Drug Utilization Review Board

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

Wednesday
December 14, 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 – December 14, 2011
DATE: December 8, 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 December 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.

Overview of OHCA Advisory Groups

Action Item – Vote on 2012 Meeting Dates – See Appendix C.

Action Item - Vote to Prior Authorize Multiple Sclerosis Medications – See Appendix D.

Action Item – Vote to Prior Authorize Darilesp® – See Appendix E.

Action Item – Vote to Prior Authorize Horizant® – See Appendix F.

Action Item – Vote to Prior Authorize Gralise™ – See Appendix G.

Action Item – Annual Review of Antihistamines – See Appendix H.

Action Item – Annual Review of Statin and Statin Combination Products – See Appendix I.

Action Item – Annual Review of Lovaza – See Appendix J.

30 Day Notice to Prior Authorize Brilinta™ and Xarelto™ – See Appendix K.

FDA and DEA Updates – See Appendix L.

Future Business

Adjournment

Oklahoma Health Care Authority
Drug Utilization Review Board
(DUR Board)
Meeting –December 14, 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. November 9, 2011 DUR Minutes – Vote
- B. November 10, 2011 DUR Recommendation Memorandum

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

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

Items to be presented by Mr. Kimble, Dr. Muchmore, Chairman

5. Overview of OHCA Advisory Groups

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

6. Action Item – Vote on 2012 Meeting Dates – See Appendix C.

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

7. Action Item – Vote to Prior Authorize Multiple Sclerosis Medications – See Appendix D.
- A. COP Recommendations

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

8. Action Item – Vote to Prior Authorize Daliresp® – See Appendix E.

A. COP Recommendations

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

9. Action Item – Vote to Prior Horizant® – See Appendix F.

A. COP Recommendations

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

10. Action Item – Vote to Prior Authorize Gralise™ – See Appendix G.

A. COP Recommendations

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

11. Action Item – Annual Review of Antihistamines – See Appendix H.

A. Current Authorization Criteria
B. Utilization Review
C. Prior Authorization Review
D. Market News and Update
E. COP Recommendations
F. Utilization Details

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

12. Action Item – Annual Review of Statin and Statin Combination Products – See Appendix I.

A. Current Authorization Criteria
B. Utilization Review
C. Prior Authorization Review
D. Market News and Update
E. COP Recommendations
F. Utilization Details

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

13. Action Item – Annual Review of Lovaza® – See Appendix J.

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

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

14. 30 Day Notice to Prior Authorize Brilinta™ and Xarelto™ – See Appendix K.

A. Brilinta™
B. Xarelto™

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

15. FDA and DEA Updates – See Appendix L.

16. Future Business

A. Annual Review of Narcotics
B. Annual Review of Ribavirin
C. New Product Reviews
D. Medical Product Reviews

17. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES of MEETING of NOVEMBER 9, 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): Linda Le, Tracy Do, Amany Hassan, Manish Mittal	X	

OKLAHOMA HEALTH CARE AUTHORITY STAFF:	PRESENT	ABSENT
Mike Fogarty, J.D., M.S.W.; Chief Executive Officer		X
Garth Splinter, M.D., M.B.A.; Director of Medicaid/Medical Services		X
Rebecca Pasternik-Ikard, Deputy State Medicaid Director		X
Nancy Nesser, Pharm.D., J.D.; Pharmacy Director	X	
Lynn Rambo-Jones, J.D.; Deputy General Counsel III	X	
Carter Kimble, MPH/Public Affairs- Information Rep.		X
Jill Ratterman, D.Ph.; Pharmacy Specialist	X	
Rodney Ramsey, Drug Reference Coordinator	X	
Kerri Wade, Senior Pharmacy Financial Analyst	X	

OTHERS PRESENT:

Renee Parks, J&J	Don Kempin, NovoNordisk	Donna Erwin, Bristol-Myers Squibb
Lon Lowrey, Novaratis	Warren Tayes, Merck	Randy McGinley, Bayer
Charlene Kaiser, Amgen	James Osborne, GSK	Brent Clarkson, Pfizer
John Omick, Novartis	Tone Jones, Sunovion	Valerie Pennington, Novartis
David Williams, Forest	Vanessa Papion, UCB	Jim Chapman, Abbott
Janie Huff, Takeda	Ron Schnare, Shire	Sam Smothers, MedImmune
Pat Trahan, Taro	Todd Bishop, Taro	

PRESENT FOR PUBLIC COMMENT:

Agenda Item No. 9 Tyrone McBayne, Takeda

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

Dr. Muchmore acknowledged the speaker for public comment:

Agenda Item No. 9 Tyrone McBayne, Takeda

ACTION: NONE REQUIRED

AGENDA ITEM NO. 3: APPROVAL OF DUR BOARD MINUTES

3A: October 12, 2011 DUR Minutes

Dr. Preslar moved to approve as submitted; seconded by Dr. Harrell.

ACTION: MOTION CARRIED

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

4A: Medication Coverage Activity Audit: October 2011

4B: Pharmacy Help Desk Activity Audit: October 2011

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: ACCELERATING UTILIZATION OF COMPARATIVE EFFECTIVENESS FINDINGS IN MEDICAID MENTAL HEALTH

Introductions by by Dr. Nesser; presentations by Sheree Neese-Todd of Rutgers MEDNET, and Dr. Molly Finnerty of Columbia.

ACTION: NONE REQUIRED

AGENDA ITEM NO. 6: VOTE TO PRIOR AUTHORIZE NATROBA™ TOPICAL SUSPENSION

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

Dr. Kuhls moved to approve as submitted; seconded by Dr. Winegardener.

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: VOTE TO PRIOR AUTHORIZE BIOLOGIC PRODUCTS FOR THE TREATMENT OF RHEUMATOID ARTHRITIS, CROHN'S DISEASE, PLAQUE PSORIASIS, AND ANKYLOSING SPONDYLITIS

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

Dr. Preslar moved to approve as submitted; seconded by Dr. Bell.

ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: VOTE TO PRIOR AUTHORIZE MOXEZA™

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

Dr. Bell moved to approve as submitted; seconded by Dr. Harrell.

ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: VOTE TO PRIOR AUTHORIZE AMTURNIDE™ AND EDARBI™

For Public Comment; Tyrone McBayne: Good afternoon ladies and gentlemen, my name is Dr. Tyrone McBayne. I'm a clinical science and outcomes manager with Takeda Pharmaceuticals. I'm actually here on behalf of Edarbi, not Amturnide. Edarbi isn't the newly approved angiotensin receptor blocker. It was actually approved on February 25th of this year and it's indicated for treatment of hypertension with alone or in combination with other antihypertensives. Now you might wonder what's the need for another antihypertensive agent, let alone another ARB. Now you may already know this but there's about 74.5 million patients in the U.S. who are afflicted with hypertension. Of those that are treated, 50% of them are still uncontrolled and they can benefit from additional blood pressure lowering. The clinical trial program for Edarbi included

seven randomized double-blind placebo-controlled and active controlled trial which ranged in length from six weeks to six months and it included patients with mild to severe hypertension. These trials were active controlled trials comparing Edarbi to maximum FDA approved doses of both olmesartan and valsartan. As you know, these are commonly prescribed products. In the actively controlled trials Edarbi gave the result in statistically significant reductions in both clinic and 24-hour mean blood pressures in comparison to both olmesartan and valsartan. The reduction in mean systolic blood pressure ranged from two to five. Now you may say this is modest, but according to previous trials, these reductions, although modest, led to and conferred a statistically significant reduction in mortality due to coronary heart disease as well as stroke. In addition, this modest reduction resulted in greater percentage of patients who actually achieve goal blood pressures. Patients who are on Edarbi have, 10% more of those patients achieve goal over both olmesartan and valsartan, so by using Edarbi, you can experience, you can expect that more people can achieve goal with Edarbi over both olmesartan and valsartan. Edarbi's recommended dose is a non-titrated single daily dose of 80 mg. A 40 mg dose, however, is also available. Edarbi does not require a dose adjustment for patients with mild to severe renal impairment, nor does it require adjustment for patients with mild to moderate hepatic impairment. Edarbi has an overall safety profile comparable to olmesartan and valsartan and it's fairly similar to placebo. The most common adverse event was diarrhea that occurred at a frequency of about 2%. Adverse reactions were generally mild, non-dose dependent and unrelated to age, gender or race. No significant drug interactions were discovered in the clinical trials. So to conclude, Takeda is pleased to make Edarbi available and an important new treatment option for patients with hypertension, particularly for those individuals who aren't managed with traditional ARBs. So with that said, I would like to open the floor for any questions you may have.
Materials included in agenda packet; presented by Dr. Moore.
Dr. Winegardener moved to approve as submitted; seconded by Dr. Bell.
ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: VOTE TO PRIOR AUTHORIZE VIIBRYD®
Materials included in agenda packet; presented by Dr. Le.
Dr. Preslar moved to approve as submitted; seconded by Dr. Kuhls.
ACTION: MOTION CARRIED

AGENDA ITEM NO. 11: 30-DAY NOTICE TO PRIOR AUTHORIZE MULTIPLE SCLEROSIS MEDICATIONS
Materials included in agenda packet; presented by Dr. Le.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 12: 30-DAY NOTICE TO PRIOR AUTHORIZE MISCELLANEOUS PRODUCTS DALIRESP®, HORIZANT®, GRALISE™
Materials included in agenda packet; presented by Dr. Le, Dr. Moore, Dr. Sipols.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: FDA & DEA UPDATES
Materials included in agenda packet; presented by Dr. Graham.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: FUTURE BUSINESS
Materials included in agenda packet; submitted by Dr. Graham.
A: Annual Review of Statins
B: Annual Review of Antihistamines
C: New Product Reviews
D: Medical Product Reviews
ACTION: NONE REQUIRED

AGENDA ITEM NO. 15: ADJOURNMENT
The meeting was adjourned at 6:40 p.m.

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

Memorandum

Date: November 10, 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 November 9, 2011

Recommendation 1: Vote to Prior Authorize Natroba® (spinosad)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends updating the current Product Based Prior Authorization tier structure as outlined below. Additionally, the College recommends placement of Natroba™ (spinosad) in Tier 3 of the current structure. An age restriction of 4 years or older and a quantity limit of 240 mL every 30 days will also apply.

Tier 1	Tier 2	Tier 3
Covered OTC Lice Products Generics with SMAC Pricing	Benzoyl Alcohol (Ulesfia™) Lotion	Lindane Lotion & Shampoo Malathion (Ovide®) Spinosad (Natroba™)

Approval Criteria:

- Approval of Tier 2 medication requires a trial with one Tier 1 medication with inadequate response or adverse effect.
- Approval of Tier 3 medication requires a trial with one Tier 2 medication with inadequate response or adverse effect.

No changes to individual product restrictions. Crotamiton will not be included in the tier system but will maintain the age and quantity restrictions.

Recommendation 2: Vote to Prior Authorize Biologic Products for Rheumatoid Arthritis, Crohn's Disease, Plaque Psoriasis, and Ankylosing Spondylitis

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends pharmacy and medical prior authorization of this class of medications with the following criteria and tier structure:

Tier 2 authorization criteria:

1. FDA approved diagnosis
2. A trial of at least one Tier 1 product in the last 90 days that did not yield adequate relief of symptoms or resulted in intolerable adverse effects.
3. Prior stabilization on the Tier 2 medication documented within the last 100 days.

Tier 3 authorization criteria:

1. FDA approved diagnosis
2. Recent trials of one Tier 1 product and all available Tier 2 medications that did not yield adequate relief of symptoms or resulted in intolerable adverse effects.
3. Prior stabilization on the Tier 3 medication documented within the last 100 days.
4. A unique FDA-approved indication not covered by Tier 2 products.

Tier 1	Tier 2	Tier 3
DMARDs appropriate to disease State : Methotrexate Hydroxychloroquine Sulfasalazine Minocycline Oral Corticosteroids Leflunomide Mesalamine 6-Mercaptopurine Azathioprine NSAIDs	Supplemental rebated medications	Abatacept (Orencia®) Adalimumab (Humira®) Alefacept (Amevive®) Anakinra (Kineret®) Certolizumab pegol (Cimzia®) Etanercept (Enbrel®) Golimumab (Simponi®) Infliximab (Remicade®) Rituximab (Rituxan®) Tocilizumab (Actemra®) Ustekinumab (Stelara®)

Recommendation 3: Vote to Prior Authorize Moxeza™ (moxifloxacin)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the placement of Moxeza™ (moxifloxacin) into Tier 3 of this PBPA category. Current criteria shall apply.

Tier 1	Tier 2	Tier 3
Gentak (Gentamicin) AK-Tob (Tobramycin) Polytrim (PolymyxinB/Trimethoprim) AK-Spore (Neo/PolyB/Gramacidin) Bleph-10, Na Sulamyd (Na Sulfacetamide)	Ciloxan Solution (Ciprofloxacin) Ocuflox (Ofloxacin)	Vigamox (Moxifloxacin) Moxeza (Moxifloxacin) Azasite (Azithromycin) Besivance (Besifloxacin HCL) Iquix (Levofloxacin) Quixin (Levofloxacin) Zymar (Gatifloxacin) Zymaxid (Gatifloxacin)

Criteria for a Tier 2 medication:

1. Approved indication/suspected infection by organism not known to be covered by Tier 1 products, or failure of a Tier 1 product.
2. Known contraindication to all indicated Tier 1 medication.
3. Prescription written by optometrists/ophthalmologists, or
4. When used for pre/post-operative prophylaxis.

Criteria for a Tier 3 medication:

1. Approved indication/suspected infection by organism not known to be covered by Tier 2 products, or failure of a Tier 2 product.
2. Known contraindication to all indicated Tier 2 medication.
3. Prescription written by optometrists/ophthalmologists, or
4. When used for pre/post-operative prophylaxis.

Recommendation 4: Vote to Prior Authorize Amturnide® (aliskirin/amlodipine/HCTZ) and Edarbi™ (azilsartan)

MOTION CARRIED by unanimous approval.

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

1. Placement of Amturnide® (aliskirin/amlodipine/HCTZ) in Tier 3 of the DRI category.
2. Placement of Edarbi™ (azilsartan) into Tier 3 of the ARB category.
3. As ARB patents expire, move generic ARBs to Tier 1 once exclusivity lapses and SMAC is applied.

Recommendation 5: Vote to Prior Authorize Viibryd® (vilazodone)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the addition of Viibryd® (vilazodone) to Tier 3 of the antidepressants Product Based Prior Authorization Category. The existing criteria will apply.

Appendix B

RETROSPECTIVE DRUG UTILIZATION REVIEW REPORT
August 2011

MODULE	DRUG INTERACTION	DUPLICATION OF THERAPY	DRUG-DISEASE PRECAUTIONS	DOSING & DURATION
Total # of messages	56,289	70,655	961,429	30,188
Limits applied	Established, Major, Males and Females, Age 19-35	Duplication of Tumor Necrosis Factors, Males and Females, Age 0-150	Contraindicated, Pregnant, Females, Age 0-21	High Dose Only, NSAIDs, Males and Females, 22-25
Total # of messages after limits were applied	111	2	596	87
Total # of members reviewed	111	2	577	87

LETTERS

Category	Prescribers	Pharmacies	Total Letters
Drug Interaction	2	2	4
Duplication of Therapy	1	2	3
Drug-Disease Precautions	0	0	0
Dosing & Duration	0	0	0
Total Letters Sent	3	4	7

Retrospective Drug Utilization Review Report

Claims Reviewed for July 2011

Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
Limits which were applied	Established, Major, Males and Females, Age 0-18	Duplication of Acetaminophen Products, Males and Females, Age 21-25	Contraindicated, Asthma, Males and Females, Age 0-12	High Dose,SSRIs & SSNRIs, Males and Females, Age 0-150

Response Summary (Prescriber)
Letters Sent: 92
Response Forms Returned: 49

The response forms returned yielded the following results:

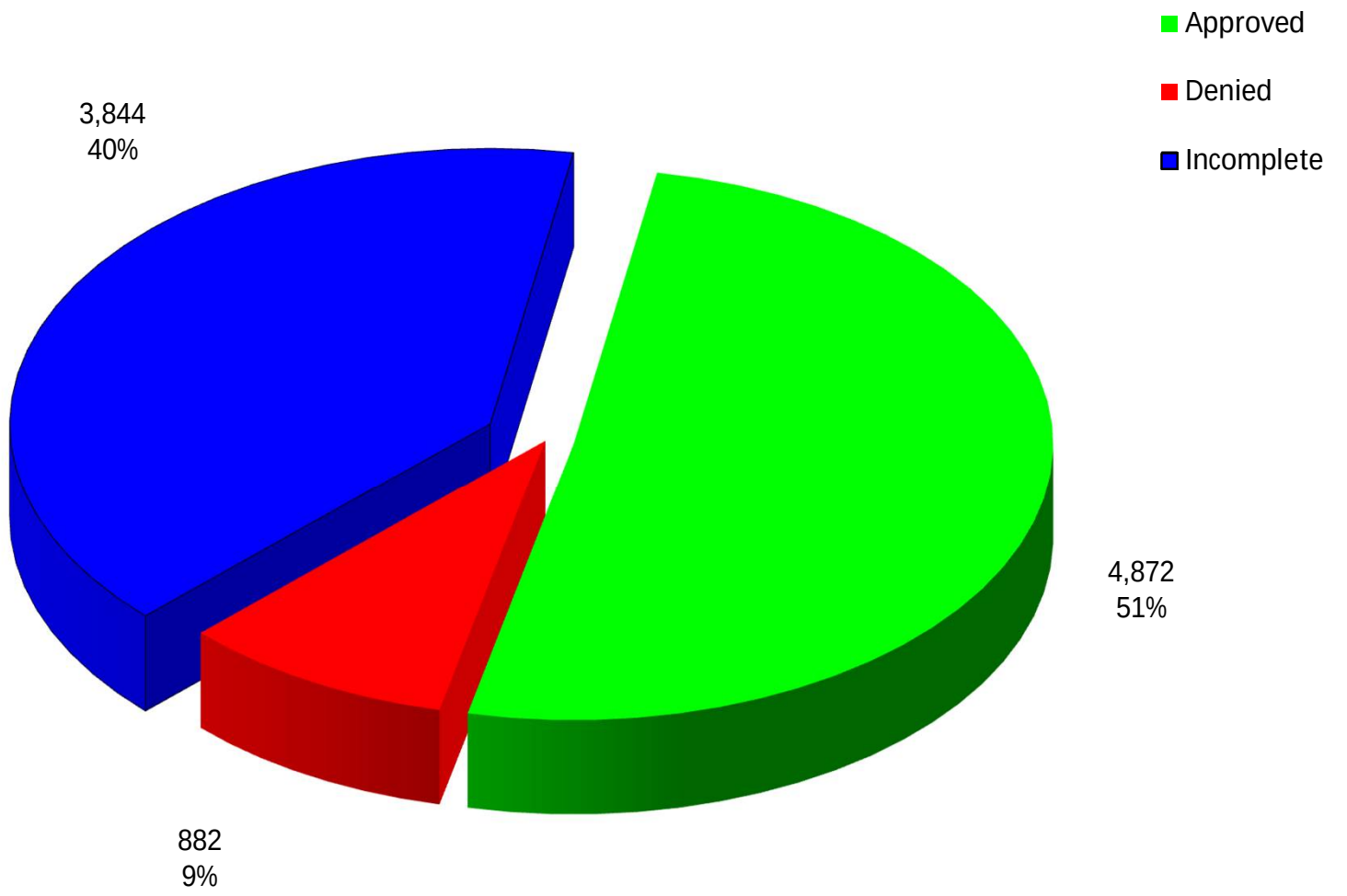
3 (6%)	*Record Error—Not my patient.*
6 (12%)	*No longer my patient.*
3 (6%)	*Medication has been changed prior to date of review letter.*
9 (18%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
18 (37%)	*I am aware of this situation and will plan to continue monitoring therapy.*
10 (20%)	*Other*

Response Summary (Pharmacy)
Letters Sent: 18
Response Forms Returned: 14

The response forms returned yielded the following results:

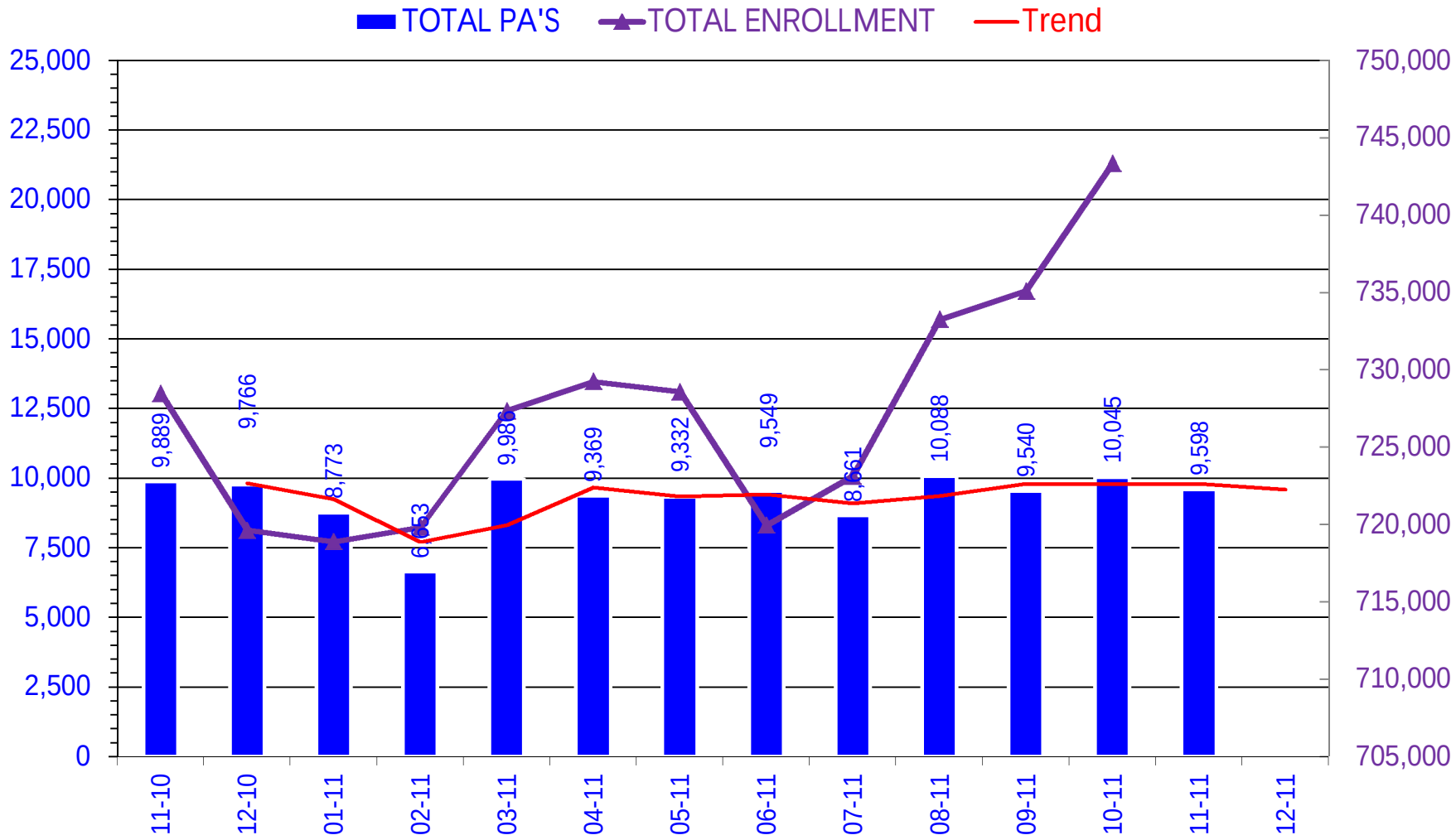
0 (0%)	*Record Error—Not my patient.*
0 (0%)	*No longer my patient.*
1 (7%)	*Medication has been changed prior to date of review letter.*
6 (43%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
3 (21%)	*I am aware of this situation and will plan to continue monitoring therapy.*
4 (29%)	*Other*

PRIOR AUTHORIZATION ACTIVITY REPORT: November 2011



PA totals include overrides

PRIOR AUTHORIZATION REPORT: November 2010 – November 2011



PA totals include overrides

Prior Authorization Activity

11/1/2011 Through 11/30/2011

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort	372	163	16	193	359
Amitiza	17	3	4	10	238
Anti-Ulcer	389	93	99	197	105
Antidepressant	289	111	17	161	345
Antihistamine	198	127	11	60	346
Antihypertensives	63	15	6	42	328
Antimigraine	84	27	13	44	302
Atypical Antipsychotics	605	360	18	227	354
Benign Prostatic Hypertrophy	4	0	0	4	0
Benzodiazepines	77	54	1	22	183
Bladder Control	66	13	9	44	363
Brovana (Arformoterol)	4	2	0	2	363
Byetta	24	8	0	16	364
Elidel/Protopic	37	10	7	20	90
ESA	145	95	6	44	111
Fibric Acid Derivatives	2	0	0	2	0
Fibromyalgia	144	44	21	79	350
Fortamet/Glumetza	6	2	0	4	363
Forteo	2	0	0	2	0
Glaucoma	19	7	0	12	363
Growth Hormones	60	49	7	4	167
HFA Rescue Inhalers	51	19	4	28	311
Insomnia	92	17	9	66	216
Misc Analgesics	38	2	32	4	226
Muscle Relaxant	156	22	86	48	120
Nasal Allergy	231	77	41	113	117
NSAIDS	170	42	17	111	319
Ocular Allergy	46	6	7	33	181
Ocular Antibiotics	39	8	1	30	18
Opioid Analgesic	302	163	10	129	246
Other	1,076	446	98	532	302
Otic Antibiotic	24	2	3	19	11
Pediculicides	149	71	13	65	17
Plavix	207	141	1	65	322
Singulair	845	438	34	373	239
Smoking Cessation	66	27	1	38	27
Statins	118	69	5	44	356
Stimulant	935	506	54	375	310
Suboxone/Subutex	152	117	2	33	75
Symlin	5	3	0	2	362
Synagis	444	209	134	101	125
Topical Antibiotics	11	5	1	5	21
Topical Antifungals	16	1	4	11	87
Topical Corticosteroids	103	7	20	76	51
Ultram ER and ODT	8	0	1	7	0
Xolair	6	0	1	5	0
Xopenex Nebs	24	4	4	16	360
Zetia (Ezetimibe)	15	8	0	7	327
Emergency PAs	10	10	0	0	
Total	**7,946**	**3,603**	**818**	**3,525**	

Overrides					
Brand	111	64	9	38	240
Dosage Change	515	494	2	19	9
High Dose	7	4	0	3	190
IHS-Brand	1	1	0	0	4
Lost/Broken Rx	98	97	0	1	13
NDC vs Age	11	9	0	2	322
Nursing Home Issue	99	94	0	5	6
Other	32	29	0	3	21
Quantity vs. Days Supply	775	474	53	248	279
Stolen	2	2	0	0	17
Third Brand Request	1	1	0	0	4
Overrides Total	**1,652**	**1,269**	**64**	**319**	
Total Regular PAs + Overrides	**9,598**	**4,872**	**882**	**3,844**	

Denial Reasons

Unable to verify required trials.	3,004
Lack required information to process request.	844
Does not meet established criteria.	832
Drug Not Deemed Medically Necessary	1

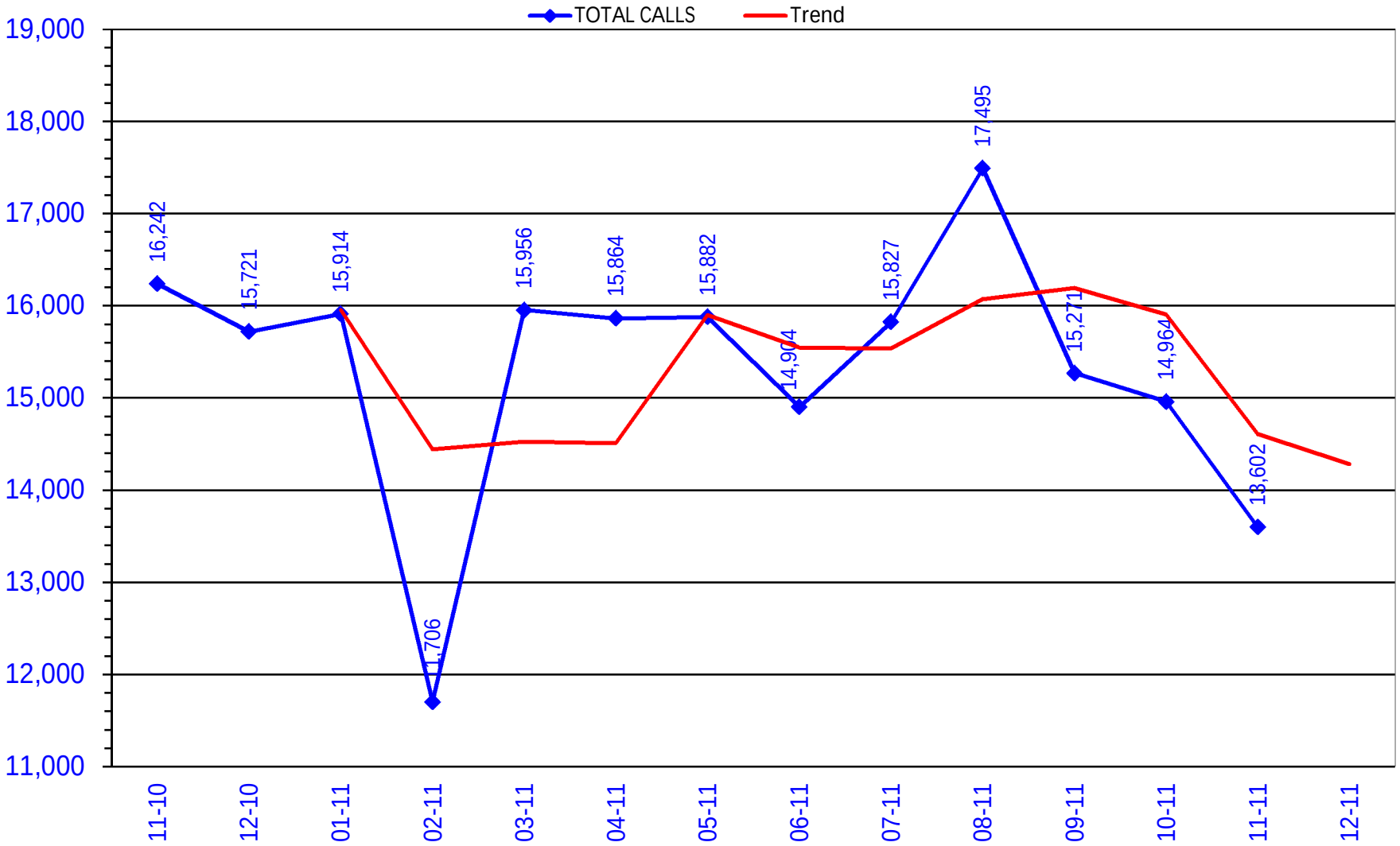
Duplicate Requests: 651

Letters: 1,776

No Process: 302

Changes to existing PAs: 571

CALL VOLUME MONTHLY REPORT:
November 2010 – November 2011



Appendix C

Vote on 2012 DUR Meeting Dates

Oklahoma Health Care Authority Drug Utilization Review Board
December 2011

Meetings are held the second Wednesday of each month.

January 11, 2012

February 8, 2012

March 14, 2012

April 11, 2012

May 9, 2012

June 13, 2012

July 11, 2012

August 8, 2012

September 12, 2012

October 10, 2012

November 14, 2012

December 12, 2012

Appendix D

Vote to Prior Authorize Multiple Sclerosis Medications

Oklahoma Health Care Authority
December 2011

This category was introduced for possible inclusion in the Product Based Prior Authorization program in September 2011. See the September, October, and November DUR packets for a more complete discussion of the category. This notice is presented to meet the statutory requirements of 63 O.S. Sec. 5030.5.

Recommendations

The College of Pharmacy recommends the following for the Multiple Sclerosis Category of Medications:

Tier 1	Tier 2
Lowest Supplemental Rebated Interferon β – 1a	Interferon β - 1a (Avonex®)
Lowest Supplemental Rebated Interferon β – 1b	Interferon β - 1a (Rebif®)
	Interferon β - 1b (Extavia®)
	Interferon β - 1b (Betaseron®)

Interferon Prior Authorization Criteria:

1. Documented diagnosis of relapsing remitting MS.
2. Tier-2 medications require failure of the preferred Tier-1 product defined as:
    a. Occurrence of an exacerbation after 6 months.
    b. Significant increase in MRI lesions after 6 months.
    c. Adverse reactions or intolerable side effects.
3. No concurrent use with other therapies.
4. Compliance will be checked for continued approval every 6 months.

Glatiramer Acetate (Copaxone®) Prior Authorization Criteria:

1. FDA approved diagnosis.
2. No concurrent use with other therapies.
3. Compliance will be checked for continued approval every 6 months.

Fingolimod (Gilenya®) Prior Authorization Criteria:

1. Documented diagnosis of relapsing remitting MS with at least one relapse in the previous 12 months, or transitioning from existing MS therapy.
2. No concurrent use with other therapies.
3. Compliance will be checked for continued approval every 6 months.

Appendix E

Vote to Prior Authorize Daliresp® (Roflumilast)

Oklahoma Health Care Authority
December 2011

Manufacturer	Forest Pharmaceuticals, Inc.
Classification	Phosphodiesterase Inhibitor
Status	Prescription Only

Recommendations

The College of Pharmacy recommends prior authorization of Daliresp® (roflumilast) with the following approval criteria:

1. Diagnosis of COPD with history of chronic bronchitis; **and**
2. FEV </= 50% of predicted; **and**
3. Smoking history >/= 20 pack-years; **and**
4. Inadequately controlled on long acting brochodilator therapy (must have 3 or more claims for long acting bronchodilators in the previous 6 months)

Appendix F

Vote to Prior Authorize Horizant® (gabapentin enacarbil)

Oklahoma Health Care Authority
December 2011

Manufacturer:	GlaxoSmithKline
FDA Status:	Prescription Only
Approved Indication:	Restless Legs Syndrome

Horizant® (gabapentin enacarbil) Summary

Horizant®, extended-release gabapentin enacarbil, a prodrug of gabapentin, was FDA approved in April, 2011 for treatment of moderate-to-severe primary Restless Legs Syndrome in adults. Gabapentin enacarbil undergoes extensive first-pass hydrolysis in enterocytes and the liver, to form gabapentin and other compounds. It is available in a 600 mg tablet for once daily dosing. Doses higher than 600 mg provided no additional benefits, but were associated with increased adverse reactions. The estimated acquisition cost is $3.48 per tab.

Recommendations

The College of Pharmacy recommends prior authorizing Horizant® using the following criteria:

1. FDA approved indication of Restless Legs Syndrome
2. Must be 18 years or older
3. Must provide documented treatment attempts at recommended dose with at least two of the following that did not yield adequate relief:
    a. carbidopo/levodopa
    b. pramipexole
    c. ropinirole
4. Reason that immediate release gabapentin cannot be used.

Appendix G

Vote to Prior Authorize Gralise™ (gabapentin extended-release)

Oklahoma Health Care Authority, December 2011

Recommendations

The College of Pharmacy recommends prior authorization of Gralise™ with the following criteria:

1. FDA-approved indication of postherpetic neuralgia.
2. Must provide documented treatment attempts at recommended dosing or contraindications to at least one agent from two of the following drug classes:
    a. Tricyclic antidepressants
    b. Anticonvulsants
    c. Topical or oral analgesics
3. Must provide a clinically significant reason why the member cannot take the immediate-release formulation of gabapentin.

Appendix H

Annual Review of Antihistamines-Fiscal Year 2011

Oklahoma HealthCare Authority
December 2011

Current Prior Authorization Criteria

Approval Criteria:

- A 14 day trial each of OTC loratadine and cetirizine within the last month is required before a Tier 2 medication can be approved.
- All Tier 2 products must be tried for 14 days each within the last 60 days before a Tier 3 medication can be approved unless no age appropriate Tier 2 product exists.
- Diagnosis must be for a chronic allergic condition or asthma.
- Prior authorization will be for 360 days.

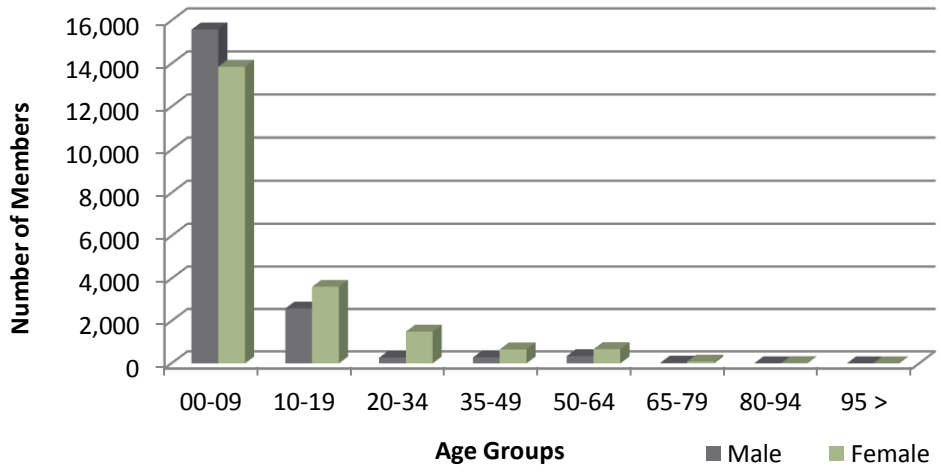
ORAL ANTIHISTAMINE MEDICATIONS		
Tier 1	**Tier 2**	**Tier 3**
OTC loratadine (Claritin®)	**Fexofenadine (Allegra®)**	**desloratadine (Clarinex®)**
OTC cetirizine (Zyrtec®)		**fexofenadine (Allegra® Syrup, ODT)**
		levocetirizine (Xyzal®)

Utilization of Antihistamines

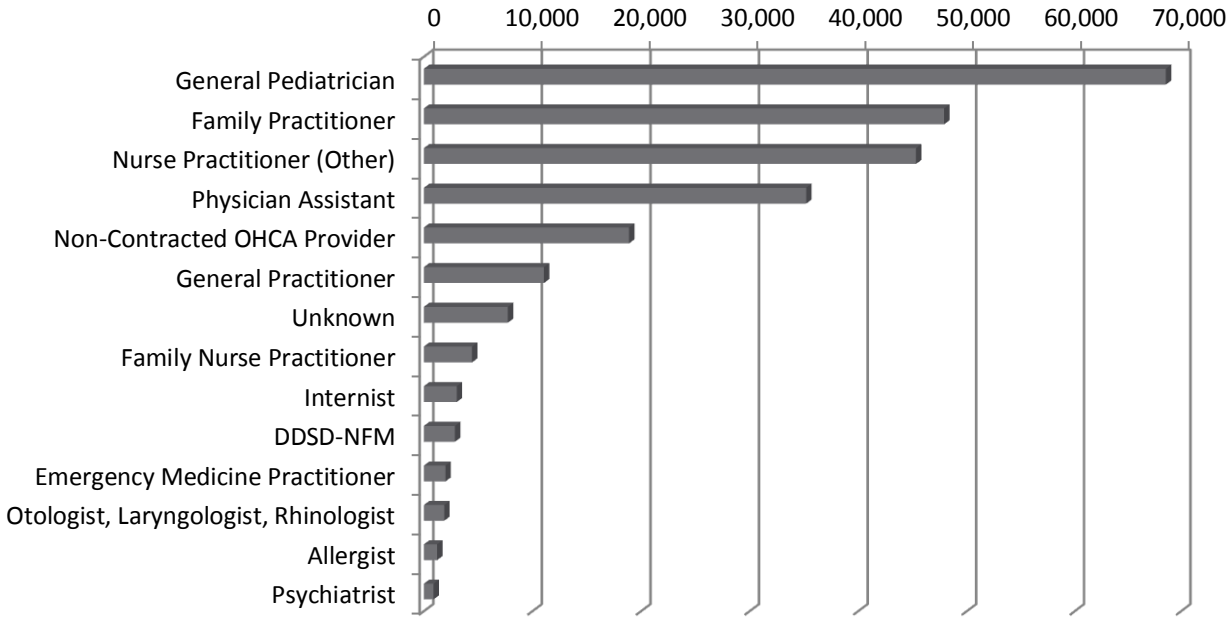
Comparison of Fiscal Years

Fiscal Year	Members	Claims	Cost	Cost/Claim	Perdiem	Units	Days
2010	86,757	196,991	$2,636,051.87	$13.38	$0.46	14,770,575	5,749,689
2011	99,465	255,455	$2,597,336.30	$10.17	$0.35	20,961,582	7,483,601
% Change	**14.60%**	**29.70%**	**-1.50%**	**-24.00%**	**-23.90%**	**41.90%**	**30.20%**
Change	**12,708**	**58,464**	**-$38,715.57**	**-$3.21**	**-$0.11**	**6,191,007**	**1,733,912**

Demographics of Members Utilizing Antihistamines: FY 2011



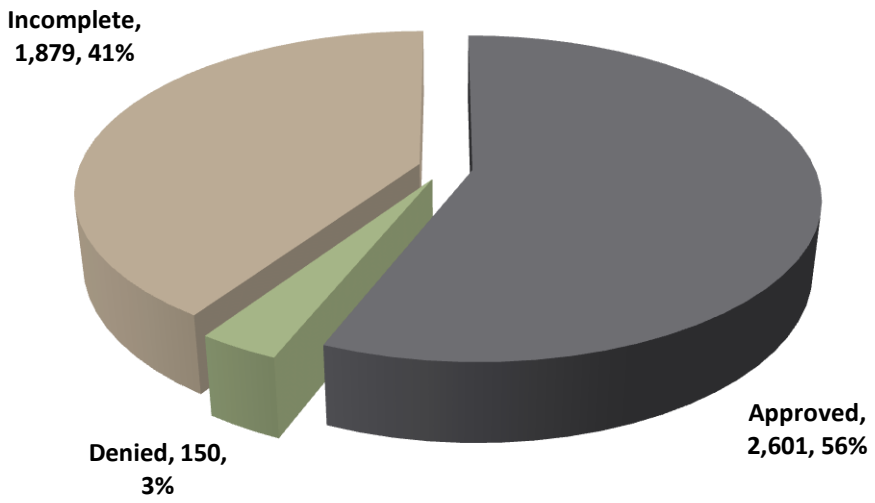
Prescribers of Antihistamines by Number of Claims: FY 2011



Prior Authorization of Antihistamines

There were a total of 4,630 petitions submitted for this PBPA category during fiscal year 2011. Please note that for this PBPA category the system will automatically search Tier 1 medications in member's claims history within a certain timeframe and if detected, the member can automatically get the Tier 2 medication without submitting a prior authorization form. The following chart shows the status of the submitted petitions.

Status of Petitions for Antihistamines: FY 2011



Market News and Updates

- **Allegra OTC® (fexofenadine)**
  - FDA-approved for OTC use January 25, 2011, and Sanofi-Aventis' version became available March 4, 2011.
  - Cost is approximately $20-25 for 45 tablets.
  - Other prescription formulations of fexofenadine have been discontinued and will not be available after current supplies are exhausted.
- **Levocetirizine dihydrochloride (Xyzal®)**
  - Entered the market November 2010, and is now available as a multi-source product with a State Maximum Allowable Cost (SMAC) designation.
  - Cost is approximately $13/30 tablets.

Conclusion and Recommendations

The College of Pharmacy recommends moving levocetirizine (Xyzal®) into Tier 2 and fexofenadine (Allegra OTC®) into Tier 3 of the PBPA criteria. The status of fexofenadine (Allegra OTC®) may be reconsidered when pricing is comparable to OTC loratadine and cetirizine. Current criteria will apply.

New tier structure:

ORAL ANTIHISTAMINE MEDICATIONS		
Tier 1	**Tier 2**	**Tier 3**
OTC loratadine (Claritin®)	**levocetirizine (Xyzal®)**	**desloratadine (Clarinex®)**
OTC cetirizine (Zyrtec®)		**fexofenadine (Allegra® OTC)**

Utilization Details of Antihistamines: Fiscal Year 2011

BRAND NAME	CLAIMS	UNITS	DAYS	MEMBERS	COST	UNITS/ DAY	CLAIMS/ MEMBER	PER DIEM	PERCENT COST
CETIRIZINE SYP 1MG/ML	72,885	8,886,270	2,047,878	35,995	$755,263.87	4.34	2.02	$0.37	29.08%
CETIRIZINE TAB 10MG	53,790	1,586,778	1,607,684	18,711	$419,656.67	0.99	2.87	$0.26	16.16%
LORATADINE TAB 10MG	44,810	1,451,838	1,458,370	17,435	$377,307.02	1	2.57	$0.26	14.53%
LORATADINE SYP 5MG/5ML	32,428	4,346,757	856,739	18,198	$359,035.85	5.07	1.78	$0.42	13.82%
CETIRIZINE SYP 5MG/5ML	13,220	1,627,268	377,842	7,287	$141,833.77	4.31	1.81	$0.38	5.46%
LORATADINE SOL 5MG/5ML	6,328	888,410	174,002	4,351	$72,790.10	5.11	1.45	$0.42	2.80%
ALLERGY RELF TAB 10MG	5,939	191,423	192,990	2,480	$53,504.90	0.99	2.39	$0.28	2.06%
CETIRIZINE TAB 5MG	4,218	124,664	125,587	1,585	$39,599.62	0.99	2.66	$0.32	1.52%
ALL DAY ALLG SYP 1MG/ML	4,073	498,411	109,819	2,153	$41,389.47	4.54	1.89	$0.38	1.59%
ALAVERT TAB 10MG	3,497	110,251	112,426	1,275	$46,742.40	0.98	2.74	$0.42	1.80%
SM LORATAD SYP 5MG/5ML	3,351	425,456	90,502	1,997	$34,960.07	4.7	1.68	$0.39	1.35%
FEXOFENADINE TAB 180MG	1,287	43,604	43,119	271	$40,005.04	1.01	4.75	$0.93	1.54%
ALLERGY TAB 10MG	1,209	36,682	36,822	493	$10,960.16	1	2.45	$0.30	0.42%
ALLEGRA SUS 30MG/5ML	1,191	244,400	32,614	296	$54,923.53	7.49	4.02	$1.68	2.11%
ALLERGY RELF SYP CHILD	1,077	139,064	27,559	641	$11,956.03	5.05	1.68	$0.43	0.46%
ALLERGY RELF TAB 10MG	891	34,728	34,929	416	$12,459.79	0.99	2.14	$0.36	0.48%
FEXOFENADINE TAB 30MG	823	46,966	24,594	166	$17,862.14	1.91	4.96	$0.73	0.69%
FEXOFENADINE TAB 60MG	758	39,803	22,471	178	$19,926.43	1.77	4.26	$0.89	0.77%
ALL DAY ALLG TAB 10MG	559	16,227	16,520	206	$4,379.46	0.98	2.71	$0.27	0.17%
LORATADINE 10MG TAB	539	17,162	17,121	304	$4,914.38	1	1.77	$0.29	0.19%
ALL DAY ALLG SOL 5MG/5ML	487	59,750	12,334	256	$5,116.37	4.84	1.9	$0.41	0.20%
ALL DAY ALLG SOL 1MG/ML	483	61,448	12,820	275	$5,378.40	4.79	1.76	$0.42	0.21%
ALLERGY TAB 10MG	373	11,159	11,429	149	$5,124.49	0.98	2.5	$0.45	0.20%
SM ALL DAY TAB ALLERGY	244	7,071	7,230	113	$1,901.69	0.98	2.16	$0.26	0.07%
CLARINEX SYP 0.5MG/ML	149	18,602	4,402	34	$8,244.08	4.23	4.38	$1.87	0.32%
XYZAL SOL	131	15,402	3,662	32	$9,389.32	4.21	4.09	$2.56	0.36%
XYZAL TAB 5MG	110	3,650	3,770	25	$11,085.76	0.97	4.4	$2.94	0.43%
ALLEGRA ODT TAB 30MG	110	5,820	3,240	30	$10,606.98	1.8	3.67	$3.27	0.41%
GNP ALL DAY TAB ALLERGY	104	2,998	2,998	53	$803.28	1	1.96	$0.27	0.03%
LEVOCETIRIZI TAB DHCL 5MG	72	2,150	2,450	32	$4,426.12	0.88	2.25	$1.81	0.17%
ALAVERT TAB 10MG	64	1,946	2,020	43	$638.16	0.96	1.49	$0.32	0.02%
CLARINEX TAB 5MG	63	2,000	1,880	12	$7,880.62	1.06	5.25	$4.19	0.30%
CETIRIZINE SOL 1MG/ML	60	8,634	1,644	34	$527.35	5.25	1.76	$0.32	0.02%
CLARINEX RDT TAB 2.5MG	33	855	990	6	$3,586.19	0.86	5.5	$3.62	0.14%
SM LORATADIN TAB 10MG	29	840	980	27	$411.70	0.86	1.07	$0.42	0.02%
SM LORATADIN TAB ALLG REL	18	456	546	10	$216.93	0.84	1.8	$0.40	0.01%
CLARINEX RDT TAB 5MG	16	480	480	3	$2,148.32	1	5.33	$4.48	0.08%
ALL DAY ALLERGY 10 MG TAB	13	388	388	4	$102.60	1	3.25	$0.26	0.00%
LORATADINE TAB ALLG REL	8	240	240	6	$116.48	1	1.33	$0.49	0.00%
SB ALLERGY TAB 10MG	8	240	240	6	$51.94	1	1.33	$0.22	0.00%
CETIRIZINE SOL 5MG/5ML	6	1,200	180	5	$101.76	6.67	1.2	$0.57	0.00%
ALLERCLEAR TAB 10MG	1	90	90	1	$6.99	1	1	$0.08	0.00%
Totals:	**255,455**	**20,961,582**	**7,483,601**	**99,465***	**$2,597,336.30**	**2.8**	**2.57**	**$0.35**	**100.00%**

**Total unduplicated number of members*

Appendix I

Fiscal Year 2011 Annual Review of Statin and Statin Combination Products

Oklahoma HealthCare Authority
December 2011

Current Prior Authorization of Statin and Statin Combination Products

For members new to statin therapy to qualify for a Tier 2 medication, there must be:

1. A trial, defined by at least 8 weeks of continuous therapy titrated to recommended dose, of Tier 1 simvastatin or pravastatin that did not yield adequate LDL reduction, but the minimum initiation dosing of the Tier 2 medication may only be at the moderate to high LDL lowering doses (i.e., doses equivalent to or 20 mg rosuvastatin or 40 mg atorvastatin).
2. Documented adverse effect or contraindication to two available lower tiered products.
3. Clinical exception for high risk members hospitalized for recent acute myocardial infarction or acute coronary syndrome for atorvastatin 40 mg or higher and rosuvastatin 20 mg or higher.

To qualify for a Tier 3 medication, there must be:

1. A trial, defined by at least 8 weeks of continuous therapy titrated to recommended dose, of a Tier 2 medication that did not yield adequate LDL reduction.
2. Documented adverse effect or contraindication to two Tier 2 products.
3. Clinical exceptions for Ezetimibe:
    a. Documented active liver disease.
    b. Documented unexplained, persistent elevations of serum transaminases.
    c. Documented statin related myopathy.

HMG-CoA Reductase Inhibitors (Statins) and Statin Combination Products		
Tier One	***Tier Two***	***Tier Three***
Fluvastatin (Lescol® & Lescol® XL)	Atorvastatin (Lipitor®)	Lovastatin (brand Altoprev®)
Lovastatin (Mevacor®)	Rosuvastatin (Crestor®)	Simvastatin/Ezetimibe (Vytorin®)
Pravastatin (Pravachol®)	Pitavastatin (Livalo®)	Ezetemibe (Zetia®)
Simvastatin (Zocor®)		
Statin/Niaspan® Combination Products		
Tier 1 Statins and/or Niaspan®	Lovastatin/Niacin CR (Advicor®)	
	Simvastatin/Niacin CR (Simcor®)	

During the summer of 2010 letters were sent to prescribers and pharmacies regarding dose equivalent conversion of tier-2 to tier-1 medications where appropriate. The conversion of members on low doses of Lipitor® and Crestor® to tier-1 medications with similar LDL-reduction potential was implemented during August 2010.

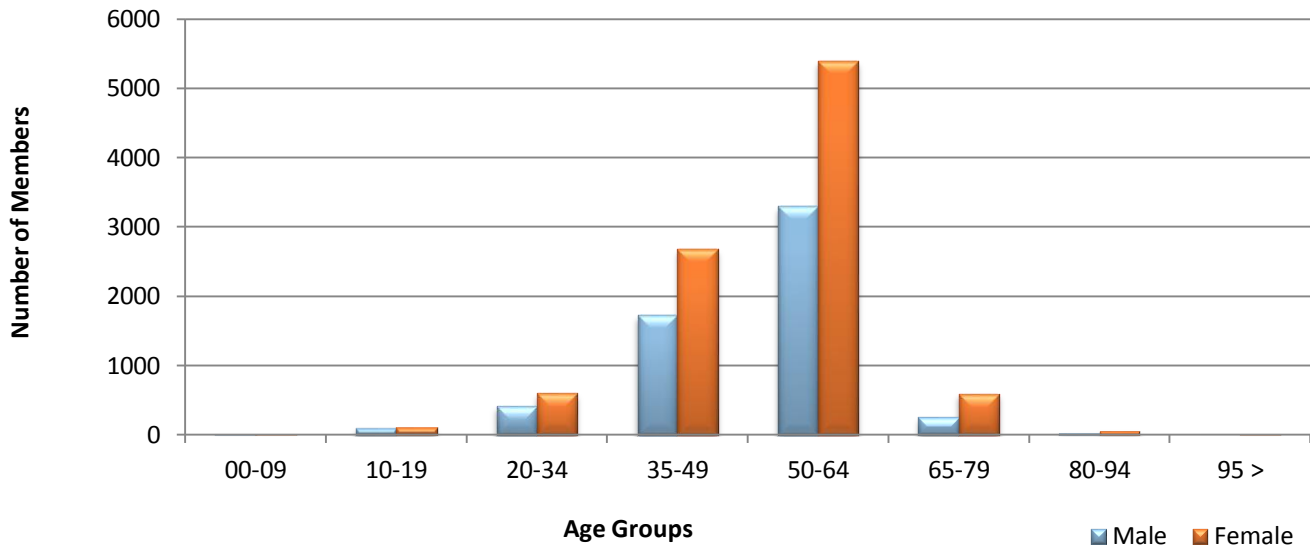
% LDL Reduction	*Pravastatin (Pravachol®)*	*Simvastatin (Zocor®)*	*Atorvastatin (Lipitor®)*	*Rosuvastatin (Crestor®)*	*Pitavastatin (Livalo®)*
25-32 %	20mg	10mg			1 mg
31-39 %	40mg	20mg	10mg		2 mg
37-45 %	80mg	40mg	20mg	5mg	4 mg
48-52 %		80mg	40mg	10mg	
55-60 %			80mg	20mg	
60-63 %				40mg	

Utilization of Statin and Statin Combination Products

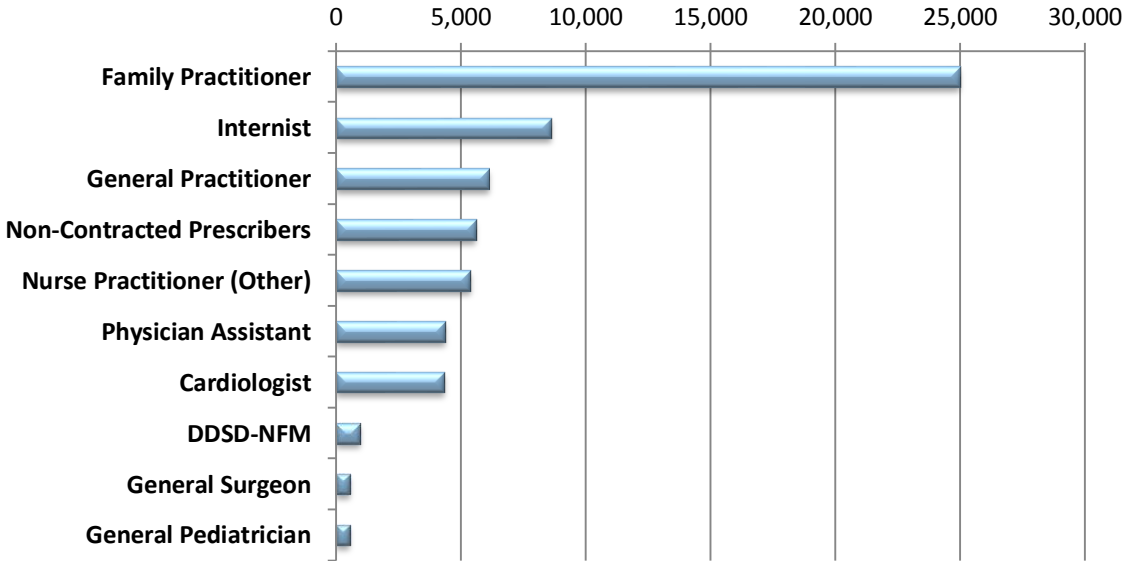
Utilization Trends

Fiscal Year	Members	Claims	Paid	Paid/Claim	Perdiem	Units	Days
2010	13,880	59,073	$4,099,347.98	$69.39	$1.69	2,451,969	2,429,669
2011	15,248	64,511	$2,331,510.47	$36.14	$0.87	2,725,667	2,689,517
% Change	9.90%	9.20%	-43.10%	-47.90%	-48.50%	11.20%	10.70%
Change	1,368	5,438	-$1,767,837.51	-$33.25	$0.82	273,698	259,848

Demographics for FY 2011

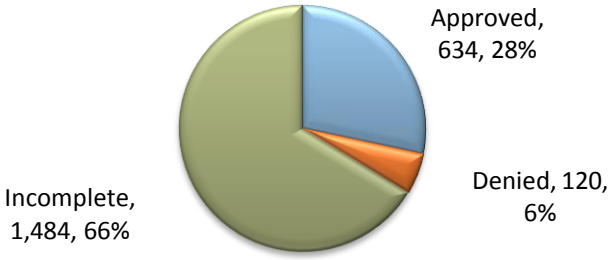


Top Prescriber Specialty by Number of Claims for FY 2011



Prior Authorization of Statin and Statin Combination Products

There were a total of 2,238 petitions submitted for this PBPA category during Fiscal Year 2011. The following chart shows the status of the submitted petitions:



Market News and Update

Anticipated Patent Expirations:
Lipitor® – December 2011
Zetia® – 2013
Vytorin® – 2013
Livalo® – 2015
Crestor® – 2016

In June of 2011, the FDA issued warnings regarding the increased risk of myopathy associated with simvastatin 80mg compared to lower doses of this drug or other drugs in the same class. The warnings also included new medications in which drug interactions may occur with simvastatin and recommendations on maximum simvastatin dosing if member is also using these medications concomitantly. The full FDA communication can be found at **http://www.fda.gov/Drugs/DrugSafety/ucm256581.htm.** After this warning was issued, clinical exceptions were allowed for members who were on interacting medications or needed LDL lowering in the range higher than could be reach with simvastatin 40mg.

Conclusions

The College of Pharmacy recommends moving Lipitor® to Tier 1 of the Statin PBPA category once the generic maximum allowable cost is comparable to Tier 1 products.

Utilization Details of Statin and Statin Combination Products: FY 2010

CHEMICAL NAME	BRAND NAME	CLAIMS	MEMBERS	COST	COST/ DAY	% COST
Simvastatin	SIMVASTATIN TAB 5MG	100	31	$630.26	$0.18	0.03%
Simvastatin	SIMVASTATIN TAB 10MG	2,813	742	$23,032.75	$0.22	1.12%
Simvastatin	ZOCOR TAB 10MG	4	1	$13.48	$0.11	0.00%
Simvastatin	SIMVASTATIN TAB 20MG	15,784	4,142	$132,333.26	$0.21	6.41%
Simvastatin	SIMVASTATIN TAB 40MG	14,218	3,922	$138,290.07	$0.23	6.70%
Simvastatin	SIMVASTATIN TAB 80MG	3,734	1,138	$38,810.87	$0.23	1.88%
	SUBTOTAL	**36,653**		**$333,110.69**	**$0.22**	**16.14%**
Pravastatin	PRAVASTATIN TAB 10MG	731	223	$5,539.98	$0.19	0.27%
Pravastatin	PRAVASTATIN TAB 20MG	4,424	1,402	$35,678.88	$0.19	1.73%
Pravastatin	PRAVASTATIN TAB 40MG	7,266	2,192	$62,063.19	$0.20	3.01%
Pravastatin	PRAVASTATIN TAB 80MG	1,036	326	$18,026.93	$0.39	0.87%
	SUBTOTAL	**13,457**		**$121,308.98**	**$0.21**	**5.88%**
Atorvastatin	LIPITOR TAB 10MG	532	329	$71,351.70	$3.22	3.45%
Atorvastatin	LIPITOR TAB 20MG	1,032	553	$192,678.24	$4.52	9.33%
Atorvastatin	LIPITOR TAB 40MG	3,307	678	$692,082.35	$4.74	33.51%
Atorvastatin	LIPITOR TAB 80MG	1,414	305	$296,215.71	$4.66	14.34%
	SUBTOTAL	**6,285**		**$1,252,328.00**	**$4.56**	**60.63%**
Lovastatin	LOVASTATIN TAB 10MG	459	134	$3,776.94	$0.19	0.18%
Lovastatin	LOVASTATIN TAB 20MG	2,608	700	$21,574.31	$0.20	1.04%
Lovastatin	LOVASTATIN TAB 40MG	1,682	429	$19,121.34	$0.27	0.93%
	SUBTOTAL	**4,749**		**$44,472.59**	**$0.22**	**2.15%**
Rosuvastatin	CRESTOR TAB 5MG	83	36	$16,154.78	$4.18	0.78%
Rosuvastatin	CRESTOR TAB 10MG	321	128	$58,512.33	$4.25	2.83%
Rosuvastatin	CRESTOR TAB 20MG	802	186	$144,305.28	$4.25	6.99%
Rosuvastatin	CRESTOR TAB 40MG	336	95	$61,196.27	$4.14	2.96%
	SUBTOTAL	**1,542**		**$280,168.66**	**$4.22**	**13.56%**
Fluvastatin	LESCOL CAP 20MG	15	5	$2,204.70	$2.94	0.11%
Fluvastatin	LESCOL CAP 40MG	34	14	$6,113.63	$3.38	0.30%
Fluvastatin	LESCOL XL TAB 80MG	60	14	$10,710.64	$3.92	0.52%
	SUBTOTAL	**109**		**$19,028.97**	**$3.60**	**0.93%**
Pitavastatin	LIVALO TAB 2MG	1	1	$105.06	$3.50	0.01%
Pitavastatin	LIVALO TAB 4MG	1	1	$105.06	$3.50	0.01%
	SUBTOTAL	**2**		**$210.12**	**$3.50**	**0.02%**
Niacin-Lovastatin	ADVICOR TAB 500-20MG	21	2	$2,179.71	$3.46	0.11%
Niacin-Lovastatin	ADVICOR TAB 1000-40	12	2	$2,123.23	$5.90	0.10%
Niacin-Simvastatin	SIMCOR TAB 500-20MG	41	13	$3,295.81	$2.70	0.16%
Niacin-Simvastatin	SIMCOR TAB 500-40MG	28	9	$2,048.58	$2.44	0.10%
Niacin-Simvastatin	SIMCOR TAB 1000-20	39	4	$5,022.77	$4.29	0.24%
	SUBTOTAL	**141**		**$14,670.10**	**$3.48**	**0.71%**
	TOTAL	**62,938**	**15,010***	**$2,065,298.11**	**$0.79**	**100.00%**

***Unduplicated total number of members.**

CHEMICAL NAME	BRAND NAME	CLAIMS	MEMBERS	COST	COST/ DAY	% COST
Ezetimibe	ZETIA TAB 10MG	582	140	$95,674.38	$3.86	35.94%
Ezetimibe-Simvastatin	VYTORIN TAB 10-40MG	514	97	$85,778.52	$3.84	32.22%
Ezetimibe-Simvastatin	VYTORIN TAB 10-20MG	225	45	$40,329.94	$3.84	15.15%
Ezetimibe-Simvastatin	VYTORIN TAB 10-80MG	213	47	$36,363.73	$3.77	13.66%
Ezetimibe-Simvastatin	VYTORIN TAB 10-10MG	39	8	$8,065.79	$3.94	3.03%
	TOTAL	**1,573**	**330***	**$266,212.36**	**$3.84**	**100.00%**

***Unduplicated total number of members.**

Appendix J

Fiscal Year 2011 Annual Review of Lovaza (omega-3-acid ethyl esters)

Oklahoma HealthCare Authority
December 2011

Current Prior Authorization of Lovaza (omega-3-acid ethyl esters)

Approval Criteria:

1. Laboratory documentation of severe hypertriglyceridemia (fasting triglycerides ≥500 mg/dL).
2. Previous failure with both nicotinic acid and fibric acid medications.

Utilization of Lovaza (omega-3-acid ethyl esters)

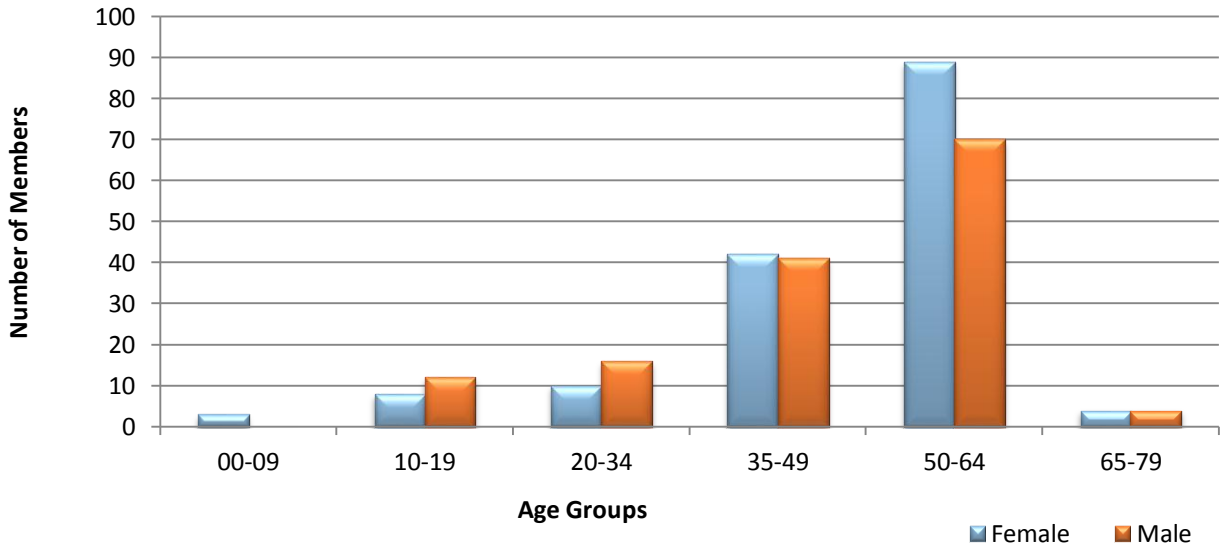
Utilization Trends

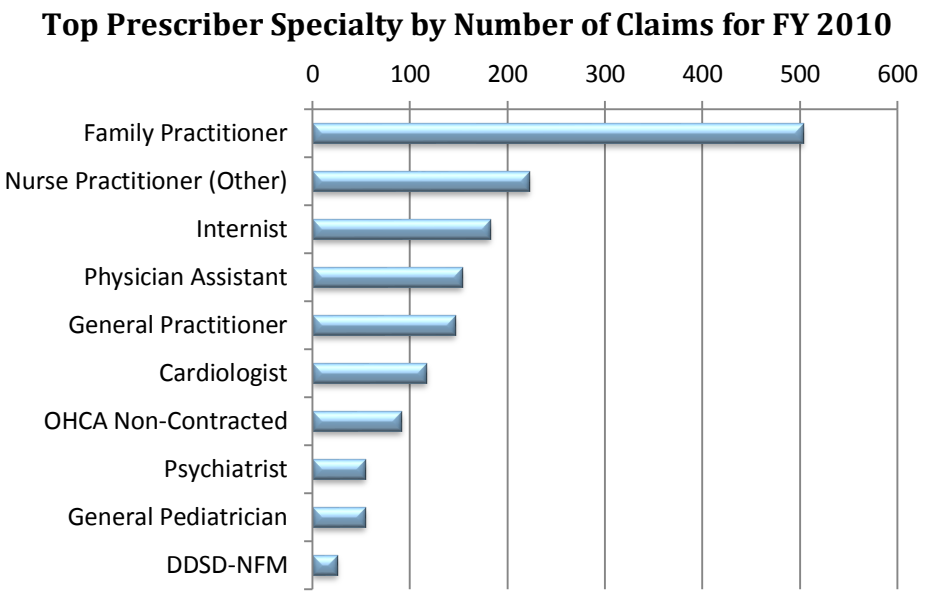
Fiscal Year	Members	Claims	Paid	Paid/Claim	Perdiem	Units	Days
2010	575	2,108	$289,641.45	$137.40	$4.53	220,634	63,996
2011	299	1,596	$229,326.24	$143.69	$4.71	167,716	48,659
% Change	-48.00%	-24.30%	-20.80%	4.60%	4.00%	-24.00%	-24.00%
Change	-276	-512	-$60,315.21	$6.29	$0.18	-52,918	-15,337

Utilization Details

BRAND NAME	CLAIMS	UNITS	DAYS	MEMBERS	COST	UNITS/DAY	CLAIMS/MEMBER	COST/ DAY
LOVAZA CAP 1GM	1,596	167,716	48,659	299	$229,326.24	3.45	5.34	$4.71

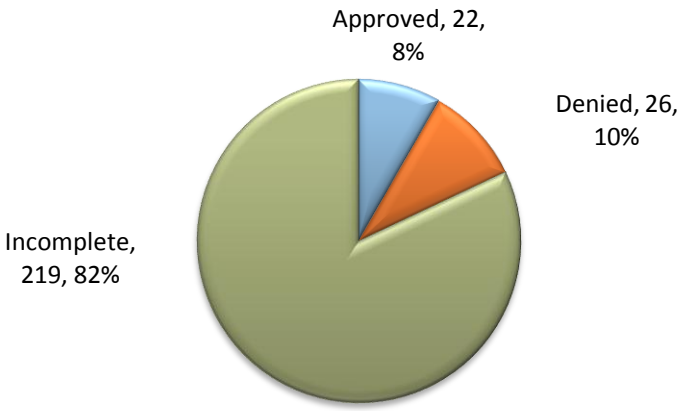
Demographics for FY 2010





Prior Authorization of Lovaza (omega-3-acid ethyl esters)

There were a total of 267 petitions submitted for this medication Fiscal Year 2011. The following chart shows the status of the submitted petitions:



Conclusions

The College of Pharmacy recommends no changes at this time.

Appendix K

30 Day Notice to Prior Authorize Xarelto® (rivaroxaban)

Oklahoma Health Care Authority, December 2011

Product Summary

Rivaroxaban is a factor Xa inhibitor indicated to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation and for the prophylaxis of deep vein thrombosis (DVT), which may lead to pulmonary embolism (PE), in patients undergoing knee or hip replacement surgery.

Comparison of Rivaroxaban with Warfarin and Enoxaparin

Rivaroxaban was compared to warfarin in a multi-national, double-blind non-inferiority study to reduce the risk of stroke and non-central nervous system (CNS) systemic embolism in patients with nonvalvular atrial fibrillation (AF). Patients had to have one or more of the following risk factors for stroke: a prior stroke, transient ischemic attack (TIA) or non-CNS systemic embolism; or two or more of the following: age ≥ 75 years, hypertension, heart failure or left ventricular ejection fraction ≤ 35% or diabetes. Rivaroxaban demonstrated non-inferiority to warfarin for the primary composite endpoint of first occurrence of stroke or non-CNS systemic embolism [HR: 0.88 (0.74, 1.030]. Superiority was not demonstrated.

For prophylaxis of DVT, two randomized, double-blind, clinical studies in patients undergoing elective hip replacement surgery were performed with rivaroxaban versus enoxaparin. The relative risk reduction was 71% (95% CI: 50, 83 p<0.001) and 76% (95% CI: 59, 86; p<0.001). In a similar study for knee replacement the relative risk reduction was 48% (95% CI: 34, 60; p<0.001).

More recently in a double-blind, placebo-controlled trial, patients with recent acute coronary syndrome were studied using rivaroxaban 2.5 or 5 mg BID versus placebo. Rivaroxaban showed significant improvement for the primary composite endpoint of death from cardiovascular causes, myocardial infarction, or stroke (HR, 0.84; 95% CI: 0.74, 0.96 p=0.008).

Nonvalvular AF	Cost	Annualized Cost
Rivaroxaban (Xarelto®) 20 mg	$7.70 (EAC per unit) qd	$2,772.00
Warfarin	$0.30 (Per Diem for all strengths)	$109.50
INR Monitoring*	$5.17	$82.72
Common Office Visit Cost*	$72.78	$1,164.48

*Annualized cost based on 16 visits per year.

DVT Prophylaxis Post Surgery	Cost	Total Therapy Cost (35 days)
Rivaroxaban (Xarelto®) 10 mg	$7.70 (EAC per unit) qd	$269.50
Enoxaparin (Lovenox®) 40 mg SC	$31.75 (EAC per 0.4 ml) qd	$1,111.32

Recommendation

The College of Pharmacy recommends prior authorization Xarelto® (rivaroxaban) with the following criteria:

1. For Xarelto® (rivaroxaban) 10 mg, the first 35 days will not require prior authorization to allow for use in DVT prophylaxis only.
2. For Xarelto® (rivaroxaban) 15 mg and 20 mg, a diagnosis with nonvalvular atrial fibrillation will be required.

PRODUCT DETAILS OF RIVAROXABAN - Xarelto®

FDA-APPROVED IN JULY 01, 2011

INDICATIONS: Xarelto® is indicated for prophylaxis of deep vein thrombosis (DVT), which may lead to pulmonary embolism (PE), in adults undergoing hip and knee replacement surgery. It is also indicated to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation.

DOSAGE FORMS:
Xarelto® is supplied:
10 mg tablets that are round, light red, biconvex and film-coated with a triangle pointing down above a "10" marked on one side and "Xa" on the other side.
15 mg tablets that are round, red, biconvex, and film-coated with a triangle pointing down above a "15" marked on one side and "Xa" on the other side.
20 mg tablets that are triangle-shaped, dark red and film-coated with a triangle pointing down above a "20" marked on one side and "Xa" on the other side.

ADMINISTRATION:

- DVT prophylaxis: The recommended dose of Xarelto® is 10 mg taken orally once daily with or without food. The initial dose should be taken at least 6 to 10 hours after surgery once hemostasis has been established.
- Nonvalvular Atrial Fibrillation:
    - CrCl > 50 ml/min: take 20 mg orally once daily with the evening meal
    - CrCl 15-50 ml/min: take 15 mg orally once daily with the evening meal
    - CrCl < 15 ml/min: avoid use

CONTRAINDICATIONS:
- Patients with hypersensitivity to Xarelto®.
- Patients with active pathological bleeding.

SPECIAL POPULATIONS:
- **Pregnancy Category C**: There are no adequate or well-controlled studies of Xarelto® in pregnant women, and dosing for pregnant women has not been established. Use Xarelto® with caution in pregnant patients because of the potential for pregnancy related hemorrhage and/or emergent delivery with an anticoagulant that is not readily reversible.

- **Labor and Delivery:** Safety and effectiveness of Xarelto® during labor and delivery have not been studied in clinical trials. However, in animal studies maternal bleeding and maternal and fetal death occurred at the Xarelto® dose of 40 mg/kg (about 17 times maximum human exposure of the unbound drug at the human dose of 10mg/d).
- **Nursing Mothers:** It is not known if Xarelto® is excreted in human milk. Xarelto® and/or its metabolites were excreted into the milk of rats. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from Xarelto®, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.
- **Pediatric Use:** The safety and effectiveness of Xarelto® in pediatric patients have not been established.
- **Geriatric Use:** Of the total number of patients in the RECORD 1-3 clinical studies evaluating Xarelto®, about 53% were 65 years and over, while about 15% were >75 years. In clinical trials the efficacy of Xarelto® in the elderly (65 years or older) was similar to that seen in patients younger than 65 years.
- **Hepatic Impairment:** The safety and pharmacokinetics of single-dose Xarelto® (10 mg) were evaluated in a study in healthy subjects (n=16) and subjects with varying degrees of hepatic impairment (see Table 5). No patients with severe hepatic impairment (Child-Pugh C) were studied. Compared to healthy subjects with normal liver function, significant increases in rivaroxaban exposure were observed in subjects with moderate hepatic impairment (Child-Pugh B). Increases in pharmacodynamic effects were also observed.
- **Renal Impairment:** The safety and pharmacokinetics of single-dose Xarelto® (10 mg) were evaluated in a study in healthy subjects [CrCl ≥80 mL/min (n=8)] and in subjects with varying degrees of renal impairment (see Table 4). Compared to healthy subjects with normal creatinine clearance, rivaroxaban exposure increased in subjects with renal impairment. Increases in pharmacodynamic effects were also observed.

WARNINGS & PRECAUTIONS:

- **Increase Risk of Stroke after Discontinuation in Nonvalvular Atrial Fibrillation:** Discontinuing Xarelto® in the absence of adequate alternative anticoagulation increases the risk of thrombotic events. An increase rate of stroke was observed during the transition from Xarelto® to warfarin in clinical trials in atrial fibrillation patients. If Xarelto® must be discontinued for a reason other than pathological bleeding, consider administering another anticoagulant.
- **Spinal/Epidural Anesthesia or Puncture:** When neuraxial anesthesia (spinal/epidural anesthesia) or spinal puncture is employed, patients treated with anticoagulant agents for prevention of thromboembolic complications are at risk of developing an epidural or spinal hematoma which can result in long-term or permanent paralysis *[see Boxed Warning]*.
- **Risk of Bleeding:** Xarelto® increases the risk of bleeding and can cause serious and fatal bleeding. Major hemorrhages including intracranial, epidural hematoma, gastrointestinal, retinal, and adrenal bleeding have been reported. Use Xarelto® with caution in conditions with increased risk of hemorrhage. Concomitant use of drugs affecting hemostasis increases the risk of bleeding. These include platelet aggregation inhibitors, other antithrombotic agents, fibrinolytic therapy, thienopyridines and chronic use of non-steroidal anti-inflammatory drugs. Bleeding can occur at any site during therapy with Xarelto®. An unexplained fall in hematocrit or blood pressure should lead to a search for a bleeding site. Promptly evaluate any signs or symptoms of blood loss.

- **Risk of Pregnancy Related Hemorrhage:** Xarelto® should be used with caution in pregnant women and only if the potential benefit justifies the potential risk to the mother and fetus. Xarelto® dosing in pregnancy has not been studied. The anticoagulant effect of Xarelto® cannot be monitored with standard laboratory testing nor readily reversed. Promptly evaluate any signs or symptoms suggesting blood loss (e.g., a drop in hemoglobin and/or hematocrit, hypotension, or fetal distress).
- **Severe Hypersensitivity Reactions:** There were postmarketing cases of anaphylaxis in patients treated with Xarelto® to reduce the risk of DVT. Patients who have a history of severe hypersensitivity reaction to Xarelto® should not receive Xarelto®

ADVERSE REACTIONS (Reported in >1%): The largest adverse effect is bleeding. Of which, mostly occurred during the first week of treatment after a surgery (for major bleeds).

- Wound Secretion
- Pain in Extremity
- Muscle Spasms
- Syncope
- Pruritus
- Blisters

Adverse reactions that at a frequency of less than 1%: for patients treated in the clinical studies.

- Dysuria

DRUG INTERACTIONS: Rivaroxaban is a substrate of CYP3A4/5, CYP2J2, and the P-gp and ATP-binding cassette G2 (ABCG2) transporters. Inhibitors and inducers of these CYP450 enzymes or transporters may result in changes in rivaroxaban exposure.

- **Drugs that Inhibit Cytochrome P450 (CYP) Enzymes:** In drug interaction studies evaluating the concomitant use with drugs that are combined P-gp and CYP3A4 inhibitors, increases in rivaroxaban exposure and pharmacodynamic effects (i.e., factor Xa inhibition and PT prolongation) were observed. Significant increases in rivaroxaban exposure may increase bleeding risk.
- In a drug interaction study, co-administration of Xarelto® (20 mg single dose with food) with a drug that is a combined P-gp and strong CYP3A4 inducer (rifampicin titrated up to 600 mg once daily) led to an approximate decrease of 50% and 22% in AUC and Cmax, respectively. Similar decreases in pharmacodynamic effects were also observed. These decreases in exposure to rivaroxaban may decrease efficacy. Avoid concomitant use of Xarelto® with drugs that are combined P-gp and strong CYP3A4 inducers (e.g., carbamazepine, phenytoin, rifampin, St. John's wort). Consider increasing the Xarelto® dose if these drugs must be coadministered.

PATIENT INFORMATION:

Instructions for Patient Use

- Advise patients to take Xarelto® only as directed.
- Remind patients not to discontinue Xarelto® prematurely without first talking to their health-care professional.
- If a dose is missed, advise the patient to take Xarelto® as soon as possible and continue on the following day with their once daily dose regimen.

Bleeding Risks
If patients have had neuraxial anesthesia or spinal puncture, and particularly, if they are taking concomitant NSAIDs or platelet inhibitors, advise patients to watch for signs and symptoms of spinal or epidural hematoma, such as tingling, numbness (especially in the lower limbs) and muscular weakness.

If any of these symptoms occur, advise the patient to contact his or her physician immediately. Advise patients to report any unusual bleeding or bruising to their physician. Inform patients that it might take them longer than usual to stop bleeding, and that they may bruise and/or bleed more easily when they are treated with Xarelto®.

Concomitant Medication and Herbals
Advise patients to inform their physicians and dentists if they are taking, or plan to take, any prescription or over-the-counter drugs or herbals, so their healthcare professionals can evaluate potential interactions.

Pregnancy and Pregnancy-Related Hemorrhage
Advise patients to inform their physician immediately if they become pregnant or intend to become pregnant during treatment with Xarelto®. Advise pregnant women receiving Xarelto® to immediately report to their physician any bleeding or symptoms of blood loss.

Nursing
Discontinue drug or discontinue nursing.

Females of Reproductive Potential
Advise patients who can become pregnant to discuss pregnancy planning with their physician.

REFERENCES

Xarelto® Label Information. Janssen Pharmaceuticals, Inc.Available online at: http://www.xareltohcp.com/sites/default/files/pdf/xarelto_0.pdf#zoom=100 . Last revised November 2011.

30 Day Notice to Prior Authorize Brilinta™ (ticagrelor)

Oklahoma Health Care Authority, December 2011

Product Summary

Ticagrelor is a $P2Y_{12}$ platelet inhibitor indicated to reduce the rate of thrombotic cardiovascular events in patients with acute coronary syndrome (ACS) (unstable angina, non-ST elevation myocardial infarction, or ST elevation myocardial infarction). In patients treated with PCI (percutaneous coronary intervention), it also reduces the rate of stent thrombosis. Ticagrelor was studied in combination with aspirin, however maintenance doses above 100 mg decrease ticagrelor's effectiveness.

Comparison of Ticagrelor and Clopidogrel

Ticagrelor was compared to clopidogrel in a randomized double-blind study. Patients could be included if they had been previously treated with clopidogrel and regardless of the intent to manage medically or invasively. The study endpoint was a composite of first occurrence of cardiovascular death, non-fatal MI (excluding silent MI), or non-fatal stroke. The hazard ratio was in favor of ticagrelor at 0.84 (0.77, 0.92; p. 0.0003).

Cost Comparison if Similar Products

	EAC per unit	Monthly Cost
Ticagrelor (Brilinta™) 90 mg twice daily	3.82	$229.20
Clopidogrel (Plavix®) 75 mg once daily	6.42	$192.60
Prasugrel (Effient®) 10 mg once daily	6.41	$192.30

Recommendation

The College of Pharmacy recommends prior authorization Brilinta™ (ticagrelor) with the following criteria:

1. Brilinta™ (ticagrelor) therapy will be approved for members who meet approved diagnostic criteria: The approved diagnosis is acute coronary syndrome (ACS) (unstable angina, non-ST elevation myocardial infarction, or ST elevation myocardial infarction) with or without percutaneous coronary intervention (PCI).
2. Length of approval: 1 year.

As with clopidogrel and prasugrel, the first 90 days will not require prior authorization.

PRODUCT DETAILS OF BRILINTA™ (TICAGRELOR)

FDA-APPROVED JULY 20, 2011

INDICATIONS: Brilinta™ is indicated as a treatment to reduce the rate of thrombotic cardiovascular events in patients with acute coronary syndrome (ACS) (unstable angina, non-ST elevation MI, or ST elevation MI). It has been shown to reduce the rate of a combined endpoint of cardiovascular death, MI, or stroke compared to clopidogrel. In patients treated with PCI, it also reduced the rate of stent thrombosis. Brilinta™ has been studied in ACS in combination with aspirin. Maintenance doses of aspirin above 100 mg decreased the effectiveness of **:** Brilinta™. Avoid maintenance doses of aspirin above 100 mg daily.

DOSAGE FORMS:

- Brilinta™ is supplied as yellow, biconvex, round tablets, film-coated marked with a "90" above "T" on one side. Each tablet contains 90 mg of ticagrelor.

ADMINISTRATION:

- The recommended dosage for patients is 180 mg (two 90 mg tablets) oral loading dose.
- Continue treatment with 90 mg twice daily.
- After initial loading dose of aspirin (325 mg) use **:** Brilinta™ with a daily maintenance dose of 70-100 mg.

CONTRAINDICATIONS:

- History of intracranial hemorrhage
- Active pathological bleeding
- Severe hepatic impairment

SPECIAL POPULATIONS:

- **Pregnancy Category C**: There are no adequate and well controlled studies of **:** Brilinta™ in pregnant women. Brilinta™ should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. In animal studies, ticagrelor caused structural abnormalities at maternal doses about 5 to 7 times the maximum recommended human dose (MRHD) based on body surface area. Brilinta™ should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
  In reproductive toxicology studies, pregnant rats received ticagrelor during organogenesis at doses from 20 to 300 mg/kg/day. The lowest dose was approximately the same as the MRHD of 90 mg twice daily for a 60 kg human on a mg/m2 basis. Adverse outcomes in offspring occurred at doses of 300 mg/kg/day (16.5 times the MRHD on a mg/m2 basis) and included supernumerary liver lobe and ribs, incomplete ossification of sternebrae, displaced articulation of pelvis, and misshapen/misaligned sternebrae. When pregnant rabbits received ticagrelor during organogenesis at doses from 21 to 63 mg/kg/day, fetuses exposed to the highest maternal dose of 63 mg/kg/day (6.8 times the MRHD on a mg/m2 basis) had delayed gall bladder development and incomplete ossification of the hyoid, pubis and sternebrae occurred. In a prenatal/postnatal study, pregnant rats received ticagrelor at doses of 10 to 180 mg/kg/day during late gestation and lactation. Pup death and effects on pup growth were observed at 180 mg/kg/day (approximately 10 times the MRHD on a mg/m2 basis). Relatively minor effects such as delays in pinna unfolding and eye opening occurred at doses of 10 and 60 mg/kg (approximately one-half and 3.2 times the MRHD on a mg/m2 basis).

It is not known whether ticagrelor or its active metabolites are excreted in human milk. Ticagrelor is excreted in rat milk. Because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from Brilinta™, a decision should be made whether to discontinue nursing or to discontinue drug, taking into account the importance of the drug to the mother.

- **Pediatric Use:** The safety and effectiveness of Brilinta™ in pediatric patients have not been established.
- **Geriatric Use:** In PLATO, 43% of patients were ≥65 years of age and 15% were ≥75 years of age. The relative risk of bleeding was similar in both treatment and age groups. No overall differences in safety or effectiveness were observed between these patients and younger patients. While this clinical experience has not identified differences in responses between the elderly and younger patients, greater sensitivity of some older individuals cannot be ruled out.
- **Hepatic Impairment:** Brilinta™ has not been studied in the patients with moderate or severe hepatic impairment. Ticagrelor is metabolized by the liver and impaired hepatic function can increase risks for bleeding and other adverse events. Hence, Brilinta™ is contraindicated for use in patients with severe hepatic impairment and its use should be considered carefully in patients with moderate hepatic impairment. No dosage adjustment is needed in patients with mild hepatic impairment
- **Renal Impairment:** No dosage adjustment is necessary for patients with renal impairment. Patients receiving dialysis have not been studied.

WARNINGS & PRECAUTIONS:

- **Bleeding:** Ticagrelor increases the risk of bleeding. Use is contraindicated in patients with active pathological bleeding and presence or history of intracranial hemorrhage. Additional risk factors for bleeding include propensity to bleed (eg, recent trauma or surgery, recent or recurrent GI bleeding, active PUD, moderate-severe hepatic impairment), CABG or other surgical procedure, concomitant use of medications that increase risk of bleeding (eg, warfarin, NSAIDs). Bleeding should be suspected if patient becomes hypotensive after undergoing recent coronary angiography, PCI, CABG, or other surgical procedure even if overt signs of bleeding do not exist. Hemostatic benefits of platelet transfusions are not known; may inhibit transfused platelets. Therapy may be resumed after a bleeding event only after the source is identified and controlled.
- **Hyperuricemia:** Use with caution in patients with a history of hyperuricemia or gouty arthritis. Renal uptake and transport of uric acid are inhibited by ticagrelor and its active metabolite and the risk of hyperuricemia may be increased. Use is not recommended in patients with uric acid nephropathy.
- **Respiratory:** Dyspnea (often mild-to-moderate and transient) was observed more frequently in patients receiving ticagrelor than clopidogrel during clinical trials; resolution of dyspnea was observed within 1 week in approximately one-third of patients. Patients with new, prolonged, or worsening dyspnea should be evaluated and if necessary, therapy discontinued.
- Discontinuation of Brilinta™**: Avoid interruption of treatment. If Brilinta™ must be temporarily discontinued (e.g., to treat bleeding or for elective surgery), restart it as soon as possible. Discontinuation of Brilinta™ will increase the risk of myocardial infarction, stent thrombosis, and death.**

ADVERSE REACTIONS (Reported in >3%):

- Uric acid increase
- Dyspnea
- Headache
- Cough
- Dizziness
- Nausea
- Atrial fibrillation
- Hypertension
- Non-cardiac chest pain
- Diarrhea
- Back pain
- Hypotension
- Fatigue
- Chest pain

Adverse reactions that at a frequency of <1 % postmarketing and/or case reports:

- Confusion, conjunctival hemorrhage, gastritis, hemarthrosis, hemoptysis, intracranial hemorrhage (including fatalities), intraocular hemorrhage, paresthesia, retinal hemorrhage, retroperitoneal hemorrhage

DRUG INTERACTIONS: Ticagrelor is predominantly metabolized by CYP3A4 and to a lesser extent CYP3A5.

- CYP3A inhibitors*:* **Avoid use of strong inhibitors of CYP3A (e.g., ketoconazole, itraconazole, voriconazole, clarithromycin, nefazodone, ritonavir, saquinavir, nelfinavir, indinavir, atazanavir and telithromycin).**
- CYP3A inducers*:* **Avoid use with potent inducers of CYP3A (e.g., rifampin, dexamethasone, phenytoin, carbamazepine and phenobarbital).**
- Aspirin*:* **Use of Brilinta™ with aspirin maintenance doses above 100 mg reduced the effectiveness of Brilinta™**
- Ticagrelor is an inhibitor of CYP3A4/5 and the P-glycoprotein transporter.
- Simvastatin, lovastatin: **Brilinta™ will result in higher serum concentrations of simvastatin and lovastatin because these drugs are metabolized by CYP3A4. Avoid simvastatin and lovastatin doses greater than 40 mg.**
- Digoxin: **Because of inhibition of the P-glycoprotein transporter, monitor digoxin levels with initiation of or any change in Brilinta™ therapy.**

PATIENT INFORMATION:

- Benefits and Risks: Tell patients to take Brilinta™ exactly as prescribed. Inform patients not to discontinue Brilinta™ without discussing it with the prescribing physician. Tell patients daily doses of aspirin should not exceed 100 mg and to avoid taking any other medications that contain aspirin.
- Tell patients to read the Medication Guide.
- Inform patients that they will bleed and bruise more easily, or take longer than usual to stop bleeding, and should report any unanticipated, prolonged or excessive bleeding, or blood in their stool or urine.

- Inform patients that Brilinta™ can cause shortness of breath. Tell them to contact their doctor if they experience unexpected shortness of breath, especially if severe.
- Tell patients to inform physicians and dentists that they are taking Brilinta™ before any surgery or dental procedure.
  Tell the doctor performing any surgery or dental procedure to talk to the prescribing physician before stopping Brilinta™.
- Tell patients to list all prescription medications, over-the-counter medications or dietary supplements they are taking or plan to take so the physician knows about other treatments that may affect bleeding risk (e.g. warfarin, heparin).

REFERENCES

Brilinta™ Label Information. AstraZeneca Pharmaceuticals, Inc. Available online at: http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?id=48936. Last revised July 2011.

Appendix L

U.S. Department of Health & Human Services

FDA U.S. Food and Drug Administration

News & Events

FDA NEWS RELEASE

For Immediate Release: Nov. 30, 2011
Media Inquiries: Sandy Walsh, 301-796-4669, sandy.walsh@fda.hhs.gov
Consumer Inquiries: 888-INFO-FDA

FDA approves first generic version of cholesterol-lowering drug Lipitor

The U.S. Food and Drug Administration today approved the first generic version of the cholesterol-lowering drug Lipitor (atorvastatin calcium tablets).

Ranbaxy Laboratories Ltd. has gained approval to make generic atorvastatin calcium tablets in 10 milligram, 20 mg, 40 mg, and 80 mg strengths. The drug will be manufactured by Ohm Laboratories in New Brunswick, N.J.

People who have high blood cholesterol levels have a greater chance of getting heart disease. By itself, the condition usually has no signs or symptoms. Thus, many people do not know that their cholesterol levels are too high.

"This medication is widely used by people who must manage their high cholesterol over time, so it is important to have affordable treatment options," said Janet Woodcock, M.D., director of the FDA's Center for Drug Evaluation and Research. "We are working very hard to get generic drugs to people as soon as the law will allow."

Not all cholesterol in your blood is bad. There are three kinds of blood cholesterol that you should know about: high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglycerides. HDL (good cholesterol) helps keep cholesterol from building up in the arteries. LDL (bad cholesterol) is the main source of cholesterol buildup and blockage in the arteries, which can prevent proper blood flow to your heart and lead to a heart attack. Triglycerides can lead to hardening of the arteries.

Atorvastatin is a statin, a type of drug that lowers cholesterol in the body by blocking an enzyme in the liver. Atorvastatin is used along with a low-fat diet to lower the LDL cholesterol and triglycerides in the blood. The drug can raise HDL cholesterol as well. Atorvastatin lowers the risk for heart attack, stroke, certain types of heart surgery, and chest pain in patients who have heart disease or risk factors for heart disease such as age, smoking, high blood pressure, low HDL, or family history of early heart disease.

In the clinical trials for Lipitor, the most commonly reported adverse reactions in patients were: inflammation of the nasal passages, joint pain, diarrhea, and urinary tract infection.

Generic drugs approved by FDA have the same high quality and strength as brand-name drugs. The generic manufacturing and packaging sites must pass the same quality standards as those of brand-name drugs.

Information about the availability of generic atorvastatin can be obtained from Ranbaxy.

For more information:

FDA: Understanding Generic Drugs [1]

National Heart Lung and Blood Institute: What is Cholesterol? [2]

Information on specific drug products, Drugs@FDA [3]

The FDA, an agency within the U.S. Department of Health and Human Services, protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products.

#

RSS Feed for FDA News Releases [4] [what is RSS? [5]]

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2. http://www.nhlbi.nih.gov/health/health-topics/topics/hbc/
3. http://www.accessdata.fda.gov/scripts/cder/drugsatfda/
4. http://www.fda.gov/AboutFDA/ContactFDA/StayInformed/RSSFeeds/PressReleases/rss.xml
5. http://www.fda.gov/AboutFDA/ContactFDA/StayInformed/RSSFeeds/ucm144575.htm

U.S. Department of Health & Human Services

FDA U.S. Food and Drug Administration

News & Events

FDA Commissioner Removes Breast Cancer Indication from Avastin Label

FDA Commissioner Margaret Hamburg is revoking the agency's accelerated approval of the breast cancer indication for Avastin (bevacizumab), manufactured by Genentech. Avastin used for metastatic breast cancer has not been shown to provide a benefit, in terms of delay in the growth of tumors, that would justify its serious and potentially life-threatening risks. Nor is there evidence that use of Avastin will either help women with breast cancer live longer or improve their quality of life.

Today's decision involves Avastin used in combination with the cancer drug paclitaxel for those patients who have not been treated with chemotherapy for their form of metastatic breast cancer known as HER2 negative. This indication must now be removed from Avastin's product labeling.

Avastin will still remain on the market as an approved treatment for certain types of colon, lung, kidney and brain cancer (glioblastoma multiforme).

Avastin was approved for metastatic breast cancer in February 2008 under the FDA's accelerated approval program, which allows a drug to be approved based on data that are not sufficiently complete to permit full approval. The accelerated approval program provides earlier patient access to promising new drugs to treat serious or life-threatening conditions while confirmatory clinical trials are conducted. If the clinical trials do not justify the continued approval of the drug or a specific drug indication, the agency may revoke its approval. In this case, the accelerated approval was based on promising results from one study that suggested that the drug could provide a meaningful increase in the amount of time from when treatment is started until the tumor grows or the death of the patient.

After the accelerated approval of Avastin for breast cancer, the drug's sponsor, Genentech, completed two additional clinical trials and submitted the data from those studies to the FDA. These data showed only a small effect on tumor growth without evidence that patients lived any longer or had a better quality of life compared to taking standard chemotherapy alone – not enough to outweigh the risk of taking the drug.

FDA's Center for Drug Evaluation and Research, which is responsible for the approval of this drug, ultimately concluded that the results of these additional studies did not justify continued approval and notified Genentech it was proposing to withdraw approval of the indication. Genentech did not agree with the Center's evaluation of the data and, following the procedures set out in FDA regulations, requested a hearing on the Center's withdrawal proposal, with a decision to be made by the Commissioner. That hearing took place June 28-29, 2011.

Dr. Hamburg has now made her decision based on a review of the arguments and evidence presented at the hearing, briefs filed by both CDER and Genentech before and after the hearing, public comments and data from multiple clinical trials.

For More Information:

- Decision of the Commissioner [1] (PDF - 4.4MB)
- Press Release [2]
- Questions and Answers: Removing Metastatic Breast Cancer as an Indication from Avastin's Product Labeling [3]
- Commissioner's Opening Statement from Media Call [4]
- Hearing Information [5]

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U.S. Department of Health & Human Services

FDA U.S. Food and Drug Administration

News & Events

FDA NEWS RELEASE

For Immediate Release: Nov. 18, 2011
Media Inquiries: Erica Jefferson, 301-796-4988, erica.jefferson@fda.hhs.gov
Consumer Inquiries: 888-INFO-FDA

FDA approves Eylea for eye disorder in older people
Maintains clearness of vision in those with wet age-related macular degeneration

The U.S. Food and Drug Administration today approved Eylea (aflibercept) to treat patients with wet (neovascular) age-related macular degeneration (AMD), a leading cause of vision loss and blindness in Americans ages 60 and older.

AMD gradually destroys a person's sharp, central vision. It affects the macula, the part of the eye that allows people to see fine detail needed to do daily tasks such as reading and driving.

There are two forms of AMD, a wet form and a dry form. The wet form of AMD includes the growth of abnormal blood vessels. The blood vessels can leak fluid into the central part of the retina, also known as the macula. When fluid leaks into the macula, the macula thickens and vision loss occurs. An early symptom of wet AMD occurs when straight lines appear to be wavy.

"Eylea is an important new treatment option for adults with wet AMD," said Edward Cox, M.D., M.P.H, director of the Office of Antimicrobial Products in FDA's Center for Drug Evaluation and Research. "It is a potentially blinding disease and the availability of new treatment options is important."

The safety and effectiveness of Eylea was evaluated in two clinical trials involving 2,412 adult patients. People in the study received either Eylea or Lucentis (ranibizumab injection). The primary endpoint in each study was a patient's clearness of vision (visual acuity) after one year of treatment.

Eylea is injected into the eye either every four weeks or every eight weeks by an ophthalmologist. The studies showed that Eylea was as effective as Lucentis in maintaining or improving visual acuity.

The most commonly reported side effects in patients receiving Eylea included eye pain, blood at the injection site (conjunctival hemorrhage), the appearance of floating spots in a person's vision (vitreous floaters), clouding of the eye lens (cataract), and an increase in eye pressure.

Eylea should not be used in those who have an active eye infection or active ocular inflammation. Eylea has not been studied in pregnant women, so the treatment should be used only in pregnant women if the potential benefits of the treatment outweigh any potential risks. Age related macular degeneration does not occur in children and Eylea has not been studied in children.

Other FDA-approved treatment options for wet AMD include: Visudyne (verteporfin for injection) approved in 2000, Macugen (pegaptanib sodium injection) approved in 2004, and Lucentis (ranibizumab injection) approved in 2006.

Eylea is marketed by Tarrytown, N.Y.-based Regeneron Pharmaceuticals Inc.

For more information:

FDA: Spotlight on Drug Innovation – Update of FDA's novel drug approvals in 2011 [1]

NEI: Facts about Age-Related Macular Degeneration [2]

The FDA, an agency within the U.S. Department of Health and Human Services, protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products.

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