceptible to infections, and the FDA recommends sterile antiseptics (including chlorhexidine gluconate, alcohol or iodine applicators, pads, and swabs) in that setting.

Manufacturers often package a prep pad with an injectable drug, selling them as a kit. But not all marketed pads are sterile. Some are marketed as non-sterile alcohol pads. If a pad does not state "sterile" on the label, health care professionals should be aware that they are using a non-sterile pad.

Health care professionals and consumers should check the label to confirm that the product is sterile, and ma also want to consider washing the area with soap and water prior to using the antiseptic for skin surface preparation.

For more information:

- Triad Group Press Release on Recall of Alcohol Prep Pads[1]
- CDC – Guideline for Prevention of Surgical Site Infection

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U.S. Food and Drug Administration

Drugs

FDA Drug Safety Communication: Avandia (rosiglitazone) labels now contain updated information about cardiovascular risks and use in certain patients

Safety Announcement

[2-03-2011] The U.S. Food and Drug Administration (FDA) is notifying the public that information on the cardiovascular risks (including heart attack) of the diabetes drug rosiglitazone has been added to the physician labeling and patient Medication Guide. This information was first announced by FDA on September 23, 2010[1] as part of new restrictions for prescribing and use of this drug.

Rosiglitazone is sold as a single-ingredient product under the brand name Avandia. Rosiglitazone is also sold as a combination product under the branc name Avandamet (contains rosiglitazone and metformin) and under the brand name Avandaryl (contains rosiglitazone and glimepiride).

In addition to describing the cardiovascular risks, the drug labels have been revised to state that rosiglitazone and rosiglitazone-containing medicines should only be used:

- In patients already being treated with these medicines
- In patients whose blood sugar cannot be controlled with other anti-diabetic medicines and who, after consulting with their healthcare professional, do not wish to use pioglitazone-containing medicines (Actos, Actoplus Met, Actoplus Met XR, or Duetact).

At this time, FDA has only approved these safety-related changes to the physician labeling and Medication Guides for the rosiglitazone-containing medicines. The Risk Evaluation and Mitigation Strategy (REMS), which will restrict rosiglitazone-containing medicines' availability, has not yet been approved and formally implemented.

FDA will be providing further information on this REMS program in the coming months. FDA expects to approve the REMS by Spring 2011, and for the manufacturer to complete implementation 6 months thereafter.

Additional Information for Patients

- You may continue to take a rosiglitazone-containing medicine if directed by your healthcare professional, but it is important that you understand the risks and benefits of the drug.
- Talk to your healthcare professional if you have concerns about rosiglitazone-containing medicines.
- Read the Medication Guide you get along with your rosiglitazone-containing medicine. It explains the risks associated with the use of rosiglitazone.
- Report any side effects from the use of rosiglitazone-containing medicines to the FDA MedWatch program, using the information at the bottom of the page in the "Contact Us" box.

Additional Information for Healthcare Professionals

- The REMS for rosiglitazone-containing medicines does not take effect at the time of this announcement. You may continue to prescribe and dispense rosiglitazone-containing medicines as directed in the revised drug label.
- You should begin discussing the risks and benefits of taking rosiglitazone-containing medicines versus other therapies with your patients, and make decisions about optimal treatment for your individual patients.
- Encourage patients to read the rosiglitazone Medication Guide given to them when they pick-up their prescription at the pharmacy
- Report adverse events involving rosiglitazone-containing medicines to the FDA MedWatch program, using the information at the bottom of the page in the "Contact Us" box.

Data Summary

On September 23, 2010, FDA announced that it would significantly restrict the use of rosiglitazone-containing medicines to patients with Type 2 diabetes who cannot control their blood sugar on other medicines. These new restrictions were in response to data that suggested an elevated risk of heart attacks in patients treated with rosiglitazone.

Related Information

- FDA significantly restricts access to the diabetes drug Avandia[2]
  9/23/2010
- Rosiglitazone maleate (marketed as Avandia, Avandamet, and Avandaryl) Information[3]
- FDA Drug Safety Podcast for Healthcare Professionals: Avandia (rosiglitazone) labels now contain updated information about cardiovascular risks and use in certain patients[4]

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