Drug Utilization Review Board

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

Wednesday
June 12, 2013
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: Chris Le, Pharm.D.

SUBJECT: Packet Contents for Board Meeting – June 12, 2013

DATE: June 5, 2013

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 June 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 Prior Authorize Kynamro™ – See Appendix C

Action Item – Annual Review of Anticonvulsant Medications And 30-Day Notice to Prior Authorize Oxtellar XR™ (Oxcarbazepine ER) And Sabril® (Vigabatrin) – See Appendix D

Action Item – Annual Review of Biologic Products for the Treatment of Rheumatoid Arthritis, Crohn's Disease, Plaque Psoriasis, and Ankylosing Spondylitis – See Appendix E.

Action Item – Annual Review of Testosterone Products – See Appendix F.

Action Item – Annual Review of Multiple Sclerosis Medications And 30 Day Notice to Prior Authorize Aubagio® (Teriflunomide) and Tecfidera™ (Dimethyl Fumarate) – See Appendix G.

Action Item – Annual Review of Leukotriene Modifiers: Singulair® (Montelukast) and Zyflo CR® (Zileuton) – See Appendix H.

Action Item – Annual Review of Horizant® and Gralise™ (Gabapentin Extended-Release) – 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 – June 12, 2013 @ 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. Cothran

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. April 10, 2013 DUR Minutes – Vote
B. April 11, 2013 DUR Recommendation Memorandum
C. Correspondence

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

4. Update on DUR / Medication Coverage Authorization Unit – See Appendix B.

A. Medication Coverage Activity for April & May 2013
B. Pharmacy Help Desk Activity for April & May 2013
C. Retrospective Drug Evaluation: Duplication of Narcotic Therapy

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

5. Action Item – Vote to Prior Authorize Kynamro™ (Mipomersen) – See Appendix C.

A. COP Recommendations

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

6. Action Item – Annual Review of Anticonvulsant Medications And 30-Day Notice to Prior Authorize Oxtellar XR™ (Oxcarbazepine ER) And Sabril® (Vigabatrin) – See Appendix D.

B. Current Authorization Criteria
C. Utilization Review
D. Prior Authorization Review
E. Market News and Updates
F. Oxtellar XR™, Fycompa™, and Sabril® Product Summaries
G. COP Recommendations
H. Utilization Details
I. Oxtellar XR™, Fycompa™, and Sabril® Product Details

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

7. Action Item – Annual Review of Biologic Products for the Treatment of Rheumatoid Arthritis, Crohn's Disease, Plaque Psoriasis, and Ankylosing Spondylitis – See Appendix E.

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

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

8. Action Item – Annual Review of Testosterone Products – See Appendix F.

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

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

9. Action Item – Annual Review of Multiple Sclerosis Medications And 30 Day Notice to Prior Authorize Aubagio® (Teriflunomide) and Tecfidera™ (Dimethyl Fumarate) – See Appendix G.

A. Current Authorization Criteria
B. Utilization Review
C. Prior Authorization Review
D. Market News and Updates
E. COP Recommendations
F. Tecfidera™ Product Details

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

10. Action Item - Annual Review of Leukotriene Modifiers: Singulair® (Montelukast) and Zyflo CR® (Zileuton) – See Appendix H.

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

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

11. Action Item – Annual Review of Horizant® and Gralise™ (Gabapentin Extended-Release) – See Appendix I.

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

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

12. FDA and DEA Updates – See Appendix J.

13. Future Business

A. Safety Reviews
B. Narcotic Prescriber Survey Results
C. New Product Reviews
D. Annual Reviews

14. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES of MEETING OF APRIL 10, 2013

BOARD MEMBERS:	PRESENT	ABSENT
Brent Bell, D.O., D.Ph.: Vice-Chairman	X	
Mark Feightner, Pharm.D.		X
Anetta Harrell, Pharm.D.	X	
Evie 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
Terry Cothran, D.Ph.; Pharmacy Director	X	
Karen Egesdal, D.Ph.; SMAC-ProDUR Coordinator/OHCA Liaison	X	
Shellie Keast, Pharm.D, M.S.; Clinical Assistant Professor	X	
Bethany Holderread, Pharm. D.; Clinical Pharmacist	X	
Chris Le, Pharm.D.; Assisant Director	X	
Mark Livesay, Operations Manager	X	
Carol Moore, Pharm.D.; Clinical Pharmacist	X	
Brandy Nawaz, 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
Jo Nel Weber, Pharm.D.; Clinical Pharmacist		X
Graduate Students: Amany Hussein, Manish Mittal	X	
Visiting Pharmacy Student(s): Juan Barajas, Kevin Nguyen, Mumba Mushili	X	

	PRESENT	ABSENT
Nico Gomez, Chief Executive Officer		X
Marlene Asmussen, R.N., Population Care Management Director	X	
Garth Splinter, M.D., M.B.A.; Medicaid Director		X
Sylvia Lopez, M.D., FAAP, Chief Medical Officer	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	
Alison Martinez, Ph.D., Geneticist	X	
Jennie Melendez, Public Affairs-Information Representative	X	
Jill Ratterman, D.Ph.; Pharmacy Specialist	X	
Kerri Wade, Senior Pharmacy Financial Analyst	X	
Stacey Hale, Pharmacy Research Analyst	X	

OTHERS PRESENT:		
Randy Huetsch, Aegerion	Toby Thompson, Pfizer	Brian Maves, Pfizer
Jim Fowler, AstraZeneca	Emerald Groom	Nicole Wilkerson
Hilary Carter, Otsuka	Warren Tayes, Merck	Roberto Pedraza
Jan Preslar	Sharon Jackson, GSK	Tone 'Jones
Clint Degner, Novartis	Don Kempin, Novo Nordisk	Audrey Rattan, Otsuka
Jon Maguire, GSK	Jim Chapman, AbbVie	Charlene Kaiser, Amgen
Ben Liniger		

PRESENT FOR PUBLIC COMMENT:	
Dan Keech	
Paul Cockrum	Bristol Meyers Squibb

AGENDA ITEM NO. 1: CALL TO ORDER
1A: Roll Call
Dr. Muchmore called the meeting to order. Roll call by Dr. Cothran established the presence of a quorum.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 2: PUBLIC COMMENT FORUM
Agenda Item: Not an agenda item Dan Keech
Agenda Item: No 5 & 6 Paul Cockrum
ACTION: NONE REQUIRED

AGENDA ITEM NO. 3: APPROVAL OF DUR BOARD MINUTES
3A: March 13, 2013 DUR Minutes
3B: March 14, 2013 DUR Recommendation Memorandum
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: Medication Coverage Activity: March 2013
4B: Pharmacy Help Desk Activity: March 2013
4C: Retrospective Drug Evaluation: Focusing on Safety
Materials included in agenda packet; presented by Dr. Le
ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: VOTE TO PRIOR AUTHORIZE JUVISYNC®, BYDUREON®, JENTADUETO®, JANUMET XR®, NESINA®, KAZANO®, AND OSENI® MEDICATIONS
5A: COP Recommendations
Materials included in agenda packet; presented by Dr. Keast.
Dr. Bell moved to approve; seconded by Dr. Harrell
ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: VOTE TO PRIOR AUTHORIZE ELIQUIS® AND TO UPDATE XARELTO® PRIOR AUTHORIZATION CRITERIA

6A: COP Recommendations

Materials included in agenda packet; presented by Dr. Holderread
Dr. Preslar moved to approve; seconded by Ms. Varalli- Claypool
ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: VOTE TO PRIOR AUTHORIZE KUVAN®

7A: COP Recommendations

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

AGENDA ITEM NO. 8: VOTE TO PRIOR AUTHORIZE GATTEX®

8A: COP Recommendations

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

AGENDA ITEM NO. 9: 30 DAY NOTICE TO PRIOR AUTHORIZE KYNAMRO™ AND VOTE TO UPDATE JUXTAPID™ PRIOR AUTHORIZATION CRITERIA

9A: Background
9B: Product Summaries
9C: Cost Comparison
9D: Product Details

Materials included in agenda packet; presented by Dr. Le.
Dr. Bell moved to approve Juxtapid™ ; seconded by Dr. Preslar
ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: INTERVENTION STRATEGIES FOR REDUCTION OF NARCOTIC OVERPRESCRIBING

10A: Prescriber Survey
10B: Narcotic Prescriber Profiling
10C: Quantity Limit Reduction
10D: COP Recommendations

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

AGENDA ITEM NO. 11: FISCAL YEAR 2012 ANNUAL REVIEW

11A: Top 100 Drugs by Reimbursement
11B: Top 50 Drugs by Total Number of Claims
11C: Expenditures by Therapeutic Class

Materials included in agenda packet; presented by Dr. Keast

AGENDA ITEM NO. 12: FDA AND DEA UPDATES

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

AGENDA ITEM NO. 13: FUTURE BUSINESS

Materials included in agenda packet; submitted by Dr. Cothran

12A: May 2013 Meeting Cancelled
12B: New Product Reviews
12C: Annual Reviews

ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: ADJOURNMENT

The meeting was adjourned at 7:36pm

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

Memorandum

Date: April 11, 2013

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

From: Chris Le, Pharm.D.
Assistant Director
Pharmacy Management Consultants

Subject: DUR Board Recommendations from Meeting of April 10, 2013

Recommendation 1: Vote to Prior Authorize Juvisync® (sitagliptin/simvastatin), Bydureon® (exenatide ER), Jentadueto® (linagliptin/metformin), Janumet XR® (sitagliptin/metformin ER), Nesina® (alogliptin), Kazano® (alogliptin/metformin), and Oseni® (alogliptin/pioglitazone)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends moving all pioglitazone products into Tier 3 from the Special PA Catetgory and placement of Jentadueto® (linagliptin/metformin), Janumet XR® (sitagliptin/metformin ER), Juvisync® (sitagliptin/simvastatin), Nesina® (alogliptin), Kazano® (alogliptin/metformin), Oseni® (alogliptin/pioglitazone), and Bydureon® (exenatide ER) into Tier 3 of the Diabetes Medication PBPA category with the following criteria:

1. To qualify for a Tier 2 medication, the member must have a trial of a Tier 1 medication (must include a trial of metformin titrated up to maximum dose), or a clinical reason why a Tier 1 medication is not appropriate.
2. For initiation with dual or triple therapy, additional Tier 2 medications can be approved based on current AACE or ADA guidelines.

3. To qualify for a Tier 3 medication, the member must have tried a Tier 2 medication in the same category and have a documented clinical reason why the Tier 2 medication is not appropriate.
4. To qualify for a Special Prior Authorized medication, the member must be currently stabilized on the requested product or have attempted at least 3 other categories of Tier 2 or Tier 3 medications, or have a documented clinical reason why the requested product is necessary for the member.
5. For members with steatohepatitis, pioglitazone can be approved after a trial of a Tier 1 medication (must include a trial of metformin titrated up to maximum dose), or a clinical reason why a Tier 1 medication is not appropriate.

*Note that Tier 3 products can be moved to Tier 2 status based on supplemental rebate status or generic pricing and availability.

Tier 1	Tier 2*	Tier 3	Special PA
Biaguanides Metformin (Glucophage®) Metformin SR (Glucophage XR®) Metformin-Glyburide (Glucovance®) Metformin-Glipizide (Metaglip®) Sulfonylureas Glyburide (Diabeta®) Glyburide Micronized (Micronase®) Glipizide (Glucotrol®) Glipizide SR (Glucotrol XL®) Glimepiride (Amaryl®) Miscellaneous Chlorpropamide Tolbutamide	DPP-4 Inhibitors Linagliptin (Tradjenta®) Saxagliptin (Onglyza®) Saxagliptin-Metformin (Kombiglyze®) Sitagliptin (Januvia®) Sitagliptin-Metformin (Janumet®) Glinides Repaglinide-Metformin (Prandimet®) Repaglinide (Prandin®) Nateglinide (Starlix®) GLP-1 Agonists Liraglutide (Victoza®) Alpha-Glucosidase Inhibitors Acarbose (Precose®)	DPP-4 Inhibitors Sitagliptin-Met ER (Janumet XR®) Sitagliptin-Simvastatin (Juvisync®) Linagliptin-Metformin (Jentadueto™) Alogliptin (Nesina®) Alogliptin-Metformin (Kazano®) Alogliptin- Pioglitazone (Oseni®) Thiazolidinediones Pioglitazone (Actos®) Pioglitazone-Metformin (Actoplus Met®, Actoplus Met XR®) Pioglitazone-Glimepiride (Duetact®) GLP-1 Agonists Exenatide (Byetta®) Exenatide Qweek (Bydureon®) Alpha-Glucosidase Inhibitors Miglitol (Glyset®)	Biaguanides Metformin solution (Riomet®) Metformin Long-Acting (Fortamet®, Glumetza®) Thiazolidinediones Rosiglitazone (Avandia®) Rosiglitazone-Metformin (Avandamet®) Rosiglitazone-Glimepiride (Avandaryl®) Amylinomimetic Pramlintide (Symlin®)

*Supplemental rebate for Tier 3 products or similarly priced generic products only.

Recommendation 2: Vote to Prior Authorize Eliquis® (Apixaban) and Update Xarelto® (Rivaroxaban) Prior Authorization Criteria

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following:

Prior Authorization of Eliquis® (apixaban) with the following Criteria:

1. FDA approved diagnosis of nonvalvular atrial fibrillation.

Updating the Prior Authorization Criteria for Xarelto® (rivaroxaban):

1. FDA approved diagnosis of one of the following: non valvular atrial fibrillation, deep vein thrombosis (DVT), pulmonary embolism (PE), or to reduce the risk of recurrent DVT and PE.
2. 10 mg: the first 35 days will not require prior authorization to allow for use for postsurgical DVT prophylaxis only.
3. 15 mg and 20 mg: a diagnosis of nonvalvular atrial fibrillation, deep vein thrombosis (DVT), pulmonary embolism (PE), or prophylaxis of recurrent DVT or PE will be required.

Recommendation 3: Vote to Prior Authorize Kuvan® (Sapropterin)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends prior authorization of Kuvan® (sapropterin) with the following criteria:

Kuvan® (Sapropterin) Approval Criteria:

1. FDA approved diagnosis of phenylketonuria.
2. Active management with phenylalanine restricted diet.
3. Initial approval will be for 30 days in duration. After which time, prescriber must verify that the member responded to treatment as defined by laboratory documentation of ≥30% decrease in blood phenylalanine levels.
4. Subsequent approvals will be for the duration of a year.

Recommendation 4: Vote to Prior Authorize Gattex® (Teduglutide)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends prior authorization of Gattex® (teduglutide) with the following criteria:

Criteria for Approval for Gattex® (Teduglutide):

1. Member must have diagnosis of severe Short Bowel Syndrome, and
2. Require parenteral nutrition at least 3 times per week, every week, for the past 12 months, with
3. Documentation of all of the following:
    a. Prior use of supportive therapies such anti-motility agents, proton pump inhibitors, bile acid sequestrants, and octreotide.
    b. Colonoscopy within the previous 6 months, with removal of polyps if present.
    c. Gastro-intestinal malignancy has been ruled out.
4. Approval will be for the duration of 3 months, after which time, prescriber must verify benefit of medication by documented reduction of at least 20% in parenteral support.
5. Subsequent approvals will be for the duration of a year.

The DUR Board recommended further evaluation of how often colonoscopy is recommended during treatment with Gattex®.

Recommendation 5: 30 Day Notice to Prior Authorize Kynamro™ (Mipomersen) and Vote to Change Juxtapid™ (Lomitapide) Prior Authorization Criteria

MOTION CARRIED by unanimous approval.

The College of pharmacy recommends prior authorization of Kynamro™ (mipomersen) with similar prior authorization criteria as Juxtapid™ (lomitapide). The College of Pharmacy also recommends the following changes to the prior authorization criteria:

Prior Authorization Criteria for Juxtapid™ (lomitapide) and Kynamro™ (mipomersen):

1. FDA approved diagnosis of homozygous familial hypercholesterolemia defined by the presence of at least one of the following criteria:
    a. Documented functional mutation(s) in both LDL receptor alleles or alleles known to affect LDL receptor functionality via genetic testing, OR
    b. Untreated total cholesterol >500 mg/dL and triglycerides <300 mg/dL and
        i. both parents with documented untreated total cholesterol >250 mg/dL or
        ii. presence of tendinous /cutaneous xanthoma prior to age 10 years.
2. Documented failure of high dose statin therapy (LDL reduction capability equivalent to atorvastatin 80mg or higher), and
3. Prescriber must be certified with Juxtapid™ or Kynamro™ REMS program.

Recommendation 5: Intervention Strategies for Reduction of Narcotic Overprescribing

MOTION CARRIED by unanimous approval.

1. The College of Pharmacy recommends implementation of quantity limit reductions after performance of prescriber surveys and general educational initiative regarding prescribing of immediate release narcotic analgesics.
2. The educational information disseminated would also include the new quantity limit restrictions of less than #120 units per month (4 units per day). This educational initiative is expected to pre-emptively reduce the number of prescriptions for high volume immediate release narcotics.
3. Following the educational initiative, quantity edits can be turned on to deny claims with quantities of #240 or greater in the first month, then tightened down to deny claims with quantities of #180 or greater in the following month, and so on, until the restriction is reduced to a maximum of #120 per 30 days (4 units per day). A manual prior authorization will be required for dosing in excess of the quantity limit.
4. During this same time, prescriber profiling will continue to be a priority as the DUR Board analyze data and recommend specific intervention(s).

In addition the DUR Board made the following recommendations:

1. Refer the top prescribers, common to all four prescriber profiling analyses, for further evaluation/audit.
2. Send letters to prescribers with information regarding their narcotic prescribing statistics, including how the prescriber ranks in regards to other prescribers.

To whom it may concern:

I am a practicing interventional cardiologist and have more than 20% of my patients with Medicaid or Sooner Care. Prior to the advent of medications like Effient and Brilinta we only had Plavix at our disposal. As we now have well established data to show the superior and more consistent anti-platelet function of the newer drugs (Effient and Brilinta), I feel having them available on the Medicaid/Sooner Care formulary would be greatly helpful.

As I have been a speaker for Effient and being well aware of the risks/benefits and especially the contraindications in the patients with prior CVA (stroke) or TIA, having an agent like Brilinta without the CVA contraindication especially when dealing with patients with atherosclerotic disease would be greatly beneficial for the patients.

Brilinta also has more indications but I did not want to write a long thesis but wanted to emphasize the most important factor for my request of having Brilinta on your formulary.

If you have further questions or would need to talk to me, you can call me in my office at the number stated below.

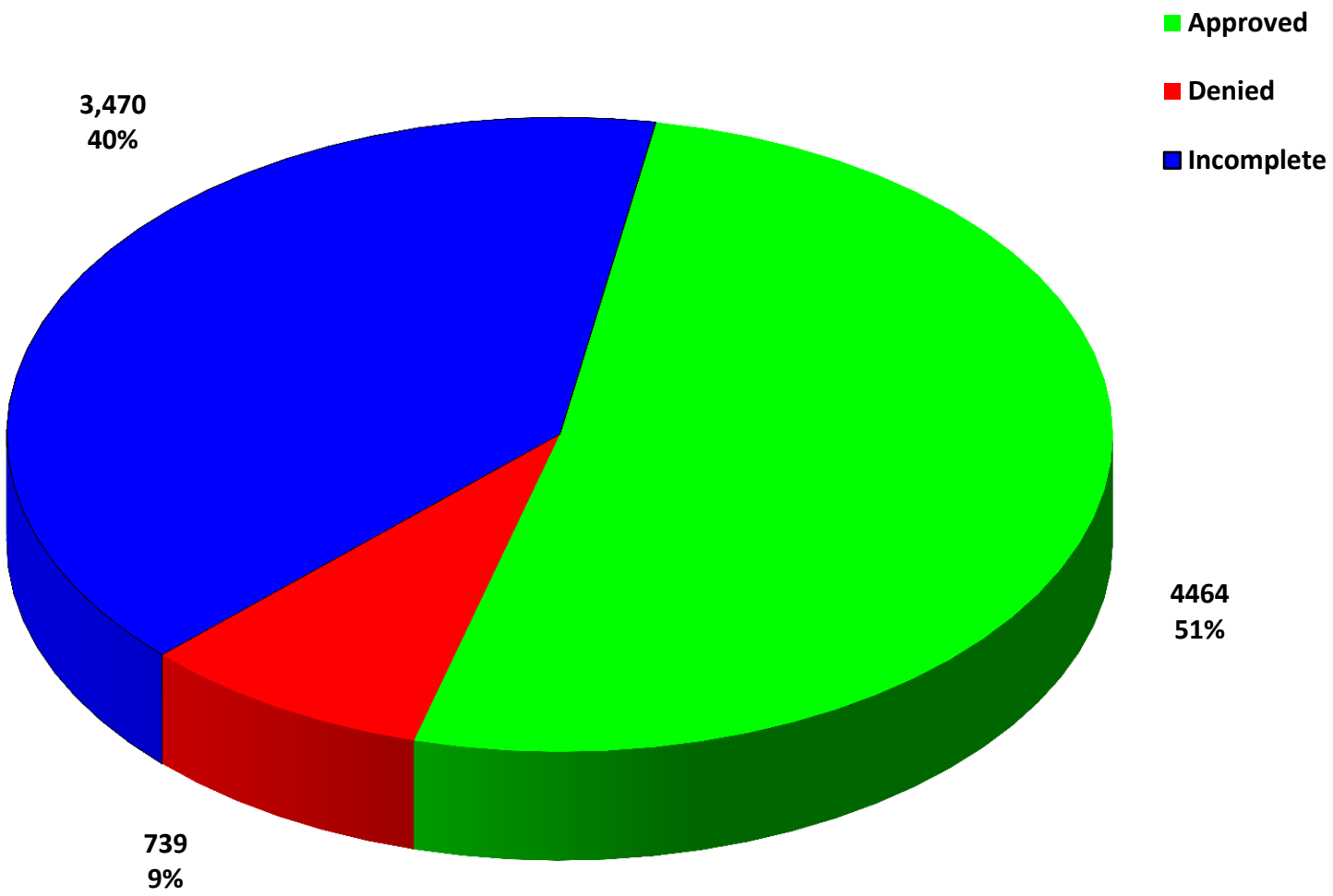
Thank you.

Sincerely,

--
Riaz A Sirajuddin, MD
Heart Solutions of Oklahoma
10413 Greenbriar Parkway
Oklahoma City, OK 73159
405-691-4665
www.heartsolutions.org

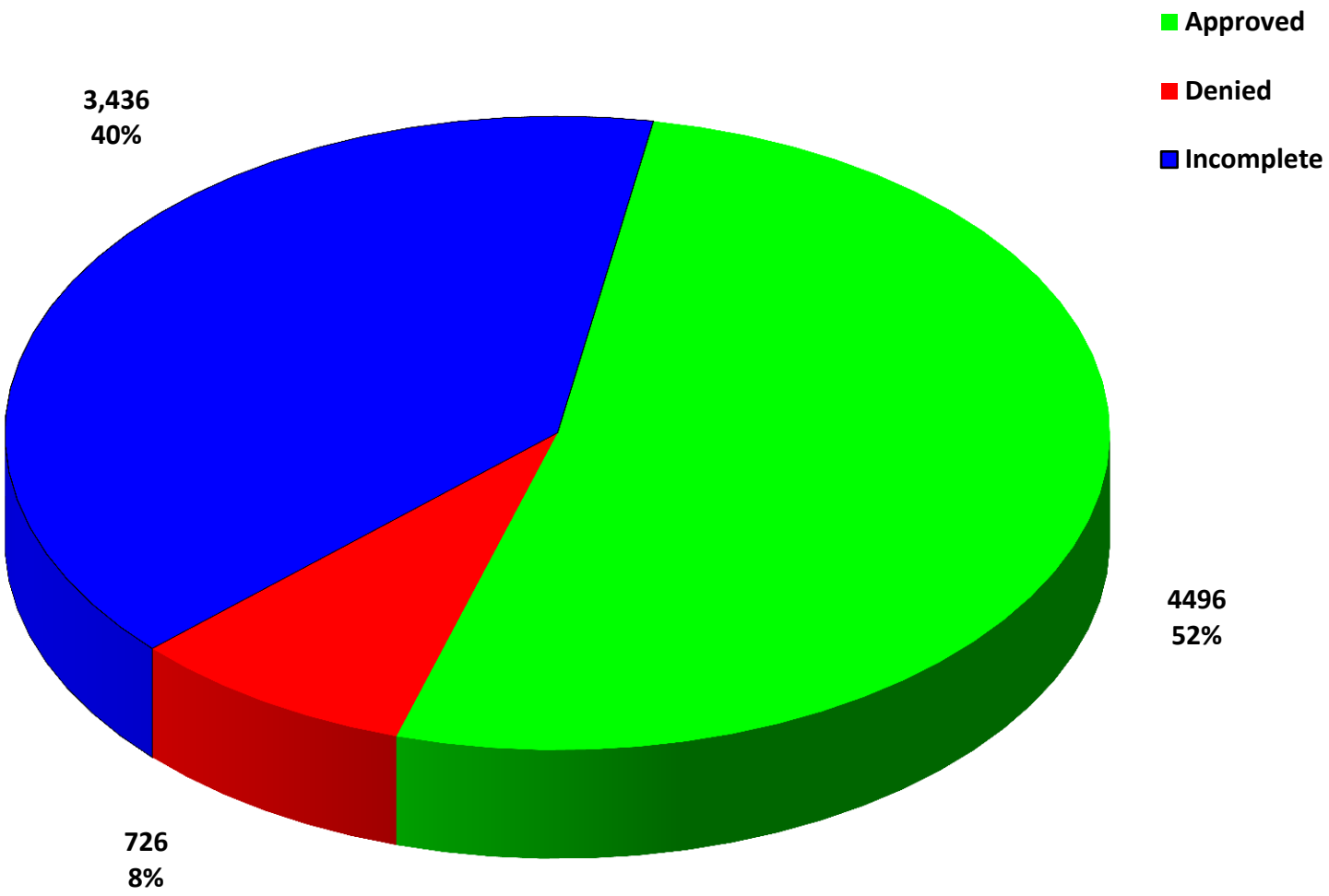
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: April 2013



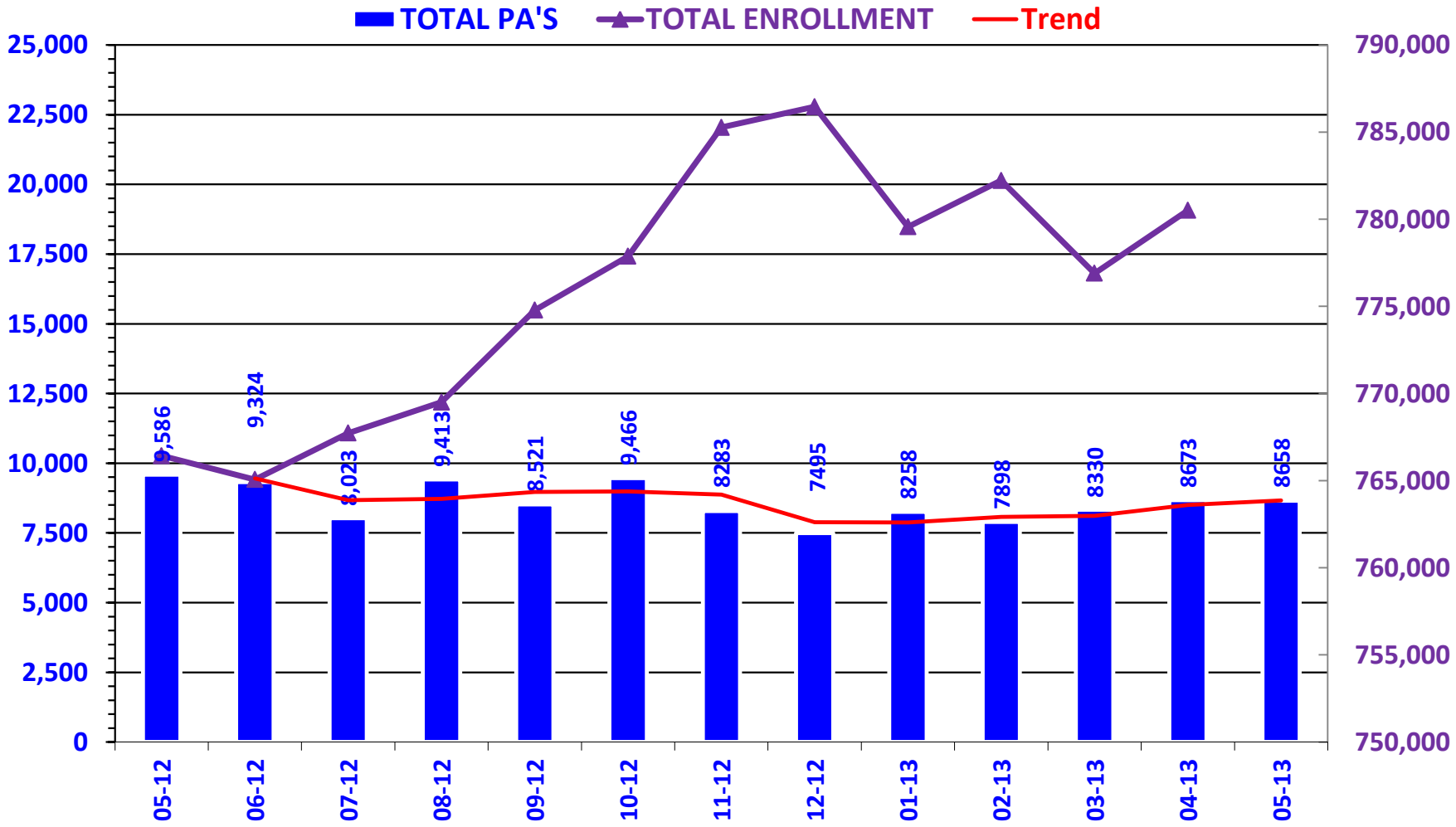
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION ACTIVITY REPORT: May 2013



PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: May 2012- May 2013



PA totals include approved/denied/incomplete/overrides

Prior Authorization Activity

4/1/2013 Through 4/30/2013

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	433	191	12	230	359
Analgesic, Narcotic	392	199	29	164	246
Angiotensin Receptor Antagonist	46	4	9	33	359
Antiasthma	1,206	648	34	524	208
Antibiotic	28	6	3	19	7
Anticoagulant	52	31	4	17	330
Anticonvulsant	76	34	4	38	302
Antidepressant	213	47	16	150	332
Antidiabetic	167	85	6	76	356
Antigout	12	6	1	5	359
Antihistamine	184	136	10	38	354
Antihyperlipidemic	16	2	2	12	361
Antimigraine	95	35	11	49	344
Antiplatelet	12	6	0	6	359
Antiulcers	305	92	62	151	165
Anxiolytic	72	54	4	14	238
Atypical Antipsychotics	420	273	10	137	339
Biologics	56	35	2	19	301
Bladder Control	72	10	9	53	291
Botox	169	156	7	6	861
Cardiovascular	47	32	6	9	309
Dermatological	125	31	49	45	95
Endocrine & Metabolic Drugs	166	74	18	74	231
Erythropoietin Stimulating Agents	52	24	1	27	101
Fibromyalgia	167	45	15	107	323
Gastrointestinal Agents	79	22	14	43	150
Genitourinary Agents	15	5	1	9	37
Glaucoma	12	5	0	7	359
Growth Hormones	52	42	2	8	164
HFA Rescue Inhalers	108	29	6	73	328
Insomnia	75	13	13	49	220
Multiple Sclerosis	18	13	0	5	176
Muscle Relaxant	128	41	45	42	42
Nasal Allergy	162	20	42	100	153
Neurological Agents	87	71	4	12	354
Nsaids	175	23	26	126	276
Ocular Allergy	88	15	7	66	120
Ophthalmic	46	8	10	28	4
Osteoporosis	37	13	1	23	358
Other*	159	23	20	116	180
Otic Antibiotic	24	4	1	19	10
Pediculicide	84	34	6	44	14
Prenatal Vitamins	10	0	0	10	0
Statins	63	30	6	27	359
Stimulant	528	330	11	187	317
Suboxone/Subutex	173	124	2	47	76
Topical Antibiotic	11	2	0	9	61
Topical Antifungal	114	3	57	54	38
Topical Corticosteroids	58	1	16	41	30

* Includes any therapeutic category with less than 10 prior authorizations for the month.

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Vitamin	46	11	23	12	334
Pharmacotherapy	122	89	2	31	100
Emergency PAs	1	1	0	0	
Total	**7,058**	**3,228**	**639**	**3,191**	
Overrides					
Brand	68	48	4	16	289
Dosage Change	384	373	2	9	8
High Dose	5	4	0	1	204
Ingredient Duplication	14	12	0	2	5
Lost/Broken Rx	73	68	3	2	5
NDC vs Age	9	8	0	1	223
Nursing Home Issue	101	91	1	9	5
Other	31	28	1	2	19
Quantity vs. Days Supply	823	530	66	227	253
Stolen	5	5	0	0	4
Temporary Unlock	46	35	10	1	18
Third Brand Request	57	34	14	9	54
Overrides Total	**1,615**	**1,236**	**100**	**279**	
Total Regular PAs + Overrides	**8,673**	**4,464**	**739**	**3,470**	

Denial Reasons	
Unable to verify required trials.	2,631
Lack required information to process request.	799
Does not meet established criteria.	756

Other PA Activity	
Duplicate Requests	562
Letters	2,664
No Process	163
Changes to existing PAs	560
Partials	1,007

* Includes any therapeutic category with less than 10 prior authorizations for the month.

Prior Authorization Activity

5/1/2013 Through 5/31/2013

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	385	182	6	197	356
Analgesic, Narcotic	418	208	35	175	240
Angiotensin Receptor Antagonist	51	8	6	37	359
Antiasthma	1,128	622	29	477	200
Antibiotic	15	3	0	12	123
Anticoagulant	58	39	2	17	337
Anticonvulsant	78	31	1	46	339
Antidepressant	264	72	21	171	346
Antidiabetic	148	82	5	61	351
Antifungal	11	4	0	7	20
Antigout	15	9	0	6	292
Antihistamine	192	153	9	30	351
Antihyperlipidemic	50	14	7	29	359
Antimigraine	76	22	12	42	318
Antiplatelet	27	21	1	5	347
Antiulcers	296	82	82	132	175
Anxiolytic	131	99	3	29	196
Atypical Antipsychotics	453	283	16	154	350
Biologics	29	15	5	9	359
Bladder Control	67	7	10	50	309
Botox	72	37	11	24	430
Cardiovascular	33	17	4	12	267
Corticosteroid	10	2	0	8	12
Dermatological	121	32	42	47	95
Endocrine & Metabolic Drugs	155	88	9	58	208
Erythropoietin Stimulating Agents	43	24	1	18	97
Fibromyalgia	157	44	20	93	336
Gastrointestinal Agents	111	39	15	57	112
Glaucoma	17	5	0	12	360
Growth Hormones	46	20	6	20	163
HFA Rescue Inhalers	88	28	6	54	336
Insomnia	80	13	16	51	180
Multiple Sclerosis	21	13	0	8	227
Muscle Relaxant	117	36	43	38	38
Nasal Allergy	145	16	37	92	102
Neurological Agents	79	63	3	13	342
Nsaids	171	25	28	118	304
Ocular Allergy	77	20	10	47	123
Ophthalmic	37	9	2	26	17
Osteoporosis	33	14	2	17	346
Other*	157	35	16	106	208
Otic Antibiotic	46	11	1	34	8
Pediculicide	97	32	7	58	11
Prenatal Vitamins	13	0	2	11	0
Smoking Cess.	10	1	1	8	87
Statins	77	23	8	46	358
Stimulant	504	322	13	169	330
Suboxone/Subutex	342	265	2	75	79
Topical Antibiotic	14	0	1	13	0

* Includes any therapeutic category with less than 10 prior authorizations for the month.

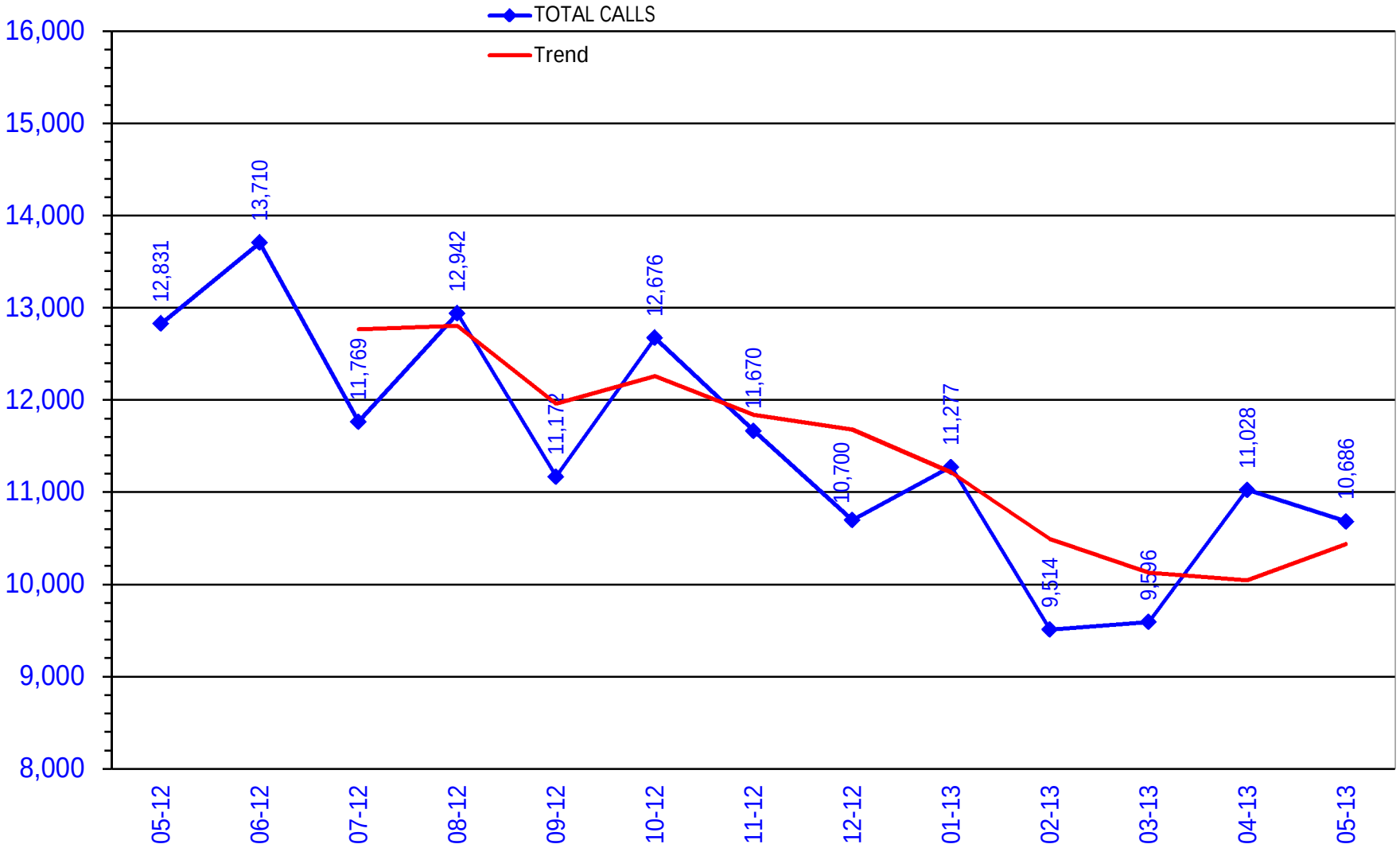
	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Topical Antifungal	71	0	28	43	0
Topical Corticosteroids	53	2	15	36	97
Vitamin	56	15	32	9	340
Pharmacotherapy	94	80	0	14	86
Emergency PAs	7	7	0	0	
Total	**7,046**	**3,294**	**631**	**3,121**	
Overrides					
Brand	48	29	6	13	291
Dosage Change	392	358	4	30	10
High Dose	3	2	0	1	268
Ingredient Duplication	10	8	0	2	7
Lost/Broken Rx	139	133	3	3	8
NDC vs Age	1	0	1	0	0
Nursing Home Issue	98	88	0	10	11
Other	44	37	2	5	25
Quantity vs. Days Supply	791	500	56	235	246
Stolen	4	3	1	0	5
Temporary Unlock	29	17	7	5	19
Third Brand Request	52	25	16	11	28
Wrong D.S. on Previous Rx	2	2	0	0	6
Overrides Total	**1,612**	**1,202**	**95**	**315**	
Total Regular PAs + Overrides	**8,658**	**4,496**	**726**	**3,436**	

Denial Reasons	
Unable to verify required trials.	2,587
Lack required information to process request.	805
Does not meet established criteria.	735

Other PA Activity	
Duplicate Requests	563
Letters	2,681
No Process	249
Changes to existing PAs	605
Partials	949

* Includes any therapeutic category with less than 10 prior authorizations for the month.

CALL VOLUME MONTHLY REPORT:
May 2012 – May 2013



RETROSPECTIVE DRUG UTILIZATION REVIEW REPORT

Duplication of Narcotic Therapy

December 2012, January, and February 2013

Parameters	Total Messages	Messages Reviewed	Members Reviewed	Members Intervened
Males and Females Age 49-60	28,492	1,935	1,859	279
Letters				
Prescribers: 385		Pharmacies: 185		Total Letters: 570

	Top 25 Narcotic Combination Messages Arranged by Total Messages Reviewed	Messages Flagged	Messages Reviewed	Members Reviewed	Members Intervened
1	Tramadol 50 MG and Hydro/apap 7.5-750 MG	6,610	296	291	45
2	Oxyco/apap 7.5-500 MG and Hydro/apap 7.5-500 MG	5,274	135	131	51
3	Morphine Sulfate ER 60 MG and Hydro/apap 7.5-500 MG	976	152	147	4
4	Oxycodone 5 MG and Hydro/apap 7.5-500 MG	1,648	103	100	31
5	Fentanyl Patch 75 MCG/HR and Hydro/apap 7.5-500 MG	729	93	88	2
6	Hydro/apap 7.5-750 MG and Hydro/apap 7.5-325 MG	1,689	55	55	7
7	Morphine Sulfate 30 MG and Morphine ER 60 MG	561	80	77	1
8	Hydro/apap 7.5/500 MG and Oxycodone ER 80	545	84	78	2
9	Oxycodone 5 MG and Oxycodone ER 80 MG	534	84	79	2
10	Tramadol 50 MG and Oxycodone/apap 7.5-500	824	41	40	18
11	Morphine Sulfate ER 60 MG and Oxyco/apap 7.5-325	407	61	59	0
12	Morphine Sulfate ER 60 MG and Oxycodone 5 MG	381	50	45	1
13	Fentanyl Patch 75 MCG/HR and Oxyco/apap 7.5-500 MG	329	45	41	2
14	Fentanyl Patch 75 MCG/HR and Oxycodone 30 MG	323	39	36	1
15	Oxycodone ER 80 MG and Oxycodone/apap 7.5/500 MG	309	48	46	2
16	APAP/codeine 300/60 MG and Hydro/apap 7.5/500 MG	840	11	11	7
17	Methadone 5 MG and Hydrocodone/apap 7.5-325 MG	420	32	31	4
18	Tramadol 50 MG and Apap/codeine 300-60 MG	348	9	8	1
19	Methadone 5 MG and Oxycodone 5 MG	340	21	20	3
20	Oxycodone 5 MG and Oxycodone/apap 7.5/500 MG	296	26	24	6
21	Hydromorphone 8 MG and Hydro/apap 7.5-750 MG	282	16	16	5
22	Morphine Sulfate 30 MG and Hydro/apap 7.5-500 MG	268	18	18	6
23	Oxycodone/apap 7.5/500 MG and Oxy/apap 10/650 MG	408	8	8	3
24	Oxycodone 5 MG and Tramadol HCl 50 MG	250	19	19	8
25	Morphine Sulf ER 60 MG and Morphine Sulf ER 200MG	220	15	15	1

RETROSPECTIVE DRUG UTILIZATION REVIEW RESPONSE REPORT

Duplication of Narcotic Therapy

Responses for July – November 2012

Response Summary (Prescriber)
Letters Sent: 1,054
Response Forms Returned: 416

22 (5%)	*Record Error—Not my patient.*
69 (17%)	*No longer my patient.*
29 (7%)	*Medication has been changed prior to date of review letter.*
125 (30%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
105 (25%)	*I am aware of this situation and will plan to continue monitoring therapy.*
106 (25%)	*Other (comments entered)*

Response Summary (Pharmacy)
Letters Sent: 547
Response Forms Returned: 295

12 (4%)	*Record Error—Not my patient.*
24 (8%)	*No longer my patient.*
7 (2%)	*Medication has been changed prior to date of review letter.*
109 (39%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
83 (28%)	*I am aware of this situation and will plan to continue monitoring therapy.*
87 (29%)	*Other (comments entered)*

All responses marked "I would like to refer this patient for review by the Pharmacy Lock-In program" were sent to the Lock-In department.

Comments From Prescriber Response Forms
REFER MEMBER FOR LOCK-IN REVIEW (APPROXIMATELY 44 COMMENTS)
WILL DISCUSS WITH DOCTOR (36)
THIS PATIENT NEEDS LONG-ACTING PAIN MEDICATION BUT CANNOT AFFORD IT UNTIL HE GETS A DIFFERENT INSURANCE COVERING IT IN JUNE OR JULY. HE HAS A NARCOTICS TOLERANCE AND GOAL IS TO DECREASE HIS DOSE. THIS PATIENT HAS MULTI-LEVEL DDD, MULTIPLE OLD INJURIES AND FRACTURES, & SEVERE OA MULTIPLE LOCATIONS. HE PLANS TO GET SURGERY WHEN HE GETS INSURANCE IN JUNE OR JULY (HE WILL HAVE TO SEE ORTHOPEDIST AGAIN 1ST)
PATIENT GETTING MEDS FROM RHEUMATOLOGY DR. XXXX. I D/C TRAMADOL AND WILL NOTIFY PT.
MY RECORD SHOWS ONLY MS ER 100MG AND OXY IR 30MG AND CLONAZEPAM 1MG WERE PRESCRIBED ON 12/19/12, NOT MORPHINE SULF 30MG. XXXX PHARMACY CONFIRMS THIS. PATIENT EXPIRED IN NURSING HOME JAN. 26.
PT'S CHART REVIEWED AS I HAD NOT SEEN PT SINCE 7/20/12. PT'S LAST RX FOR HYDROCODONE/ACET 7.5/325 WAS (ILLEGIBLE?) & TRAMADOL GIVEN BY ANOTHER DR FROM O.U.FM. REVIEWED PT'S INFO W/ OTHER PROVIDER. WILL CONTACT PT FOR APPT, IF UNABLE TO REACH WILL SEND LETTER. THANKS.
PATIENT IS NOW BEING SLOWLY TAPERED DOWN ON HER NARCOTICS.
WAS MINE WHILE IN NURSING FACILITY. MAY NOT CONTINUE AS OUTPATIENT
HER CHRONIC NARCOTIC USE HAS BEEN DISCUSSED ON MULTIPLE OCCASIONS, WHILE SHE WAS AN INPATIENT, WITH HER PCP AND MYSELF. SHE IS CURRENTLY BEING MANAGED BY PALLIATIVE CARE/HOSPICE SPECIALISTS, OR WAS THE LAST TIME I LOOKED INTO HER CASE, TO THE BEST OF MY KNOWLEDGE. I AM NO LONGER INVOLVED IN HER DAY-TO-DAY CARE
WILL DISCUSS WITH PRESCRIBER. PATIENT APPEARS TO GET OXYCONTIN & OXYCODONE VERY CONSISTANTLY (q 30 DAYS) AND GOT ONE RX OF 3-DAY SUPPLY IN BETWEEN
PATIENT RARELY FILLS AT MY PHARMACY BUT IT APPEARS MOST MEDS ARE FROM PAIN MANAGEMENT - MAY VERIFY W/ M.D.
THIS IS NOT OUT PATIENT - CHECK XXXX M.D. THE LAST TIME THIS HAPPENED W/ THIS # I CALLED & WE FIGURED OUT IT WAS XXXX M.D. THANK YOU.
OXYCODONE FILLED HERE 12-4-12 // HYDROCODONE FILLED HERE 10-25-12 // WE CAUGHT HER W/ A FORGERY & CUT HER OFF. I CALLED DHS ABOUT THIS.
AT THE SAME TIME I RECEIVED LETTER, TRAMADOL BECAME NARCOTIC AND REPORTED TO PMP. PATIENT HAD NOT DISCLOSED BEFORE THAT TIME THAT SHE WAS GETTING TRAMADOL FROM PCP.
BOTH MEDICATIONS WERE PRESCRIBED BY DR. XXXX, WHO IS A PAIN MANAGEMENT SPECIALIST. THE PATIENT HAS A CONTRACT WITH DR. XXXX. WE DO NOT FEEL THE PHARMACY LOCK-IN PROGRAM IS NECESSARY AT THIS TIME.
BOTH MEDICATIONS WERE PRESCRIBED BY DR. XXXX. THE COMBINATION OF A LONG ACTING MEDICATION FOR BASAL PAIN CONTROL AND A SHORT ACTING MEDICATION FOR BREAK-THRU PAIN DOES NOT WARRANT THE PHARMACY LOCK-IN PROGRAM FOR THIS PATIENT AT THIS TIME.
NO LONGER SEEING PATIENT ACTIVELY. PROBLEM RESOLVED. THANK YOU. PLEASE FOLLOW UP AS NEEDED.
I AM NOT PT'S PCP. ONLY SEE IN ER & IN HOSPITAL.
PATIENT IS FILLING AT MULTIPLE PHARMACIES. I WILL CALL THE MULTIPLE DOCTORS AND ASK FOR THEIR ADVICE.
PT WAS RECENTLY DISMISSED FROM MY PRACTICE FOR NOT FOLLOWING TREATMENT PRESCRIBED & NARCOTIC SEEKING
REFER MEMBER FOR LOCK-IN REVIEW. THIS OFFICE WAS JUST MADE AWARE THAT HE IS GETTING MEDICATIONS FROM OTHER PROVIDERS. WE WILL NOT BE GIVING HIM PAIN MEDICATIONS IN THE FUTURE.
PT WILL BE REFERRED FOR SUBSTANCE ABUSE RISK SCREENING. FURTHER MEDICAL MANAGEMENT WILL BE DETERMINED AFTER THE SCREENING RESULTS HAVE BEEN REVIEWED.

PT WILL NOT RECEIVE PAIN MEDICATION OR CONTROLLED DRUGS FROM THIS OFFICE. PT. INFORMED 3/4/13
AFTER CALLING THE OTHER PHARMACIES I FOUND OUT THAT XXXX's REPORTING PROCESS TO DRUG TRACKER HAS AN ERROR ON SOME PATIENTS. THEY ADMITTED FILLING THE NARCOTICS EVERY MONTH BUT I WAS UNABLE TO SEE IT ON TRACKER. DR. XXXX NOTIFIED - PATIENT WILL NO LONGER RECEIVE RX'S... XXXX, ARNP NOTIFIED, PATIENT NOTIFIED.
ONLY FILLED HERE ONCE ON 12/19 - BUT SHE GET SMALL QTY'S
PT HAS BEEN SENT TO PAIN MANAGEMENT.
PATIENT WAS SEEN BY ME WHILE IN HOSPITAL.
I WILL STOP 1 MEDICATION.
MEDICATION CHANGED OVER TO TRAMADOL 50MG QID ONLY.
WILL STOP TRAMADOL.
WE HAVE ONLY FILLED FOR THIS PT ONE TIME. IT IS CLEAR FROM THE PRINTOUT PROVIDED THAT SHE IS GETTING NARCOTICS FROM MORE THAN ONE PHYSICIAN AND MORE THAN ONE PHARMACY.
WE PRESCRIBED THE TRAMADOL BUT NOT THE OXYCODONE.
PATIENT HAS PAIN CONTRACT WITH PHYSICIAN. DOCTOR IS AWARE OF THERAPY.
I ONLY HAVE OFFICE RECORDS FOR PERCOCET 10/325 ON 12/20/2012 AND A REFILL USING NORCO 10/325 ON 1/15/2013. HE REPORTED TAKING OXYCODONE FOR CHRONIC PAIN FROM ANOTHER PHYSICIAN. POST SURGICAL SCRIPTS ARE NOT AVAILABLE IN MY OFFICE CHART. I LAST SAW PT 2/12/13 & NO SCRIPT GIVEN.
I SAW HER AS AN EMERGENCY DEPARTMENT PATIENT BUT I AM NOT HER PCP.
DR XXXX IS NO LONGER A PROVIDER HERE AT OUR FACILITY. THE PATIENT IN QUESTION IS NO LONGER RECEIVING HYDROCODONE FROM OUR FACILITY.
THE PATIENT WAS RX'D THE HYDROCODONE IN AN ER VISIT. I HAVE NOT RX'D PATIENT WITH HYDROCODONE.
HE GOT A SMALL RX FROM ANOTHER SOURCE OF ENDOCET. HAVE ADDRESSED WITH PATIENT.
DIAGNOSIS FIBROMYALGIA.
PATIENT WAS IN WITH PAIN MANAGEMENT BUT THAT PHYSICIAN HAD TO STOP SEEING PATIENTS DUE TO AN ILLNESS. HE WAS THE ONE WHO PRESCRIBED ULTRAM. PT CAME TO ME FOR NEW PAIN MANAGEMENT REFERRAL AND INFORMED ME ULTRAM WAS NOT HELPING SO HAD HER STOP ULTRAM AND ORDERED THE LORTAB FOR HER TO TAKE INSTEAD.
GETTING NEW PAIN MED DOCTOR.
I SAW THIS PATIENT IN THE ER, I WROTE A ONE TIME PRESCRIPTION. THANK YOU.
LAST OFFICE VISIT 4-18-12 NEITHER OF THOSE ARE ON OUR MOST RECENT MED LIST. I AGREE - IT'S A DUPLICATION.
DISCUSSED IN PAST, THIS WILL HELP ME MAKE CHANGE AT NEXT VISIT.
PATIENT NOT UNDER MY CARE DURING THIS PERIOD.
PT HAS RA AND LUPUS. HAS BEEN STABLE FOR MANY YEARS.
PATIENT HAD RECENT SURGERY. SURGEON HAS BEEN RX'ING CURRENT PAIN MED. THE DATES YOU LISTED ON 12/1/12 AND 12/19/12 DO NOT CORRESPOND WITH RX WRITTEN BY ME.
WILL DISCUSS WITH PRESCRIBER. TRAMADOL NEVER PICKED UP AT OTHER PHARMACY. PT WAS COUNSELED TO NOT TAKE TRAMADOL WITH HYD/APAP. PT IS CURRENTLY UNDER CARE OF ONE DOCTOR AND TRAMADOL WAS STOPPED IN DECEMBER. PT CURRENTLY ON HYD/APAP AND IS FILLING AT REGULAR INTERVALS.

I GAVE PATIENT LIMITED DOSE OVER A COUPLE MONTHS WHILE REFERRING TO A DIFFERENT PHYSICIAN.
THE OXYCODONE 7.5/325 WAS NOT FILLED BY COUCH. SHE HAS HAD NO OXYCODONE SINCE DECEMBER 2012, SO I ASSUME HER CONDITION HAS IMPROVED OR BEEN RESOLVED.
I DISCONTINUED THE HYDROCODONE FOR MR. XXXX IN JUNE, 2012. HE CONTINUES TO REQUIRE OXYCONTIN & OXYCODONE TO FUNCTION AT ALL.
LOOKS LIKE AN ER VISIT.
MEDICATION HAS BEEN CHANGED.
NORCO 10/325 HAS BEEN REMOVED. OXYCODONE WILL BE CONTINUED FOR BREAKTHROUGH PAIN.
PATIENT IS NO LONGER RECEIVING PAIN MEDICATIONS FROM MY OFFICE SECONDARY TO COMPLIANCE ISSUES & DRUG SEEKING BEHAVIOR.
HAS BEEN TAKING THE SAME DOSE FOR 2 YEARS ON REGULAR BASIS. NO INCREASE IN HIS PRESCRIPTIONS OR FREQUENCY. I HAVE CONTACTED HIM, I WAS UNAWARE OF HYDROCODONE PRESCRIPTION - REVIEWED IT. WILL CONTINUE CURRENT MANAGEMENT.
PT IS DECEASED. EXPIRED 2-2-13
I PRESCRIBED NARCOTIC PAIN RELIEF MEDICATIONS IN ASSOCIATION WITH SEVERAL RECONSTRUCTIVE OPERATIONS, WHICH HAVE NOW BEEN COMPLETED, THEN I STOPPED PRESCRIBING THEM.
I SAW THE PATIENT ONCE, FOR TREATMENT OF A SUPERFICIAL BURN.
I HAVE ONLY FILLED ONE PRESCRIPTION FOR THIS PATIENT IN THE LAST 6 MONTHS. CANNOT MAKE DETERMINATION.
SHE IS NOT TAKING TRAMADOL AND HYDROCODONE TOGETHER. SHE IS TRYING TO GET OFF OF TRAMADOL.
PATIENT IS NEW TO THIS FACILITY // REPORTS PCP HE HAD PREVIOUSLY NO LONGER TAKES MEDICAID. PATIENT IS AWARE HE WILL NOT RECEIVE LORTAB OR VALIUM HERE AND FLEXRIL AND TRAMADOL MUST LAST 30 DAYS.
I AM THE ONLY PRACTITIONER TREATING HER CHRONIC PAIN W/ NARCOTICS. WE CHECKED THE OK PMP WHICH CONFIRMS.
THIS LOOKS LIKE A ONE TIME OCCURANCE . FOR #15 // I DO NOT SEE PROBLEM.
LAST TIME GIVEN LORTAB WAS JULY 23, 2012. NORCO WAS GIVEN 11-5-2012. NO OXYCONTIN WAS GIVEN BY ME OR THIS CLINIC.
I HAVE COUNSELLED THIS PATIENT REPEATEDLY. I HAVE GIVEN HER A 30 DAY SCRIPT TO HELP HER WEAN OFF SLOWLY IF SHE WILL FOLLOW INSTRUCTION. SHE HAS BEEN DISMISSED FROM OUR PRACTICE FOR NON-COMPLIANCE.
POST CANCER ORAL/THROAT // OBVIOUSLY AWARE OF OUR RX'S - NOT AWARE OF OTHERS - DO YOU SEND THIS TYPE OF NOTIFICATION TO THE PRESCRIBERS? // I CAN LET DR. XXXX AND XXXXX KNOW - DON'T KNOW WHO OTHER PRESCRIBERS ARE // I NOTICE DIAZEPAM 10MG FROM DIFFERENT PHARMACY & DIFFERENT DR. WE HAVE DIAZEPAM IN HIS PROFILE ALSO BUT HE HAS BEEN PAYING CASH // MY CELL XXXXXX
PT HAS NOT RECEIVED ANY MORE TRAMADOL SINCE I HAVE BECOME AWARE THAT TRAMADOL IS NOW A NARCOTIC CLASS // TRAMADOL WAS USED FOR MILDER PAIN & HYDROCODONE FOR MODERATE TO SEVERE PAIN - FYI, I NO LONGER GIVE TRAMADOL.
SHE HAS ONLY FILLED OXY/APAP ONE TIME AT OUR STORE. NOT FAMILIAR W/ SITUATION & WILL NOT DISCUSS W/ PATIENT.
WILL DISCUSS WITH PRESCRIBER // WE HAVEN'T FILLED FOR HER SINCE THE 11/15/12 RX, ACCORDING TO RECORDS, SHE IS MORE RECENTLY FILLING AT XXXX MEDICAL PHARMACY IN DURANT & RECEIVED MORE HYDROCODONE FROM YET ANOTHER DR AT THAT PHARMACY. WE WILL CALL DR & MAKE NOTE ON PROFILE HERE AT WAL MART
TO MY KNOWLEDGE THE PATIENT IS NOT TAKING TRAMADOL. I WILL CHECK WITH THE PATIENT TO CONFIRM THAT HE IS NOT TAKING TRAMADOL.
ALL OF THESE PRESCRIBERS APPEAR TO BE FROM THE SAME OFFICE.

PATIENT ONLY FILLED ONCE AT THIS LOCATION. NOT FAMILIAR W/ PT. HISTORY
HER PCP MANAGES PAIN CONTROL FOR THE MOST PART. APPRECIATE THE NOTE.
NO LONGER ON TRAMADOL BUT I WILL MONITOR THIS WHEN PT FILLS HERE VIA PMP.
I SAW HER ONLY ONE TIME 11-19-12 BETWEEN 11-1-12 AND 11-30-12. I DID NOT KNOW THAT SHE WAS GETTING MEDS FROM OTHER PHYSICIANS. I WILL TALK TO HER NEXT VISIT. THANKS FOR THE INFO.
ONLY TIME THEY GOT ANYTHING FROM US WAS IN NOV 2012.
WE GAVE LAST SCRIPT JAN 2013. TOLD PATIENT HE NEEDED MEDICAL PAIN MANAGEMENT.
WILL DC TRAMADOL ON NEXT VISIT.
WILL D/C HYDROCODONE AND USE ONLY OXYCODONE.
I WAS AWARE OF PREVIOUS PAIN MEDICINE USE. HOWEVER RECENT SURGERY NECESSITATED THE TEMPORARY PRESCRIPTION FROM ME. SHE WILL NOT LIKELY NEED ANY FURTHER NARCOTICS FROM ME.
PATIENT HAS MIGRAINES, AND SHE USES HYDROCODONE FOR MORE SEVERE PAIN. TRAMADOL IS USED WHEN LESS SEVERE. THE PHYSICIANS ARE AWARE OF THE ISSUE. THANK YOU.
NO FURTHER NARCOTIC RX'S WILL BE PROVIDED BY THIS OFFICE & PT WILL BE DISMISSED.
I AM AN URGENT CARE DOCTOR GIVING EPISODIC CARE. TRAMADOL WAS NOT HELPING WITH HER SEVERE PAIN, SO I INSTEAD GAVE HER PERCOCETS WHICH DOES HELP WITH SEVERE PAIN. I DID NOT PRESCRIBE TRAMADOL FOR HER & I USUALLY ADVISE TO NOT TAKE BOTH AT THE SAME TIME.
THIS IS & WAS MY ONLY INTERACTION WITH MRS. XXXX. FROM THE MEDICATION PROFILE IT APPEARS SHE IS USING THE MORPHINE ER FOR MAINTENANCE AND HYDROCODONE FOR BREAKTHROUGH PAIN. IF SO, THIS IS APPROPRIATE. ALSO, IF YOU NOTE ON THE RX FROM 10/1/12 THE RX WAS SUBMITTED FOR LORTAB, THEN REVERSED AND CORRECTED TO NORCO 7.5.
REFER FOR LOCK-IN // I WAS ONLY AWARE PARTIALLY, OF RECENTLY - WAS NOT AWARE OF HISTORY DATING BACK SO FAR. THANK YOU. CURRENTLY AWARE AND WILL CONTINUE MONITORING. UNDER CARE FOR POST SURGICAL RECONSTRUCTION OF LIMB, AND PAIN MANAGEMENT ONLY DURING THE PERIOD OF RECENT, AND ONLY FOR MEDICATION I PRESCRIBED. I WILL CONTINUE TO MONITOR CLOSELY.
I AM A HOSPITALIST BUT I WAS NOT AWARE OF A POTENTIAL SITUATION WITH THIS PATIENT'S NARCOTICS. IF XXXXX IS READMITTED TO US WE WILL RE-ASSES AT THAT TIME. ANY FURTHER ISSUES SHOULD BE DIRECTED TO THE PRIMARY CARE PROVIDER. THANK YOU!
PATIENT SEEN AT RED BIRD CLINIC IN SALLISAW. I WAS A (?) DR FOR ONLY A SHORT TIME & NOT GOING BACK.
PT SEEN ONCE FOR A LIMITED EXAM - PT REFERRED TO ORAL SURGEON FOR EXTRACTION - PT COMPLETED TREATMENT AT OS - NO NEED FOR CONTINUED PAIN MEDICATION AT THIS TIME.
PATIENT WAS TERMINATED FROM BOTH OU INTERNAL MEDICINE AND OU FAMILY MEDICINE
I WAS AWARE // PT. DISMISSSED FROM MY SUBOXONE CLINIC
PATIENT HAS NOT FILLED AT OUR PHARMACY SINCE 10/31/12. WILL FLAG PATIENT'S ACCOUNT FOR INTERVENTION.
SEEN AS ER/URGENT CARE PT ONLY
PT HASN'T FILLED HERE SINCE 10-17-12 // WILL MAKE NOTE TO WATCH CONTROLS
THE RX FOR HYDROCODONE/APAP 5-500 WAS FROM THE ER WHILE THE RX FOR OXYCODONE/APAP 5-325 WAS FROM HER PCP. WE WILL MONITOR THE SITUATION IN THE FUTURE.
I SAW THIS PATIENT AS AN ER PHYSICIAN

Appendix C

Vote to Prior Authorize Kynamro™ (Mipomersen)

Oklahoma Health Care Authority
June 2013

Recommendations:

The College of pharmacy recommends prior authorization of Kynamro™ (mipomersen) with the following criteria:

Prior Authorization Criteria for Kynamro™ (Mipomersen):

1. FDA approved diagnosis of homozygous familial hypercholesterolemia defined by the presence of at least one of the following criteria:
    a. Documented functional mutation(s) in both LDL receptor alleles or alleles known to affect LDL receptor functionality via genetic testing; or
    b. Untreated total cholesterol >500 mg/dL and triglycerides <300 mg/dL *and*
        i. both parents with documented untreated total cholesterol >250 mg/dL; or
        ii. presence of tendinous /cutaneous xanthoma prior to age 10 years.
1. Documented failure of high dose statin therapy (LDL reduction capability equivalent to atorvastatin 80mg or higher); and
2. Prescriber must be certified with Kynamro™ REMS program.

Appendix D

FY 2012 Annual Review of Anticonvulsant Medications And 30-Day Notice to Prior Authorize Oxtellar XR™ (Oxcarbazepine ER) And Sabril® (Vigabatrin)

Oklahoma Health Care Authority
June 2013

Current Prior Authorization Criteria

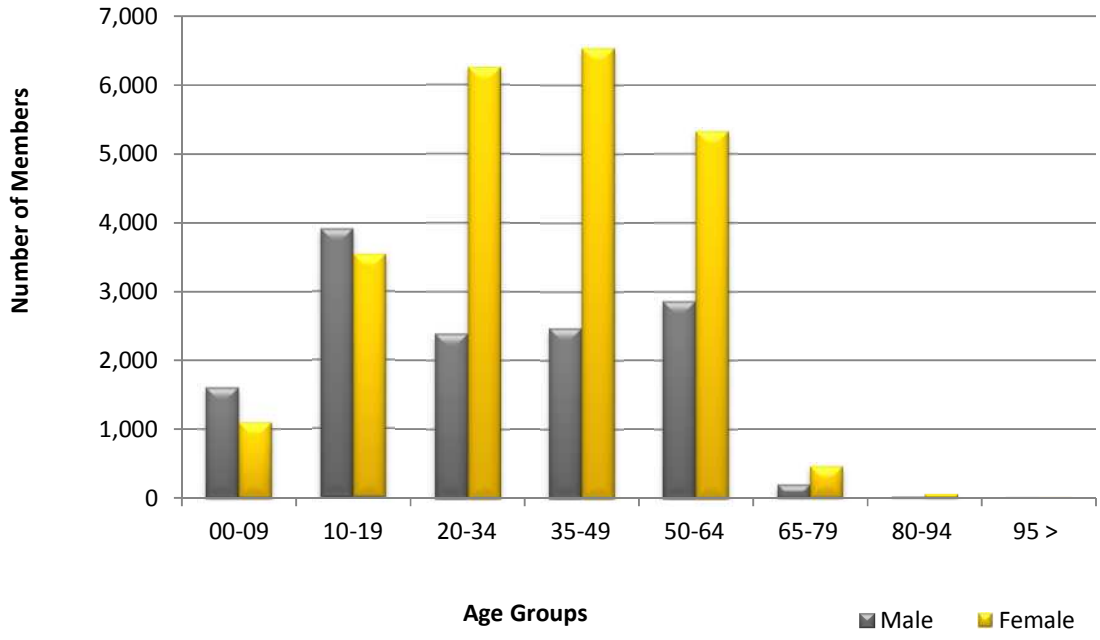
1. Anticonvulsants are included in the current mandatory generic plan.
    a. All brand-name anticonvulsants (with a generic equivalent) require prior authorization.
        i. Brand-name medications (with a generic equivalent) will be approved for all members who are currently stable on these medications and have a seizure diagnosis.
2. Prior authorization is required for certain non-standard dosage forms of medications when the drug is available in standard dosage forms.
    a. Members 12 and older must have a documented medical reason demonstrating need for non-standard dosage forms.
    b. Criteria for approval of extended-release formulations:
        i. Previously stabilized on the short-acting formulation.
        ii. Dosing is not more than once daily.
        iii. Member must provide a reason why the short-acting formulation is not adequate.
    c. Dose packs are not approved if standard dosage forms are available.
3. Quantity limit restrictions have been placed on lower strength tablets and capsules. The highest strengths continue to have no quantity restrictions unless a maximum dose is specified for a particular medication. (Please see Attachment A for additional details)
4. **Felbamate® (Felbatol) Approval Criteria**:
    a. Initial prescription written by a neurologist.
    b. Member has failed therapy with at least three other medications commonly used for seizures.
5. **Onfi® (clobazam) Approval Criteria:**
    a. Diagnosis of severe seizures or generalized tonic, atonic or myoclonic seizures; and
    b. Previous failure of at least two non-benzodiazepine anticonvulsants; and
    c. Previous failure of clonazepam
    d. For continuation prescriber must include information regarding improved response/effectiveness of this medication.

Utilization of Anticonvulsant Medications

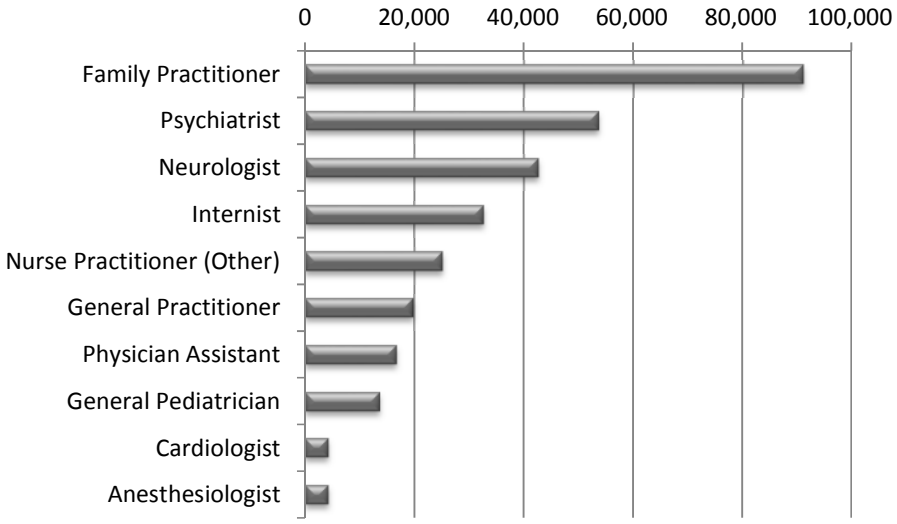
Comparison of Fiscal Years for Anticonvulsants

Fiscal Year	Members	Claims	Cost	Cost/Claim	Perdiem	Units	Days
2011	33,265	223,470	$12,617,576.29	$56.46	$1.88	23,804,514	6,713,989
2012	36,762	250,352	$13,795,867.22	$55.11	$1.83	25,374,999	7,551,683
% Change	**10.50%**	**12.00%**	**9.30%**	**-2.40%**	**-2.70%**	**6.60%**	**12.50%**
Change	**3,497**	**26,882**	**$1,178,290.93**	**-$1.35**	**-$0.05**	**1,570,485**	**837,694**

FY 2012 Demographics of Members Utilizing Anticonvulsants



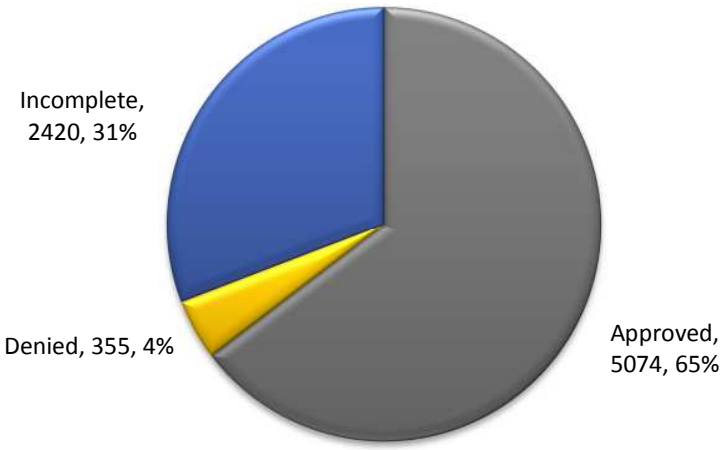
FY 2012 Prescribers of Anticonvulsants by Number of Claims



Prior Authorization of Anticonvulsants

There were a total of 7849 petitions submitted for anticonvulsants during fiscal year 2012. The following chart shows the status of the submitted petitions.

Status of Petitions for of Anticonvulsants



Market News and Update

- **Anticipated Patent Expirations:** [1]
  - Sabril® (vigabatrin)-August 2014
  - Vimpat® (lacosamide)-March 2017
  - Onfi® (clobazam)-October 2018
  - Lyrica® (pregabalin)-December 2018
  - Banzel® (rufinamide)-November 2022
- **Updated Package Labeling:**
  - **Keppra® (levetiracetam)**: Warning of increased risk of Stevens-Johnson's Syndrome or toxic epidermal necrolysis. (12/2011)[2]
  - **Dilantin® (phenytoin):** Black box warning associated with increased cardiovascular risk with rapid intravenous infusion exceeding 50mg per minute. Additional label changes included the risk of serious dermatologic reactions, and the risk of local toxicity associated with the injection formulation. A contraindication was also added stating that coadministration with delavirdine is not advised due to potential for loss of virologic response.(12/2011)[3]
  - **Zonegran® (zonisamide):** Potential adverse reactions of rhabdomyolysis and pancreatitis. (01/2012)[4]
  - **Vimpat®(lacosamide):** Increased risk for cardiac disorders (bradycardia), psychiatric disorders (hallucinations) and skin and tissue disorders (rash). (02/2013)[5]
  - **Dilantin® (phenytoin):** Potential drug interaction with non-depolarizing neuromuscular blocking agents. The drug interaction results in decreased effectiveness of the non-depolarizing neuromuscular blocking agent. (03/2013)[6]
- **New Indications and Approvals:**
  - **10/2012** The FDA approved Oxtellar XR™ (oxcarbazepine ER) for adjunctive therapy in the treatment of partial seizures in adults and in children 6 to 17 years of age.[7]
  - **10/2012** The FDA approves Fycompa™ (perampanel) to treat partial onset seizures in patients with epilepsy ages 12 years and older.[8]
- **FDA updates:**
  - **01/2012** Lundbeck Inc. ceases production of mephobarbital tablets and the company's remaining inventory was set to expire in March 2012.[9]
  - **04/2013** The FDA warns the public that Potiga® (ezogabine) can cause blue skin discoloration and eye abnormalities characterized by pigment changes in the retina. All patients taking Potiga® should have a baseline eye exam, followed by periodic eye exams. Potiga® should be discontinued if ophthalmic changes are observed unless no other treatment options are available. If a patient develops skin discoloration, serious consideration should be given to changing to an alternate medication.[10]

Oxtellar XR™ (Oxcarbazepine Extended-Release) Summary[11]

- **Indications:** Oxtellar XR™ (oxcarbazepine ER) is an antiepileptic drug indicated for adjunctive therapy in the treatment of partial seizures in adults and children aged 6 to 17 years.

- **Dosing:** Oxtellar XR™ is available as 150mg, 300mg and 600mg extended-release tablets. The recommended daily dose is 1200mg to 2400mg by mouth once daily. Adults should initiate therapy with a dose of 600mg daily and if necessary the dose should be increased weekly in intervals of 600mg per day to the recommended daily dose. Dosing in pediatric patients is based upon weight. Children should be initiated on 8 mg/kg to 10 mg/kg per day and increased weekly in increments of 8 mg/kg to 10 mg/kg daily (not to exceed 600mg), to achieve target daily dose. Dosage adjustments are recommended for patients with the following characteristics:

    - Patients with creatinine clearance less than 30mL/minute should start at 300mg per day and increase slowly.
    - Geriatric patients should start at a lower dose of 300mg or 450mg per day and increase slowly.

  When converting from oxcarbazepine immediate-release to Oxtellar XR™, higher doses of Oxtellar XR™ may be necessary. Tablets should be taken on an empty stomach at least one hour before food or at least two hours after food.

- **Efficacy:** The Oxtellar XR™ Primary Trial compared the efficacy of Oxtellar XR™ with placebo by evaluating a percentage change from baseline in seizure frequency per 28 days. The randomized, placebo-controlled, multinational, double-blind trial evaluated adults with a diagnosis of refractory epilepsy who had a least three partial seizures per 28 days during an eight-week baseline period. The three-arm trial compared placebo to Oxtellar XR™ 1200mg per day or 2400mg per day with a primary outcome of mean percentage change from baseline in seizure frequency per 28 days during the treatment period relative to the baseline period. Oxtellar XR™ 2400mg was found to have a statistically significant decrease in average percent change in seizure frequency compared to placebo (-42.9% for Oxtellar XR™ 2400mg vs. -28.7% for placebo; P =0.003). Oxtellar XR™ 1200mg did not reach statistical significance (-38.2% for Oxtellar XR™ 1200mg vs. -28.7% for placebo; P =0.078).

- **Cost:** The following is a comparison of costs.

Estimated Acquisition Cost Per Tablet		
Strength	Oxtellar XR™ (oxcarbazepine ER)	Generic oxcarbazepine Immediate Release
150 mg	ER: $3.15	$0.28
300 mg	ER: $4.37	$0.34
600 mg	ER: $8.00	$0.59

Fycompa™ (Perampanel) Summary[12, 13]

- **Indications:** Fycompa™ (perampanel) is a non-competitive AMPA glutamate receptor antagonist indicated for adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalized seizures in patients with epilepsy aged 12 years and older.

- **Dosing:** Fycompa™ is available as 2mg, 4mg, 6mg, 8mg, 10mg and 12mg tablets. The recommended daily dose is 8mg to 12mg by mouth once daily. Patients should initiate therapy with a dose of 2mg daily at bedtime and if necessary the dose should be increased no more frequently than weekly in increments of 2mg per day to the recommended daily dose. The maximum recommended daily dose is 12mg once daily. Dosage adjustments are recommended for patients with the following characteristics:
    - Patients with mild or moderate hepatic impairment should start at 2mg per day and increase no more frequently than every 2 weeks with a maximum daily dose of 6mg daily.
    - Geriatric patients should increase dosing no more frequently than every two weeks.
- When Fycompa™ is used concomitantly with enzyme-inducing antiepileptic medications, including phenytoin, carbamazepine, and oxcarbazepine, the starting dose is 4mg. Tablets can be taken with or without regard to food. The FDA recommended that Fycompa™ be classified as a scheduled drug. The DEA is currently reviewing the recommendation to determine a final scheduling designation.

- **Efficacy:** Two phase III trials compared the efficacy of Fycompa™ with placebo by evaluating a percentage change from baseline in seizure frequency. The randomized, placebo-controlled, double-blind trials evaluated patients with persisting seizures despite treatment with one to three anti-epileptic medications. One trial compared placebo to Fycompa™ 2mg, 4mg, or 8mg while the other compared placebo to Fycompa™ 8mg or 12mg. The primary outcomes of both trials were median percent change in seizure frequency and 50% responder rate. The median percent change in seizure frequency was statistically significant when compared to placebo for perampanel 8mg and 12mg with reductions of -26.3%, and -34.5% (p =0.0261 for 8mg and p = 0.0158 for 12 mg). Fifty percent responder rates during the maintenance period were not statistically significant for Fycompa™ 8mg or 12mg. In the alternate phase III trial, median percent change in seizure frequency was -13.6%, -23.3%, and -30.8% for Fycompa™ 2mg, 4mg, and 8mg/day. The difference from placebo was statistically significant for Fycompa™ 4mg/day (p =0.0026) and 8mg/day (p = 0.0001). Only the 4mg/day and 8mg/day had statistically significant 50% responder rates (28.5% (p =0.0132) for 4mg/day & 34.9% (p = 0.0003) for 8mg/day).

- **Cost:** The cost for Fycompa™ is not available.

Sabril® (Vigabatrin) Summary[14]

- **Indications:** Sabril® (vigabatrin) is an irreversible inhibitor of γ-aminobutyric acid transaminase (GABA-T) indicated for adjunctive therapy in the treatment of refractory complex partial seizures in adults who have responded inadequately to several alternative treatments. The powder formulation is indicated as monotherapy for infantile spasms in ages one month to two years of age.

- The American Academy of Neurology guidelines state good evidence (level B) supports the use of adrenocorticotropic hormone (ACTH), but state weak evidence (level C) supports the use of Sabril® for short-term treatment of infantile spasms. The recent update indicates that ACTH may be offered over Sabril®.[16]

- **Dosing:** Sabril® is available as a 500mg tablet and a powder for oral solution (500mg packet). The recommended daily dose for adults is 1,500mg by mouth twice daily. Patients should initiate therapy with a dose of 500mg twice daily and if necessary the dose should be increased weekly in increments of 500mg per day to the recommended daily dose. A 6,000mg/day dose has not been

shown to confer additional benefit compared to the 3,000mg/day. Dosage adjustments are recommended for patients with the following characteristics:
    - Patients with mild, moderate, or severe renal impairment should have the dose decreased by 25%, 50% or 75% respectively.
    - Geriatric patients should use Sabril® with caution as it is known to be substantially excreted by the kidney and the risk of toxic reactions may be greater.

- Sabril® powder for pediatric patients initial dosing is 50mg/kg/day in two divided doses and can be titrated up by 25-50mg/kg/day increments every 3 days up to a maximum of 150mg/kg/day. The entire contents of the packets should be dissolved into 10mL of water per packet and taken by mouth with or without food.
- Sabril® is only available through the SHARE program due to risk of permanent vision loss. To enroll in SHARE, prescribers must understand the risks of Sabril® and complete the enrollment agreement form stating that they will:
    - Review the medication guide with patients/parents/legal guardians.
    - Educate patients on the risks of Sabril®.
    - Order and review vision assessments upon initiation of treatment, every 3 months while on therapy, and approximately 3 to 6 months after discontinuation. The vision assessments must be submitted to the SHARE program after every assessment.
    - Remove patients from Sabril® if they do not experience a meaningful reduction in seizures. A treatment maintenance form must be submitted to the SHARE program after the initial evaluation.
    - Counsel patients who fail to comply with the program requirements.
    - Remove all patients from Sabril® who fail to comply with the program requirements after appropriate counseling.

- **Efficacy:** The efficacy of Sabril® for the treatment of complex partial seizures was evaluated in a randomized, double-blind, placebo-controlled, parallel study. The study consisted of a pre-treatment (baseline) period of 8 weeks followed by a 16-week treatment phase during which patients were treated with Sabril® or placebo. The primary outcome was the reduction in mean monthly complex partial seizure frequency. Sabril® 3,000mg/day was found to be superior in reducing seizure frequency with statistically significant results (Sabril® 8.3 baseline to 5.5; Placebo: 9.0 baseline to 7.5 ($P<0.05$))
- The efficacy of Sabril® for the treatment of infantile spasms was evaluated in a multicenter, randomized, double-blind, placebo-controlled, parallel study. The study consisted of a pre-treatment (baseline) period of 2-3 days followed by a 5-day treatment phase during which patients were treated with Sabril® or placebo. The primary outcome was the average percent change in daily spasm frequency, assessed during a 2-hour window evaluation, comparing baseline to the final 2 days of the 5-day treatment phase. The average change in frequency of spasms using the 2-hour evaluation window was not statistically significant. A post-hoc analysis using a 24-hour clinical evaluation window found a statistically significant difference in the overall percentage of reduction in spasms between the Sabril® group (68.9%) and the placebo group (17.0%) ($p=0.030$).

- **Cost:** The cost per 500mg tablet and 500mg packets are $59.52 per unit.

Conclusions and Recommendations:

The College of Pharmacy recommends the following:

1. Prior Authorization of Oxtellar XR™ (oxcarbazepine ER) with the following criteria:
    a. A patient specific, clinically significant reason why member cannot use the short-acting formulation.
    b. A quantity limit of 30 per 30 days will apply on the lower strength tablets (150mg and 300mg).
2. Prior authorization of Sabril® (vigabatrin) for all members 3 years of age and older. Use of Sabril® in members younger than 3 years of age will not require prior authorization. For members 3 years of age or older, the following criteria will apply:
    a. The member must have FDA approved diagnosis of refractory complex seizures, and
    b. Treatment with at least three other antiepileptic medications that has failed to yield adequate clinical response, and
    c. Prescriptions must be written by a neurologist.
    d. Prescriber, member, and pharmacy must all register in the SHARE program and maintain enrollment throughout therapy.
    e. A quantity limit of 180 per 30 days will apply on both the tablets and packets.

Attachment A

Anticonvulsant Dosing and Restrictions				
Drug name	**How Supplied**	**Normal daily dosing**	**Max dose**	**Restrictions**
Barbiturates				
Mephobarbital (Mebaral)	32, 50, 100mg tablet	400-600mg div TID-QID, or given HS	600 mg/day	Discontinued production
Phenobarbital (Luminal)	15, 16.2, 30, 32.4, 60, 64.8, 97.2, 100 mg tablet	Adult: 50-100mg BID-TID, Ped: 15-50mg BID-TID		
Phenobarbital elixir	20 mg/mL oral elixir	Adult: 60-200mg/day, Ped: 3-6mg/kg/day		
Phenobarbital injection	65 mg/mL, 130mg/mL injection	100 -320mg slow IV or IM		
Hydantoins				
Fosphenytoin (Cerebyx)	100mg PE/2mL, 500mg PE/10mL injections	LD: 10-20mg PE/kg IV or IM, MD: 4-6mg PE/kg/day	Max IV rate 150mg PE/min	
Phenytoin (Dilantin)	50 mg chew tablet	Adults: ID: 100mg TID, MD: 300-400mg, Ped: 4-8mg/kg/day div BID-TID	Adult:600mg/day Ped: 300mg/day	180/30
	100 mg/4mL, 125 mg/5mL oral suspension	Adult: 125mg TID, Ped: 4-8mg/kg/day div BID-TID	Adult:625mg/day Ped: 300mg/day	360mL/30
	50 mg/mL injection	LD: 15-20 mg/kg, MD: 2 mL IV Q 6-8 hrs	Adult:600mg/day Ped: 300mg/day	
	100 mg ER capsule	Adult: 100 mg TID-QID or 300mg QD, Ped: 4-8mg/kg/day div BID-TID		180/30
	200 mg ER capsule			90/30
	300 mg ER capsule			
Succinimides				
Ethosuximide (Zarontin)	250 mg capsule	Individualized, Adults: ID 500 mg/day & Ped: ID 250mg/day	1500 mg/day	180/30
	250mg/5mL oral syrup			
Methsuximide (Celontin)	300 mg capsule	300 mg QD	1200mg/day	
Valproic acid and derivatives				
Valproic acid (Depakene)	250 mg/5 mL oral syrup	ID: 10-15 mg/kg/day, doses >250 mg/day should be given in divided doses	60 mg/kg/day 75 kg= 4,500mg/day 25 kg= 1,500mg/day	1020mL/34
	250mg capsule			
Valproic acid (Stavzor)	125 mg DR capsule			120/30
	250 mg DR capsule			120/30
	500 mg DR capsule			
Divalproex sodium (Depakote)	125 mg sprinkle capsule			Age ≤11yo, 360/30
	125 mg DR tablet			90/30
	250 mg DR tablet			90/30
	500 mg DR tablet			
	250 mg ER tablet			90/30
	500 mg ER tablet			
Valproate inj (Depacon)	100 mg/mL injection			1350mL/30

Drug name	How Supplied	Normal daily dosing	Max dose	Restrictions
Carbamazepine Derivatives				
Carbamazepine (Tegretol)	100 mg chew tablet	Adults: 400mg/day (BID for ER, TID-QID for others), Ped: ≤6yo: 10-20mg/kg/day div QID 6-12yo: 400-800mg div QID (div BID for ER)	Adult: 1,600mg/day, PED: 35mg/kg or 1,000mg/day	
	100 mg/5 mL oral suspension			1500mL/30
	200 mg tablet			
	100 mg XR tablet			90/30
	200 mg XR tablet			90/30
	400 mg XR tablet			
Carbamazepine (Carbatrol)	100 mg ER capsule			150/30
	200 mg ER capsule			150/30
	300 mg ER capsule			150/30
Oxcarbazepine (Trileptal)	300 mg/5 mL oral suspension	Adults: 1,200mg/day, given BID, Ped:2-4yo 60mg/kg/day div BID 4-16yo: 600- 2100mg/day	Ped: 2100mg/day Adult: 2,400mg/day	1200mL/30
	150 mg tablet			90/30
	300 mg tablet			90/30
	600 mg tablet			
Oxcarbazepine (Oxtellar XR)	150mg ER tablet	Adults:1200-2400mg/QD, Ped: 8-10mg/kg QD	Adult: 2,400mg/day, Ped: 600mg/day	30/30
	300mg ER tablet			30/30
	600mg ER tablet			120/30
Lamotrigine				
Lamotrigine (Lamictal)	5 mg chew tablet	Ranges from 100-600mg/day in divided doses		Age ≤11yo 240/30
	25 mg chew tablet			Age ≤11yo 120/30
	25 mg tablet			180/30
	100 mg tablet			60/30
	150 mg tablet			120/30
	200 mg tablet			
	25 mg ODT tablet			Age ≤11yo 90/30
	50 mg ODT tablet			Age ≤11yo 90/30
	100 mg ODT tablet			Age ≤11yo 90/30
	200 mg ODT tablet			Age ≤11yo
	25 mg XR tablet			Dosage form 30/30
	50 mg XR tablet			Dosage form 30/30
	100 mg XR tablet			Dosage form 30/30
	200 mg XR tablet			Dosage form

Drug name	How Supplied	Normal daily dosing	Max dose	Restrictions
				60/30
	250 mg XR tablet			Dosage form 60/30
	300 mg XR tablet			Dosage form 90/30
Levetiracetam				
Levetiracetam (Keppra)	100 mg/mL oral solution	Adults: 3000mg/day, Ped: 6mos-4yo: 50mg/kg/day div BID, 4-16yo: 60mg/kg/day div BID	Adults: 3000mg/day, Ped: 6mos-4yo: 50mg/kg/day, 4-16yo: 60mg/kg/day	900mL/30
	500 mg/5mL oral solution			
	250 mg tablet			60/30
	500 mg tablet			120/30
	750 mg tablet			120/30
	1000 mg tablet			
	500 mg XR tablet			60/30
	750 mg XR tablet			
Topiramate				
Topiramate (Topamax)	15 mg sprinkle capsule	Adults: 200-400 mg/day divided BID, Ped: 2-16 yo: 5-9mg/kg/day	400mg/day	Age ≤11yo 120/30
	25 mg sprinkle capsule			Age ≤11yo 120/30
	25 mg tablet			90/30
	50 mg tablet			90/30
	100 mg tablet			90/30
	200 mg tablet			
Other anticonvulsants				
Felbamate (Felbatol)	400 mg tablet	Adult: 1200-3600mg/day div TID-QID, Ped: 15-45mg/kg/day div TID-QID	Adults: 3600mg/day Ped: 45mg/kg/day	PA & 240/30
	600 mg tablet			PA
	600mg/5mL oral suspension			PA
Gabapentin (Neurontin)	250mg/5mL oral solution	Adult: 900-1800mg/day div TID, Ped: 5-12yo: 25-35mg/kg/day div TID	3600mg/day	2,250mL/30
	100 mg capsule			150/30
	300 mg capsule			300/30
	400 mg capsule			90/30
	600 mg tablet			180/30
	800 mg tablet			
Lacosamide (Vimpat)	50 mg tablet	Adult: 200-400mg/day div BID, Ped: Not FDA approved	400 mg/day	60/30
	100 mg tablet			60/30
	150 mg tablet			60/30
	200 mg tablet			
	10mg/mL oral solution			
Primidone (Mysoline)	50 mg tablet	Adult:250 mg TID-QID Ped: 10-25mg/kg TID	2000 mg/day	120/30
	250 mg tablet			

Drug name	How Supplied	Normal daily dosing	Max dose	Restrictions
Rufinamide (Banzel)	200 mg tablet	Adult: 3200mg/day div BID, Ped: 45mg/kg/day div BID	3200 mg/day	90/30
	400 mg tablet			
	40mg/mL oral suspension			
Zonisamide (Zonegran)	25 mg capsule	Adult:100-600mg/day div QD-BID, Ped: Not approved <16 yo	600 mg/day	90/30
	50 mg capsule			90/30
	100 mg capsule			
Pregabalin (Lyrica)	25 mg capsule	Adult:150-600 mg/day, div BID-TID, Ped: Not FDA approved	600 mg/day	90/30
	50 mg capsule			90/30
	75 mg capsule			90/30
	100 mg capsule			90/30
	150 mg capsule			90/30
	200 mg capsule			60/30
	225 mg capsule			
	300 mg capsule			
Acetazolamide (Diamox)	125 and 250mg tablets	8-30mg/kg/day div, range 375-1000 mg/day	1000mg/day	
Ezogabine (Potiga)	50, 200, 300, 400mg tablets	Adult: 200-400mg TID, Ped: Not FDA approved		90/30
Tiagabine (Gabitril)	2,4 mg tablets	Adult: 4-56mg/day div BID-QID Ped:2-32mg/day div BID-QID	Adult:56mg/day Ped: 32mg/day	
Vigabatrin (Sabril)	500 mg tablet, 500 mg oral powder for solution	Adult & >16 yo: 500-1500mg BID	1500mg BID	

Anticonvulsant Utilization Details

CHEMICAL NAME	BRAND NAME	CLAIMS	MEMBERS	COST	COST/ DAY	% COST
Acetazolamide	ACETAZOLAMID TAB 250MG	308	101	$9,761.37	$1.08	
Acetazolamide	ACETAZOLAMID CAP 500MG ER	176	72	$31,467.26	$6.29	
Acetazolamide	ACETAZOLAMID TAB 125MG	59	14	$1,999.41	$1.03	
	SUBTOTAL	**543**	**184**	**$43,228.04**	**$2.70**	**0.31%**
Carbamazepine	CARBAMAZEPIN TAB 200MG	5,765	1,120	$54,558.17	$0.31	
Carbamazepine	CARBAMAZEPIN CHW 100MG	1,378	273	$27,360.48	$0.67	
Carbamazepine	EPITOL TAB 200MG	894	225	$5,145.21	$0.19	
Carbamazepine	CARBAMAZEPIN TAB 200MG ER	684	167	$40,714.20	$1.96	
Carbamazepine	CARBAMAZEPIN TAB 400MG ER	647	102	$61,872.33	$3.16	
Carbamazepine	CARBAMAZEPIN SUS 100/5ML	479	59	$44,338.37	$3.51	
Carbamazepine	CARBAMAZEPIN CAP 300MG ER	436	75	$55,124.77	$4.21	
Carbamazepine	CARBATROL CAP 300MG ER	316	54	$46,218.11	$4.87	
Carbamazepine	CARBATROL CAP 200MG ER	307	49	$64,169.37	$6.94	
Carbamazepine	CARBAMAZEPIN CAP 200MG ER	283	54	$44,220.53	$5.29	
Carbamazepine	TEGRETOL XR TAB 200MG	279	42	$31,603.50	$3.78	
Carbamazepine	TEGRETOL XR TAB 100MG	273	55	$12,404.47	$1.44	
Carbamazepine	TEGRETOL XR TAB 400MG	203	29	$32,756.45	$5.08	
Carbamazepine	TEGRETOL TAB 200MG	144	21	$21,931.16	$4.92	
Carbamazepine	TEGRETOL SUS 100/5ML	141	15	$21,707.65	$5.18	
Carbamazepine	CARBATROL CAP 100MG ER	73	15	$10,959.50	$5.02	
Carbamazepine	CARBAMAZEPIN CAP 100MG ER	73	23	$5,582.26	$2.41	
Carbamazepine	TEGRETOL CHW 100MG	67	8	$4,970.47	$2.72	
	SUBTOTAL	**12,442**	**1,980**	**$585,637.00**	**$1.57**	**4.24%**
Divalproex	DIVALPROEX TAB 500MG ER	8,976	1,762	$248,521.48	$0.92	
Divalproex	DIVALPROEX TAB 500MG DR	8,647	1,735	$176,506.89	$0.67	
Divalproex	DIVALPROEX TAB 250MG DR	6,344	1,665	$105,712.72	$0.55	
Divalproex	DIVALPROEX TAB 250MG ER	3,735	927	$88,065.98	$0.79	
Divalproex	DIVALPROEX SPR CAP 125MG	2,861	510	$238,139.73	$2.89	
Valproate	VALPROIC ACD SYP 250/5ML	1,903	272	$36,801.34	$0.68	
Valproic Acid	VALPROIC ACD CAP 250MG	1,854	368	$50,884.15	$0.91	
Divalproex	DIVALPROEX TAB 125MG DR	1,362	344	$20,874.14	$0.51	
Divalproex	DEPAKOTE SPR CAP 125MG	542	77	$98,246.37	$6.15	
Valproate	VALPROIC ACD SOL 250/5ML	541	94	$8,236.84	$0.52	
Divalproex	DEPAKOTE ER TAB 500MG	333	67	$90,032.00	$9.15	
Divalproex	DEPAKOTE ER TAB 250MG	205	36	$41,296.59	$6.75	
Divalproex	DEPAKOTE TAB 250MG DR	196	49	$30,900.65	$5.36	
Divalproex	DEPAKOTE TAB 500MG DR	184	33	$68,891.18	$12.44	
Valproate	DEPAKENE SYP 250/5ML	64	9	$7,931.08	$4.19	
Divalproex	DEPAKOTE TAB 125MG DR	62	15	$4,889.01	$2.64	
Valproic Acid	STAVZOR CAP 500MG DR	35	11	$9,721.23	$8.92	
Valproic Acid	STAVZOR CAP 250MG DR	33	7	$4,454.29	$4.58	
Valproic Acid	STAVZOR CAP 125MG DR	5	1	$381.64	$2.54	
	SUBTOTAL	**37,882**	**6,044**	**$1,330,487.31**	**$1.17**	**9.64%**
Ethosuximide	ETHOSUXIMIDE CAP 250MG	631	104	$47,306.67	$2.53	
Ethosuximide	ETHOSUXIMIDE SOL 250/5ML	589	103	$17,753.30	$1.03	
Ethosuximide	ZARONTIN CAP 250MG	43	7	$6,304.12	$4.89	
Ethosuximide	ZARONTIN SOL 250/5ML	4	2	$274.72	$2.29	
	SUBTOTAL	**1,267**	**197**	**$71,638.81**	**$1.92**	**0.52%**
Ezogabine	POTIGA TAB 50MG	4	2	$894.17	$8.60	
Ezogabine	POTIGA TAB 200MG	2	1	$1,255.56	$20.93	
	SUBTOTAL	**6**	**2**	**$2,149.73**	**$13.11**	**0.16%**
Felbamate	FELBATOL TAB 600MG	181	32	$98,533.10	$18.63	
Felbamate	FELBAMATE TAB 600MG	138	19	$70,657.81	$17.23	
Felbamate	FELBATOL SUS 600/5ML	114	15	$99,001.88	$30.67	
Felbamate	FELBATOL TAB 400MG	97	14	$45,003.79	$14.80	
Felbamate	FELBAMATE SUS 600/5ML	42	8	$39,941.22	$35.89	
Felbamate	FELBAMATE TAB 400MG	31	7	$8,954.19	$9.08	

CHEMICAL NAME	BRAND NAME	CLAIMS	MEMBERS	COST	COST/ DAY	% COST
	SUBTOTAL	603	63	$362,091.99	$20.39	2.62%
Fosphenytoin	FOSPHENYTOIN INJ 100/2ML (PHENYTOIN EQUIV)	4	2	$24.63	$6.16	
	SUBTOTAL	4	2	$24.63	$6.16	0.0%
Gabapentin	GABAPENTIN CAP 300MG	27,759	8,642	$427,044.37	$0.49	
Gabapentin	GABAPENTIN TAB 600MG	12,990	2,933	$536,842.84	$1.35	
Gabapentin	GABAPENTIN CAP 100MG	6,788	2,801	$66,192.79	$0.33	
Gabapentin	GABAPENTIN TAB 800MG	5,331	1,046	$384,938.69	$2.38	
Gabapentin	GABAPENTIN CAP 400MG	3,249	941	$48,478.67	$0.50	
Gabapentin	GABAPENTIN SOL 250/5ML	421	73	$44,344.90	$3.90	
Gabapentin	NEURONTIN SOL 250/5ML	23	13	$3,512.00	$6.82	
Gabapentin	NEURONTIN CAP 300MG	13	2	$2,357.01	$5.16	
Gabapentin	NEURONTIN TAB 800MG	13	1	$5,509.14	$14.65	
Gabapentin	NEURONTIN TAB 600MG	4	1	$1,547.78	$5.53	
	SUBTOTAL	56,591	13,755	$1,520,768.19	$0.87	11.02%
Lacosamide	VIMPAT TAB 100MG	878	165	$404,827.82	$15.62	
Lacosamide	VIMPAT TAB 200MG	653	96	$302,870.20	$15.49	
Lacosamide	VIMPAT TAB 50MG	400	106	$113,060.96	$9.84	
Lacosamide	VIMPAT TAB 150MG	305	64	$130,543.37	$14.47	
Lacosamide	VIMPAT SOL 10MG/ML	222	43	$70,875.06	$11.80	
	SUBTOTAL	2,458	336	$1,022,177.41	$14.20	7.41%
Lamotrigine	LAMOTRIGINE TAB 100MG	8,654	2,198	$97,546.46	$0.37	
Lamotrigine	LAMOTRIGINE TAB 200MG	7,071	1,301	$85,139.44	$0.38	
Lamotrigine	LAMOTRIGINE TAB 25MG	6,299	2,555	$87,978.19	$0.47	
Lamotrigine	LAMOTRIGINE TAB 150MG	3,511	706	$39,947.83	$0.37	
Lamotrigine	LAMOTRIGINE CHW 25MG	477	117	$18,907.30	$1.33	
Lamotrigine	LAMICTAL XR TAB 200MG	430	73	$218,025.82	$16.99	
Lamotrigine	LAMICTAL TAB 200MG	344	47	$131,141.05	$12.60	
Lamotrigine	LAMOTRIGINE CHW 5MG	197	67	$6,618.51	$1.16	
Lamotrigine	LAMICTAL TAB 100MG	172	32	$81,012.71	$15.86	
Lamotrigine	LAMICTAL ODT TAB 100MG	156	55	$41,287.79	$8.94	
Lamotrigine	LAMICTAL XR TAB 100MG	155	33	$99,541.67	$21.52	
Lamotrigine	LAMICTAL ODT TAB 50MG	142	41	$41,373.20	$9.01	
Lamotrigine	LAMICTAL TAB 150MG	138	18	$51,672.46	$12.58	
Lamotrigine	LAMICTAL KIT START 25 MG (42) & 100 MG (7)	102	99	$25,613.02	$8.45	
Lamotrigine	LAMICTAL ODT TAB 200MG	102	26	$35,913.42	$11.66	
Lamotrigine	LAMICTAL ODT TAB 25MG	64	19	$22,898.98	$12.10	
Lamotrigine	LAMICTAL XR TAB 50MG	64	17	$17,931.00	$9.62	
Lamotrigine	LAMICTAL TAB 25MG	64	13	$40,821.83	$21.82	
Lamotrigine	LAMICTAL XR TAB 300MG	62	11	$35,866.91	$18.11	
Lamotrigine	LAMICTAL CHW 25MG	23	2	$38,145.25	$55.28	
Lamotrigine	LAMICTAL ODT KIT 25 MG (14) & 50 MG (14) & 100 MG (7)	21	21	$5,257.01	$8.73	
Lamotrigine	LAMICTAL XR TAB 25MG	8	2	$1,276.40	$5.32	
Lamotrigine	LAMICTAL KIT START 25 MG (35)	5	5	$851.53	$7.10	
Lamotrigine	LAMICTAL ODT KIT 25 MG (21) & 50 MG (7)	4	4	$724.84	$6.09	
Lamotrigine	LAMICTAL XR TAB 250MG	3	1	$1,610.85	$17.90	
Lamotrigine	LAMICTAL ODT KIT 50 MG (42) & 100 MG (14)	1	1	$518.86	$14.82	
Lamotrigine	LAMICTAL KIT START 25 MG (84) & 100 MG (14)	1	1	$499.83	$16.66	
	SUBTOTAL	28,270	5,199	$1,228,122.16	$1.43	8.90%
Levetiracetam	LEVETIRACETA SOL 100MG/ML	7,926	1,150	$314,477.47	$1.35	
Levetiracetam	LEVETIRACETA TAB 500MG	7,637	1,607	$151,184.60	$0.66	
Levetiracetam	LEVETIRACETA TAB 1000MG	3,096	502	$152,701.69	$1.67	
Levetiracetam	LEVETIRACETA TAB 750MG	2,682	461	$81,832.20	$1.03	
Levetiracetam	LEVETIRACETA TAB 250MG	1,307	315	$23,053.45	$0.60	
Levetiracetam	KEPPRA XR TAB 500MG	481	110	$201,757.41	$14.02	
Levetiracetam	LEVETIRACETA TAB 500MG ER	348	87	$17,679.43	$1.67	
Levetiracetam	KEPPRA SOL 100MG/ML	294	40	$97,180.39	$11.10	
Levetiracetam	KEPPRA TAB 500MG	282	42	$117,805.76	$13.96	
Levetiracetam	KEPPRA XR TAB 750MG	281	46	$175,972.56	$21.24	
Levetiracetam	KEPPRA TAB 1000MG	188	25	$143,906.45	$26.31	

CHEMICAL NAME	BRAND NAME	CLAIMS	MEMBERS	COST	COST/ DAY	% COST
Levetiracetam	LEVETIRACETA TAB 750MG ER	161	46	$27,813.67	$5.62	
Levetiracetam	KEPPRA TAB 750MG	104	14	$65,931.51	$21.13	
Levetiracetam	KEPPRA TAB 250MG	57	9	$16,062.90	$9.39	
Levetiracetam	KEPPRA INJ 500/5ML	1	1	$85.68	$85.68	
Levetiracetam	LEVETIRACETM INJ 500/5ML	1	1	$7.53	$7.53	
	SUBTOTAL	24,846	3,660	$1,587,452.70	$2.15	11.5%
Mephobarbital	MEBARAL TAB 50MG	18	3	$1,794.22	$3.43	
Mephobarbital	MEBARAL TAB 100MG	15	2	$2,142.55	$4.76	
Mephobarbital	MEBARAL TAB 32MG	14	3	$1,620.64	$3.86	
	SUBTOTAL	47	8	$5,557.41	$3.99	0.04%
Methsuximide	CELONTIN CAP 300MG	89	8	$11,222.30	$4.26	
	SUBTOTAL	89	8	$11,222.30	$4.26	0.08%
Oxcarbazepine	OXCARBAZEPIN TAB 300MG	8,096	1,793	$213,300.86	$0.88	
Oxcarbazepine	OXCARBAZEPIN TAB 600MG	6,522	1,070	$302,668.10	$1.55	
Oxcarbazepine	OXCARBAZEPIN TAB 150MG	4,955	1,368	$90,719.00	$0.61	
Oxcarbazepine	TRILEPTAL SUS 300MG/5M	2,514	381	$718,781.37	$9.84	
Oxcarbazepine	OXCARBAZEPIN SUS 300MG/5M	343	167	$60,936.58	$6.53	
Oxcarbazepine	TRILEPTAL TAB 600MG	138	17	$79,187.28	$18.93	
Oxcarbazepine	TRILEPTAL TAB 300MG	62	14	$20,203.79	$10.47	
Oxcarbazepine	TRILEPTAL TAB 150MG	17	4	$3,029.79	$4.52	
	SUBTOTAL	22,647	3,884	$1,488,826.77	$2.21	10.79%
Phenobarbital	PHENOBARB TAB 30MG	1,931	273	$17,331.21	$0.30	
Phenobarbital	PHENOBARB ELX 20MG/5ML	1,909	275	$51,737.67	$1.04	
Phenobarbital	PHENOBARB TAB 64.8MG	1,904	255	$15,610.67	$0.27	
Phenobarbital	PHENOBARB TAB 32.4MG	1,586	246	$13,126.95	$0.28	
Phenobarbital	PHENOBARB TAB 60MG	1,107	166	$8,721.41	$0.25	
Phenobarbital	PHENOBARB TAB 97.2MG	650	100	$5,278.87	$0.25	
Phenobarbital	PHENOBARB TAB 15MG	381	56	$2,704.55	$0.25	
Phenobarbital	PHENOBARB TAB 100MG	337	52	$2,675.07	$0.26	
Phenobarbital	PHENOBARB TAB 16.2MG	190	32	$1,424.41	$0.25	
Phenobarbital	PHENOBARB SOL 20MG/5ML	3	3	$87.47	$1.04	
Phenobarbital	PHENOBARB INJ 130MG/ML	2	2	$137.29	$45.76	
	SUBTOTAL	10,000	1,171	$118,835.57	$0.40	0.86%
Phenytoin	PHENYTOIN EX CAP 100MG	8,689	1,509	$234,041.18	$0.90	
Phenytoin	DILANTIN EX CAP 100MG	1,541	260	$101,289.31	$2.16	
Phenytoin	PHENYTOIN SUS 125/5ML	760	96	$31,188.45	$1.63	
Phenytoin	DILANTIN CHW 50MG	701	113	$31,759.28	$1.47	
Phenytoin	DILANTIN EX CAP 30MG	130	23	$4,488.47	$1.19	
Phenytoin	PHENYTOIN EX CAP 300MG	98	33	$4,492.31	$1.41	
Phenytoin	PHENYTOIN EX CAP 200MG	62	20	$2,820.96	$1.34	
Phenytoin	PHENYTEK EX CAP 300MG	50	9	$2,980.25	$1.68	
Phenytoin	PHENYTEK EX CAP 200MG	50	10	$2,864.75	$2.05	
Phenytoin	PHENYTOIN SUS 100/4ML	44	2	$867.00	$2.69	
Phenytoin	DILANTIN-125 SUS 125/5ML	36	5	$2,410.28	$2.34	
	SUBTOTAL	12,161	1,885	$419,202.24	$1.16	3.04%
Pregabalin	LYRICA CAP 150MG	3,263	651	$645,114.00	$6.58	
Pregabalin	LYRICA CAP 75MG	2,896	768	$526,266.27	$6.06	
Pregabalin	LYRICA CAP 100MG	2,165	499	$466,618.06	$7.17	
Pregabalin	LYRICA CAP 50MG	1,214	412	$240,846.08	$6.70	
Pregabalin	LYRICA CAP 300MG	806	133	$144,058.70	$5.77	
Pregabalin	LYRICA CAP 200MG	567	115	$103,576.34	$6.13	
Pregabalin	LYRICA CAP 225MG	258	51	$45,636.12	$5.87	
Pregabalin	LYRICA CAP 25MG	125	46	$19,650.90	$5.21	
	SUBTOTAL	11,294	2,107	$2,191,766.47	$6.46	15.89%
Primidone	PRIMIDONE TAB 50MG	481	113	$8,745.48	$0.55	
Primidone	PRIMIDONE TAB 250MG	435	56	$8,631.90	$0.64	
Primidone	MYSOLINE TAB 250MG	17	2	$10,890.69	$17.85	
	SUBTOTAL	933	160	$28,268.07	$0.94	0.20%

CHEMICAL NAME	BRAND NAME	CLAIMS	MEMBERS	COST	COST/ DAY	% COST
Rufinamide	BANZEL TAB 400MG	409	55	$377,945.44	$30.99	
Rufinamide	BANZEL TAB 200MG	193	34	$41,762.08	$7.32	
Rufinamide	BANZEL SUS 40MG/ML	44	8	$29,961.22	$24.64	
	SUBTOTAL	**646**	**78**	**$449,668.74**	**$23.52**	**3.26%**
Tiagabine	GABITRIL TAB 4MG	175	30	$94,878.85	$17.92	
Tiagabine	GABITRIL TAB 12MG	32	8	$14,475.43	$14.03	
Tiagabine	GABITRIL TAB 2MG	13	2	$6,751.87	$17.05	
Tiagabine	GABITRIL TAB 16MG	8	3	$2,389.98	$9.96	
	SUBTOTAL	**228**	**40**	**$118,496.13**	**$17.02**	**0.86%**
Topiramate	TOPIRAMATE TAB 100MG	7,090	1,568	$95,571.26	$0.44	
Topiramate	TOPIRAMATE TAB 50MG	6,481	2,011	$76,145.99	$0.39	
Topiramate	TOPIRAMATE TAB 25MG	5,691	2,424	$67,333.08	$0.40	
Topiramate	TOPIRAMATE TAB 200MG	2,909	445	$48,938.28	$0.55	
Topiramate	TOPIRAMATE SPR CAP 25MG	405	111	$29,379.88	$2.48	
Topiramate	TOPIRAMATE SPR CAP 15MG	317	101	$31,729.45	$3.49	
Topiramate	TOPAMAX TAB 100MG	152	26	$83,389.54	$18.12	
Topiramate	TOPAMAX TAB 200MG	111	22	$66,692.63	$19.57	
Topiramate	TOPAMAX SPR CAP 25MG	55	9	$36,139.03	$22.23	
Topiramate	TOPAMAX SPR CAP 15MG	46	13	$15,442.72	$11.19	
Topiramate	TOPAMAX TAB 25MG	35	6	$6,234.33	$5.98	
Topiramate	TOPAMAX TAB 50MG	25	7	$12,267.65	$16.36	
	SUBTOTAL	**23,317**	**5,299**	**$569,263.84**	**$0.80**	**4.13%**
Vigabatrin	SABRIL POW 500MG	96	11	$377,180.34	$131.88	
Vigabatrin	SABRIL TAB 500MG	26	2	$159,515.36	$204.51	
	SUBTOTAL	**122**	**13**	**$536,695.70**	**$147.44**	**3.89%**
Zonisamide	ZONISAMIDE CAP 100MG	2,277	334	$51,994.64	$0.77	
Zonisamide	ZONISAMIDE CAP 25MG	898	181	$13,708.08	$0.52	
Zonisamide	ZONISAMIDE CAP 50MG	755	136	$10,014.57	$0.45	
Zonisamide	ZONEGRAN CAP 100MG	63	8	$29,404.17	$14.61	
Zonisamide	ZONEGRAN CAP 25MG	12	2	$726.49	$2.08	
	SUBTOTAL	**4,005**	**497**	**$105,847.95**	**$0.89**	**0.77%**
	TOTAL	**250,401**	**46,572***	**$13,797,429.16**	**$1.83**	**100%**

***Total number of unduplicated members**

Anticonvulsant (Benzodiazepine) Utilization Details

GENERIC NAME	BRAND NAME	CLAIMS	MEMBERS	COST	COST/ DAY	% COST
Clobazam	ONFI TAB 10MG	214	65	$104,222.08	$16.57	73.22%
Clobazam	ONFI TAB 5MG	69	28	$12,523.52	$6.36	8.80%
Clobazam	ONFI TAB 20MG	49	15	$25,607.05	$18.20	17.99%
	SUBTOTAL	**332**	**96**	**$142,352.65**	**$14.73**	**100.00%**
	TOTAL	**332**	**96**	**$142,352.65**	**$14.73**	**100.00%**

***Total number of unduplicated members**

Product Details of Oxtellar XR™ (Oxcarbazepine Extended-Release)[11]

INDICATIONS: Oxtellar XR™ is indicated as adjunctive therapy for the treatment of partial seizures in adults and in children 6 years to 17 years of age.

DOSAGE FORMS: 150 mg, 300 mg, and 600 mg extended-release tablets.

ADMINISTRATION:

- The recommended dose of Oxtellar XR™ is 1,200mg to 2,400mg per day, given once daily.
- Initiate treatment at a dose of 600 mg per day given once daily for one week. Subsequent dose increases can be made at weekly intervals in 600 mg per day increments to achieve the recommended daily dose.
- Tablets should be taken on an empty stomach at least one hour before food or at least two hours after food.

CONTRAINDICATIONS:

- Severe hypersensitivity to Oxtellar XR™

SPECIAL POPULATIONS:

- **Pregnancy:** There are no adequate and well-controlled studies with Oxtellar XR™ in pregnant women. Oxtellar XR™ should be used during pregnancy only if the potential benefit justifies the potential risk. Oxtellar XR™ is closely related structurally to carbamazepine, which is considered to be teratogenic in humans. (Category C)
- **Nursing Mothers:** Oxcarbazepine is excreted in human milk. Because of the potential for serious adverse reactions to Oxtellar XR™ in nursing infants, a decision should be made about whether to discontinue nursing or to discontinue the drug in nursing women, taking into account the importance of the drug to the mother.
- **Pediatrics**: Oxtellar XR™ is indicated in children ages 6 to 17 years of age. Target dose is based upon weight. Dosing should be initiated with 8 mg/kg to 10 mg/kg once per day and if necessary increased weekly, not to exceed 600 mg. Safety and effectiveness in pediatric patients younger than 6 years of age has not been established.
- **Geriatrics**: AUC values were measured to be 30%-60% higher in the elderly (60-82 years of age) than in younger volunteers. Manufacturers recommend starting at lower dose (300 mg or 450 mg per day) and increasing slowly.
- **Hepatic Impairment:** Oxtellar XR™ has not been evaluated in patients with severe hepatic impairment and is not recommended in these patients.
- **Renal Impairment:** Patients with a creatinine clearance less than 30mL/minute should start at 300mg per day and increase slowly. Manufacturers recommend that patients with end-stage renal disease who are on dialysis use the immediate release formulation instead of Oxtellar XR™.

WARNINGS AND PRECAUTIONS:

- Clinically significant hyponatremia (sodium <125 mmol/L) may develop during use of Oxtellar XR™. Serum sodium concentrations should be monitored during treatment with Oxtellar XR™, particularly if the patient receives concomitant medications known to decrease serum sodium levels.

- Cases of anaphylaxis and angioedema have been reported in patients after taking the first or subsequent doses of immediate-release oxcarbazepine. If a patient develops any of these reactions after treatment with Oxtellar XR™, discontinue the drug and initiate an alternative treatment. Do not rechallenge these patients with Oxtellar XR™.
- Serious dermatological reactions, including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), have occurred in patients treated with immediate-release oxcarbazepine. If a patient develops a skin reaction while taking Oxtellar XR™, consider discontinuing use and prescribing another AED.
- Oxtellar XR™ can increase the risk of suicidal thoughts or behavior. Patients should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.
- Pancytopenia, agranulocytosis, and leukopenia have been seen in patients treated with immediate-release oxcarbazepine during post-marketing experience. Discontinuation of Oxtellar XR™ should be considered if any evidence of these hematologic reactions develops.

ADVERSE REACTIONS: (≥5% and >placebo)

- Gastrointestinal: vomiting
- Neurologic: abnormal gait, dizziness, headache, impairment of balance, somnolence, tremor, asthenia
- Ophthalmic: diplopia

DRUG INTERACTIONS:

- Oxtellar XR™ is an inducer of CYP450 3A family (CYP3A4 and CYP3A5).
- Coadministration of Oxtellar XR™ and oral contraceptives can decrease the plasma concentration of the hormonal contraceptive.
- Concomitant use of CYP450 inducers such as phenytoin, phenobarbital, and carbamazepine with Oxtellar XR™ can decrease plasma concentrations of Oxtellar XR™.

PATIENT COUNSELING INFORMATION:

- You should not discontinue Oxtellar XR™ without talking to your physician first. Stopping Oxtellar XR™ suddenly increases your risk of having a seizure.
- Oxtellar XR™ may cause the level of sodium in your blood to be low especially if you are taking other medications that can lower sodium. It is important to report symptoms such as nausea, tiredness, lack of energy, confusion, or more frequent or more severe seizures as these symptoms can be signs of low sodium.
- Oxtellar XR™ may also cause allergic reactions. Call your healthcare provider right away if you experience any of the following: swelling of your face or tongue, trouble swallowing or bleeding, rash, sever muscle pain, hives, fever, swollen glands, painful sores in the mouth, sever fatigue or weakness, yellowing of your skin or eyes, frequent infections, or unusual bleeding or bruising.
- Oxtellar XR™ can cause an increase in suicidal thoughts or actions. Call your healthcare provider right away if you experience worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.
- Oxtellar XR™ may cause your birth control medicine to be less effective. Talk to your healthcare provider about the best birth control method to use.
- Take Oxtellar XR™ whole by mouth once daily at least one hour before food or 2 hours after food. Do not cut, crush, or chew the tablet.

Product Details of Fycompa™ (Perampanel) [12, 13]

INDICATIONS: Fycompa™ is indicated as adjunctive therapy for the treatment of partial-onset seizures with or without secondary generalized seizures in patients with epilepsy aged 12 years and older. Fycompa™ is a noncompetitive antagonist of the alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) glutamate receptor found on postsynaptic neurons. Glutamate is the primary excitatory neurotransmitter in the central nervous system (CNS). Fycompa™ is the first FDA-approved non-competitive AMPA glutamate receptor antagonist.

DOSAGE FORMS:

- 2mg, 4mg, 6mg, 8mg, 10mg, and 12mg tablets.
- The FDA recommended that Fycompa™ be classified as a scheduled drug. The DEA is currently reviewing the recommendation to determine a final scheduling designation.

ADMINISTRATION:

- The recommended dose of Fycompa™ is 8mg to 12mg per day.
- Initiate treatment at a dose of 2 mg per day given once daily at bedtime for one week. Subsequent dose increases can be made at weekly intervals in 2mg per day increments to achieve the recommended daily dose.
- Tablets should be taken once daily at bedtime.

CONTRAINDICATIONS:

- Specific contraindications have not been determined.

SPECIAL POPULATIONS:

- **Pregnancy:** There are no adequate and well-controlled studies with Fycompa™ in pregnant women. Fycompa™ should be used during pregnancy only if the potential benefit justifies the potential risk. (Category C)
- **Nursing Mothers:** Fycompa™ is excreted in rat milk. It is not known whether this drug is excreted in human milk. Caution should be exercised.
- **Pediatrics**: Fycompa™ is indicated in children aged 12 years and older with dosing equivalent to adult dosing. Safety and effectiveness in pediatric patients younger than 12 years of age has not been established.
- **Geriatrics**: Clinical studies of Fycompa™ did not include sufficient numbers of patients aged 65 and over to determine the safety and efficacy of Fycompa™ in the elderly population. Manufacturers recommend increasing slowly with titrations no more frequently than every two weeks.
- **Hepatic Impairment:** The maximum recommended daily dose is 6 mg for patients with mild hepatic impairment and 4 mg for patients with moderate hepatic impairment. Use of Fycompa™ in patients with severe hepatic impairment is not recommended.
- **Renal Impairment:** Patients with moderate renal impairment should be monitored closely and a slower titration may be considered based on tolerability. Manufacturers do not recommend use of Fycompa™ in patients with severe renal impairment or who are on dialysis.

WARNINGS AND PRECAUTIONS:

- Fycompa™ has been associated with severe aggression and hostility related reactions. Monitoring is recommended and a dose reduction or permanent discontinuation may be required.
- Fycompa™ can increase the risk of suicidal thoughts or behavior. Patients should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.
- Patients taking Fycompa™ can have an increased risk of falls. Some reports indicate cases leading to serious injuries including head injuries and bone fracture.
- Fycompa™ can cause dose-dependent increases in somnolence and fatigue. Prescribers should advise patients against engaging in hazardous activities requiring mental alertness, such as operating motor vehicles or dangerous machinery, until the effect of Fycompa™is known.

ADVERSE REACTIONS: (≥4%and >placebo)

- Gastrointestinal: Nausea
- Neurologic: abnormal gait, dizziness, impairment of balance, somnolence, fatigue, falls, ataxia, gait disturbance, vertigo
- Mood: irritability
- Metabolic: weight gain

DRUG INTERACTIONS:

- Coadministration of Fycompa™ 12mg daily and oral contraceptives can decrease the plasma concentration of the hormonal contraceptive.
- Concomitant use of CYP450 inducers such as phenytoin, oxcarbazepine, and carbamazepine with Fycompa™ can decrease plasma concentrations of Fycompa™.
- In the presence of concomitant enzyme-inducing antiepileptic drugs (AED), initial dosing should be 4 mg once daily.
- Concomitant use of Fycompa™ and CNS depressants including alcohol may increase CNS depression.

PATIENT COUNSELING INFORMATION:

- You should not discontinue Fycompa™ without talking to your physician first. Stopping Fycompa™ suddenly increases your risk of having a seizure.
- Fycompa™ can cause psychiatric problems. Call your healthcare provider right away if you experience new or worsening aggressive behavior, hostility, anger, anxiety, irritability and/or any unusual changes in mood or behavior.
- Fycompa™ can cause an increase in suicidal thoughts or actions. Call your healthcare provider right away if you experience worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.
- Fycompa™ may cause dizziness, fatigue, vertigo, and problems walking normally. These symptoms can increase your risk for falls and you should not drive or operate heavy machinery until you know how Fycompa™ will affect you.
- Fycompa™ may cause your birth control medicine to be less effective. Talk to your healthcare provider about the best birth control method to use.
- Avoid alcohol while taking Fycompa™ as it may enhance the impairment effects of alcohol.
- Take Fycompa™ whole by mouth once daily at bedtime.

Product Details of Sabril® (Vigabatrin) [14]

INDICATIONS: Sabril® is an irreversible inhibitor of γ-aminobutyric acid transaminase (GABA-T) indicated for adjunctive therapy in the treatment of refractory complex partial seizures in adults who have responded inadequately to several alternative treatments. The powder formulation is indicated as monotherapy for the treatment of infantile spasms in ages one month to two years of age.

DOSAGE FORMS:

- 500mg tablet and 500mg powder packets for oral solution.
- Sabril® is available only under a special restricted distribution program called the SHARE program. Only pharmacies, prescribers, and patients registered with the program are able to dispense, prescribe, and take Sabril®.
    - To enroll in SHARE, prescribers must understand the risks of Sabril® and complete the enrollment agreement form stating that they will:
        1. Review the medication guide with every patient.
        2. Educate patients on the risks of Sabril®.
        3. Order and review vision assessments upon initiation of treatment and every three months.
        4. Remove patients from Sabril® if they do not experience a meaningful reduction in seizures.
        5. Counsel patients who fail to comply with the program requirements.
        6. Remove all patients from Sabril® who fail to comply with the program requirements after appropriate counseling.

ADMINISTRATION:

- Adults:
    - The recommended dose of Sabril® is 1,500mg twice daily.
    - Initiate therapy with a dose of 500mg twice daily and if necessary the dose should be increased weekly in increments of 500mg per day to the recommended daily dose.
    - A 6,000mg/day dose has not been shown to confer additional benefit compared to the 3,000mg/day.
    - Tablets should be taken twice daily by mouth without regard to food.
- Pediatric patients:
    - The recommended dose of Sabril® is 150mg/kg/day divided twice daily.
    - Initiate therapy with a dose of 50mg/kg/day in two divided doses and if necessary the dose can be increased every 3 days in increments of 25-50mg/kg/day up to a maximum of 150mg/kg/day.
    - The entire contents of the packets should be dissolved into 10mL of water per packet and taken by mouth without regard to food. Each dose should be prepared immediately before use and administered cold or at room temperature. Discard any unused portion of the solution.

CONTRAINDICATIONS:

- Specific contraindications have not been determined.

SPECIAL POPULATIONS:

- **Pregnancy:** There are no adequate and well-controlled studies with Sabril® in pregnant women. It should be used during pregnancy only if the potential benefit justifies the potential risk. It is important to note that Sabril® produced teratogenic effects when administered to pregnant animals. (Category C)
- **Nursing Mothers**: Sabril® is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.
- **Pediatrics**: Sabril® is indicated in pediatric patients aged one month to 2 years for the treatment of infantile spasms. Safety and effectiveness in pediatric patients younger than 16 years of age with complex partial seizures has not been established. Abnormal MRI signal changes and neurotoxicity have been observed in infants.
- **Geriatrics**: Clinical studies of Sabril® did not include sufficient numbers of patients aged 65 and over to determine the safety and efficacy in the elderly population. Manufacturers recommend careful dose selection and monitoring renal function.
- **Renal Impairment:** Patients with mild, moderate, or severe renal impairment should have the dose decreased by 25%, 50% or 75% respectively.

WARNINGS AND PRECAUTIONS:

- Sabril® has been associated with vision loss and the package insert contains a black box warning stating that because of the risk of vision loss, a patient who fails to show substantial clinical benefit within 3 months of initiation of treatment should be withdrawn from Sabril®. Monitoring of vision is required.
- Sabril® can increase the risk of suicidal thoughts or behavior. Patients should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.
- Abnormal MRI signal changes have been observed in some infants treated for infantile spasms with Sabril®. MRI surveillance may be necessary.
- Neurotoxicity including convulsions and hypomyelination was observed in juvenile rats exposed to Sabril®.
- Use of Sabril® has been associated with anemia. Hematology changes should be monitored.
- Sabril® caused symptoms of peripheral neuropathy in some studies; however there is insufficient evidence to determine whether these symptoms were related to duration of treatment, cumulative dose, or if they were reversible upon discontinuation.
- Sabril® has been associated with weight gain. Patient weight should be monitored.
- Edema has been reported with use of Sabril®.

ADVERSE REACTIONS: (≥5%and >placebo)

- Gastrointestinal: Nausea, vomiting, diarrhea, constipation, abdominal pain
- Neurologic: dizziness, somnolence, fatigue, asthenia, headache, nystagmus, tremor, memory impairment, paraesthesia, impairment in coordination, disturbance in attention
- Musculoskeletal: Arthralgia
- Ophthalmic: Blurred vision, Diplopia
- Psychiatric: Depression
- Metabolic: weight gain
- Other: Peripheral edema
- Infections: Nasopharngitis, upper respiratory tract infection, influenza

DRUG INTERACTIONS:

- Coadministration of Sabril® and phenytoin can reduce phenytoin plasma levels.
- Concomitant use Sabril® with phenobarbital or sodium valproate can decrease plasma concentrations of phenobarbital and sodium valproate.
- Coadministration of clonazepam and Sabril® can result in an increase the mean C_{max} of clonazepam.

PATIENT COUNSELING INFORMATION:

- You should not discontinue Sabril® without talking to your physician first. Stopping Sabril® suddenly increases your risk of having a seizure.
- Sabril® can damage your vision, particularly your peripheral vision. Tell your doctor right away if you have vision changes, and be sure to keep all appointments to monitor your vision.
- Sabril® can cause an increase in suicidal thoughts or actions. Call your healthcare provider right away if you experience worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.
- Sabril® may cause dizziness, fatigue, and problems walking normally. These symptoms can increase your risk for falls and you should not drive or operate heavy machinery until you know how Sabril® will affect you.
- Take Sabril® whole by mouth twice daily. The packets must be dissolved in 10mL per packet of cold or room temperature water immediately before administration and taken by mouth twice daily.

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Appendix E

Annual Review of Biologic Products for the Treatment of Rheumatoid Arthritis, Crohn's Disease, Plaque Psoriasis, and Ankylosing Spondylitis

Oklahoma Health Care Authority
Month 2013

Current Prior Authorization Criteria

The prior authorization of this category was implemented January 2012.

Tier-2 Authorization Criteria

1. A FDA approved diagnosis, and
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, or
3. Prior stabilization on the Tier 2 medication documented within the last 100 days.

Tier-3 Authorization Criteria

1. A FDA approved diagnosis, and
2. Recent trials of at least one Tier 1 product and all available, disease specific, Tier 2 medications that did not yield adequate relief of symptoms or resulted in intolerable adverse effects, or
3. Prior stabilization on the Tier 3 medication documented within the last 100 days, or
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	Adalimumab (Humira®) Certolizumab pegol (Cimzia®) Etanercept (Enbrel®) Golimumab (Simponi®) Ustekinumab (Stelara®)	Abatacept (Orencia®) Alefacept (Amevive®) Anakinra (Kineret®) Infliximab (Remicade®) Rituximab (Rituxan®) Tocilizumab (Actemra®) Tofacitinib (Xeljanz®)

Utilization of Biologics

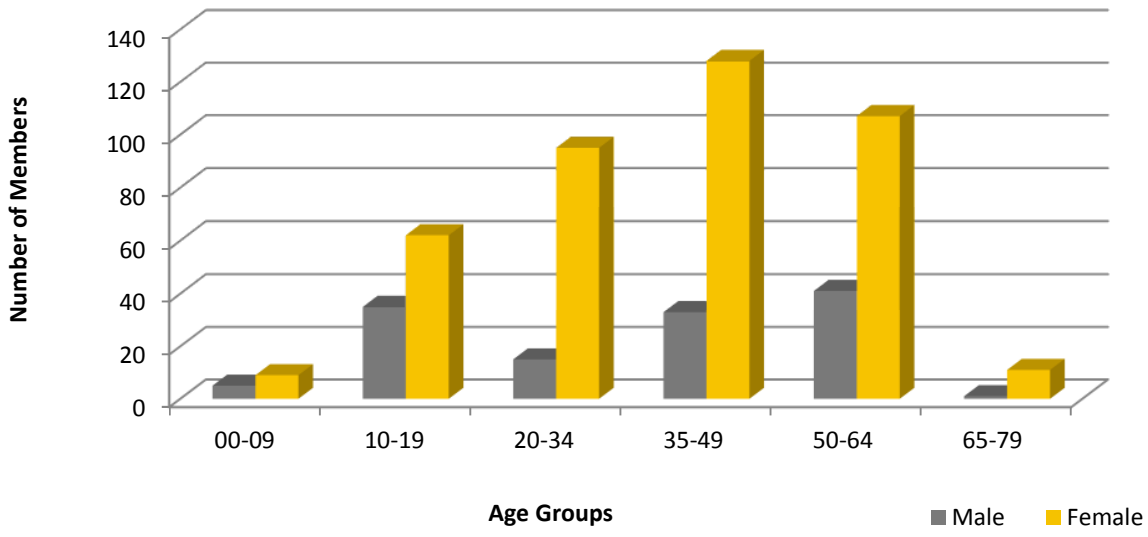
Comparison of Calendar Years for Biologics (Pharmacy)

Calendar Year	Members	Claims	Cost	Cost/Claim	Cost/Day	Units	Days
2011	480	2,572	$5,767,130.20	$2,242.27	$76.50	21,842	75,387
2012	542	2,999	$7,608,963.25	$2,537.17	$86.81	19,228	87,647
% Change	12.92%	16.60%	33.75%	13.15%	13.48%	-11.97%	16.26%
Change	62	427	$1,841,233.05	$294.90	$10.31	-2,614	12,260

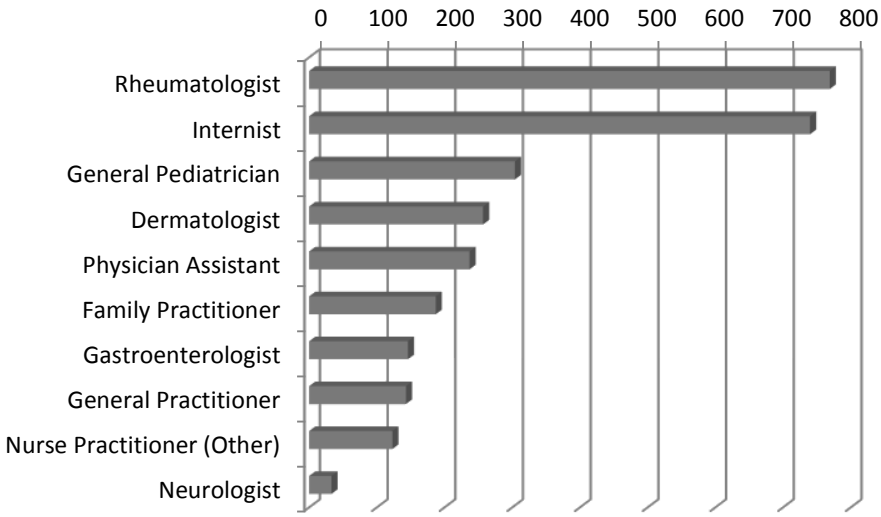
Comparison of Calendar Years for Biologics (Medical)

Calendar Year	Members	Claims	Cost	Cost/Claim	Units
2011	90	430	$722,009.17	$1,679.09	38,342
2012	76	380	$769,822.81	$2,025.85	52,177
% Change	-15.55%	-11.63%	6.62%	20.65%	36.08%
Change	-14	-50	$47,813.64	$346.76	13,835

CY 2012 Demographics of Members Utilizing Biologics



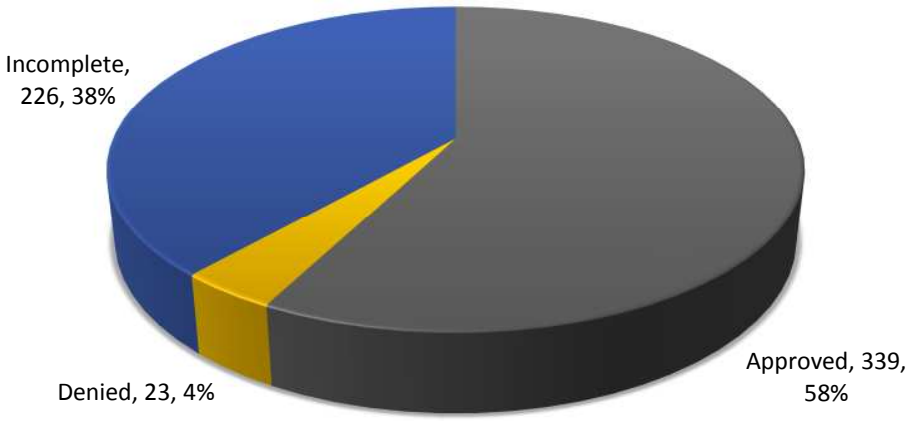
CY 2012 Prescribers of Biologics by Number of Claims



Prior Authorization of Biologic Medications

There were a total of 588 petitions submitted for this category during calendar year 2012. Computer edits are in place to detect tier-1 medications in member's recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions.

Status of Petitions for Biologics



Market News and Updates

- **Anticipated Patent Expirations:** [1]
  - Rituxan® (rituximab)- September 2016
  - Humira® (adalimumab)- December 2016
  - Remicade® (infliximab)-September 2018
  - Enbrel® (etanercept)- Amgen's patent has been extended until November 2028.
- **Updated Package Labeling :**
  - Remicade® and Humira®- adverse reaction of sarcoidosis (10/2011)[2]
  - Humira® and Simponi®- warning of risk of optic neuritis (12/2011)[2]
  - Rituxan®- adverse reaction of hypogammaglobulinemia (02/2012)[3]
  - Humira®- adverse reaction of liver failure (05/2012)[3]
  - Actemra®- warning of increased risk of liver enzyme elevations, low neutrophil counts, low platelet counts, and lipid elevations in patients with polyarticular and systemic juvenile idiopathic arthritis (04/2013)[4]
  - Simponi®- warning of risk of melanoma (04/2013)[4]
- **New Products/Indications:**
  - Humira®- treatment of moderate-to severe ulcerative colitis in adults. (09/2012)[5]
  - Rituxan®- 90-minute infusion starting at Cycle 2 for patients with non-Hodgkin's lymphoma (NHL) who did not experience a grade 3 or 4 infusion-related adverse reaction during Cycle 1. (10/2012) [6]
  - Xeljanz®- treatment for adults with moderately to severely active rheumatoid arthritis who have had an inadequate response to, or who are intolerant of, methotrexate. (11/2012)[7]
  - Simponi®- treatment of adults with moderate to severe ulcerative colitis. (05/2013)[8]
- **FDA Updates:**
  - **04/2011** The FDA informed the public of reports of a rare cancer of white blood cells (Hepatosplenic T-Cell Lymphoma) primarily in young adults being treated for Crohn's disease and ulcerative colitis with Tumor Necrosis Factor (TNF) blockers (Remicade® and Humira®), as well as azathioprine and mercaptopurine.[9]
  - **09/2011** The FDA announced that the Boxed Warning for the entire class of TNF blockers (Remicade®, Enbrel®, Humira®, Cimzia®, and Simponi®) has been updated to include the risk of infection from two bacterial pathogens, *Legionella* and *Listeria.*[10]
  - **11/2011** The FDA updated the public about its ongoing safety review of TNF blockers and malignancy in children, adolescents, and young adults. The FDA is requiring the manufacturers of TNF blockers to perform enhanced safety surveillance for these products.[11]

Conclusion and Recommendations

The College of Pharmacy recommends no changes to this PBPA category at this time.

Utilization Details of Biologics (Pharmacy Claims): Calendar Year 2012

CHEMICAL NAME	BRAND NAME	CLAIMS	MEMBERS	COST	COST/DAY	% COST
Abatacept	ORENCIA INJ 250MG	13	4	$11,700.40	$45.00	
Abatacept	ORENCIA INJ 125MG/ML	72	13	$153,242.75	$74.32	
	SUBTOTAL	**85**	**17**	**$164,943.15**	**$71.03**	**2.16%**
Adalimumab	HUMIRA PEN KIT 40MG/0.8	887	176	$2,183,905.44	$82.19	
Adalimumab	HUMIRA KIT 40MG/0.8	328	69	$791,883.89	$83.71	
Adalimumab	HUMIRA PEN KIT PSORIASI	28	20	$118,970.19	$128.20	
Adalimumab	HUMIRA PEN KIT CROHNS	23	18	$145,938.41	$204.40	
Adalimumab	HUMIRA KIT 20MG/0.4	12	3	$25,167.04	$84.45	
	SUBTOTAL	**1,278**	**238**	**$3,265,864.97**	**$86.01**	**42.9%**
Alefacept	AMEVIVE INJ 15MG	0	0	$0.00	$0.00	
	SUBTOTAL	**0**	**0**	**$0.00**	**$0.00**	**0.00%**
Anakinra	KINERET INJ	63	7	$118,888.47	$67.24	
	SUBTOTAL	**63**	**7**	**$118,888.47**	**$67.24**	**1.56%**
Certolizumab	CIMZIA KIT 200MG/ML	113	24	$264,640.11	$82.96	
Certolizumab	CIMZIA KIT STARTER	12	11	$74,578.24	$130.38	
Certolizumab	CIMZIA KIT	1	1	$2,082.69	$74.38	
	SUBTOTAL	**126**	**26**	**$341,301.04**	**$90.05**	**4.49%**
Etanercept	ENBREL SRCLK INJ 50MG/ML	652	138	$1,597,230.22	$84.30	
Etanercept	ENBREL INJ 50MG/ML	285	61	$645,719.42	$80.12	
Etanercept	ENBREL INJ 25MG	199	32	$309,778.88	$57.28	
Etanercept	ENBREL INJ 25/0.5ML	57	19	$101,941.23	$64.07	
	SUBTOTAL	**1,193**	**221**	**$2,654,669.75**	**$78.06**	**34.9%**
Golimumab	SIMPONI INJ 50MG	109	20	$244,350.79	$75.05	
	SUBTOTAL	**109**	**20**	**$244,350.79**	**$75.05**	**3.21%**
Infliximab	REMICADE INJ 100MG	64	16	$294,746.76	$194.68	
	SUBTOTAL	**64**	**16**	**$294,746.76**	**$194.68**	**3.87%**
Natalizumab	TYSABRI INJ	38	6	$133,305.99	$143.49	
	SUBTOTAL	**38**	**6**	**$133,305.99**	**$143.49**	**1.75%**
Rituximab	RITUXAN INJ 100MG	5	3	$31,966.22	$541.80	
Rituximab	RITUXAN INJ 500MG	1	1	$12,839.62	$458.56	
	SUBTOTAL	**6**	**3**	**$44,805.84**	**$515.01**	**0.59%**
Tocilizumab	ACTEMRA INJ 200/10ML	1	1	$2,183.78	$77.99	
	SUBTOTAL	**1**	**1**	**$2,183.78**	**$77.99**	**0.029%**
Ustekinumab	STELARA 90 MCG	20	8	$244,275.45	$216.94	
Ustekinumab	STELARA 45MG/0.5ML	16	7	$99,627.26	$117.21	
	SUBTOTAL	**36**	**15**	**$343,902.71**	**$174.04**	**4.52%**
	TOTAL	**2,999**	**542***	**$7,608,963.25**	**$86.81**	**100%**

***Total number of unduplicated members**

Utilization Details of Biologics (Medical Claims): Calendar Year 2012

CHEMICAL NAME	BRAND NAME	CLAIMS	MEMBERS	COST	UNITS	% COST
Abatacept	ORENCIA INJ	62	12	$91,941.31	4,374	11.94%
Infliximab	REMICADE INJ 100MG	236	56	$553,283.49	10,934	71.87%
Tocilizumab	ACTEMRA INJ 200/10ML	82	8	$124,598.01	36,869	16.19%
	TOTAL	**380**	**76***	**$769,822.81**	**52,177**	**100%**

***Total number of unduplicated members**

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Appendix F

Annual Review of Testosterone Products – Calendar Year 2012

Oklahoma Health Care Authority
June 2013

Current Prior Authorization Criteria

The prior authorization of testosterone products was voted by the DUR Board in June 2011 and implemented in October 2011. Medical prior authorization of testosterone products were implemented in the fall of 2012. The current approval criteria are as follows:

1. Approved diagnosis:
    a. Testicular failure due to cryptorchidism, bilateral torsions, orchitis, vanishing testis syndrome, or orchidectomy
    b. Idiopathic gonadotropin or luteinizing-hormone-releasing hormone (LHRH) deficiency, or pituitary hypothalamic injury from tumors, trauma, or radiation
    c. Delayed puberty
    d. Advanced inoperable metastatic mammary cancer in females 1 to 5 years postmenopausal, or premenopausal women with breast cancer benefitting from oophorectomy and have been determined to have a hormone-responsive tumor
2. Must include two labs showing pre-medication testosterone level below 300ng/dL (where applicable) and other labs necessary to demonstrate diagnosis
3. Oral agents are only approved in cases where member cannot use all other available formulations of testosterone

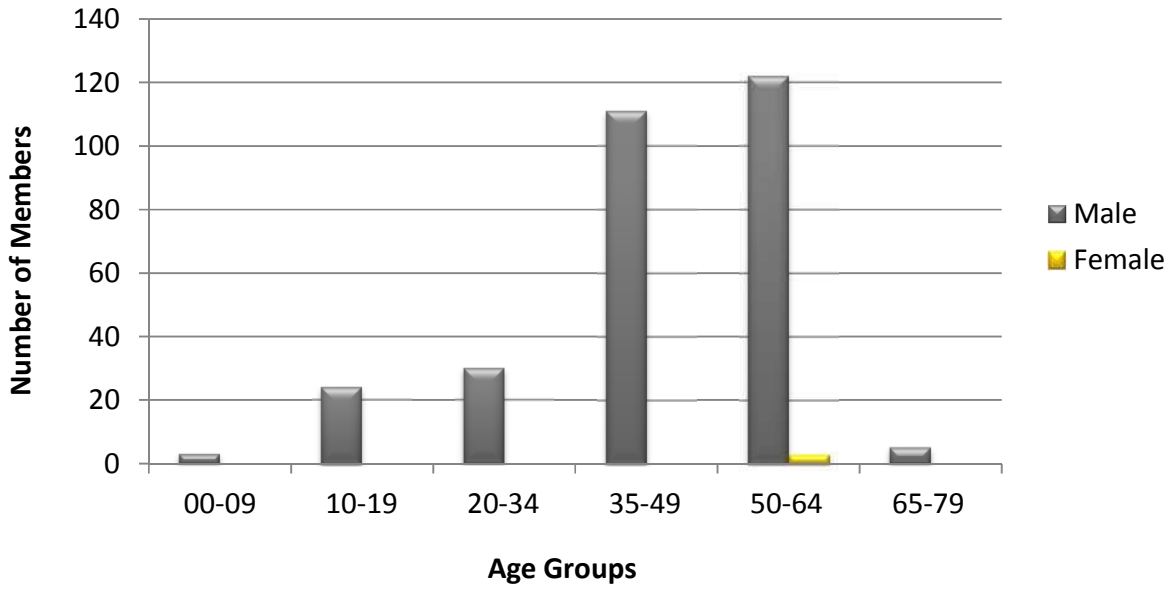
ROUTE OF ADMINISTRATION	CURRENT PRODUCTS
Buccal	Testosterone (**Striant®**)
Powder	Methyltestosterone Powder
Oral	Fluoxymesterone **(Androxy® Tab)** Methyltestosterone **(Testred® Cap, Android® Cap, Methitest® Tab)**
Intramuscular Injection	Testosterone Cypionate **(Depo-Testosterone®)** Testosterone Enanthate
Transdermal	Testosterone Patch **(Androderm®)** Testosterone Topical Gel/Solution **(Androgel®, Testim®, Fortesta®, Axiron®)**

Utilization of Testosterone Products

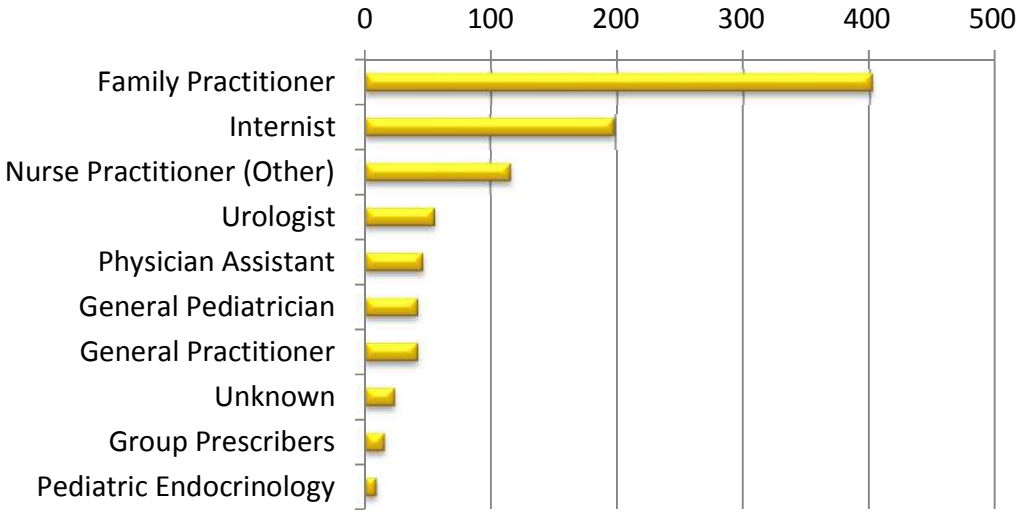
Comparison of Calendar Years

Calendar Year	Members	Claims	Cost	Cost/Claim	Perdiem	Units	Days
2011	521	1,247	$252,182.95	$202.23	$4.35	99,900	57,988
2012	298	982	$236,553.31	$240.89	$5.41	71,693	43,738
% Change	-42.80%	-21.30%	-6.20%	19.10%	24.40%	-28.20%	-24.60%
Change	-223	-265	-$15,629.64	$38.66	$1.06	-28,207	-14,250

Demographics of Members Utilizing Testosterone Products: CY 2012



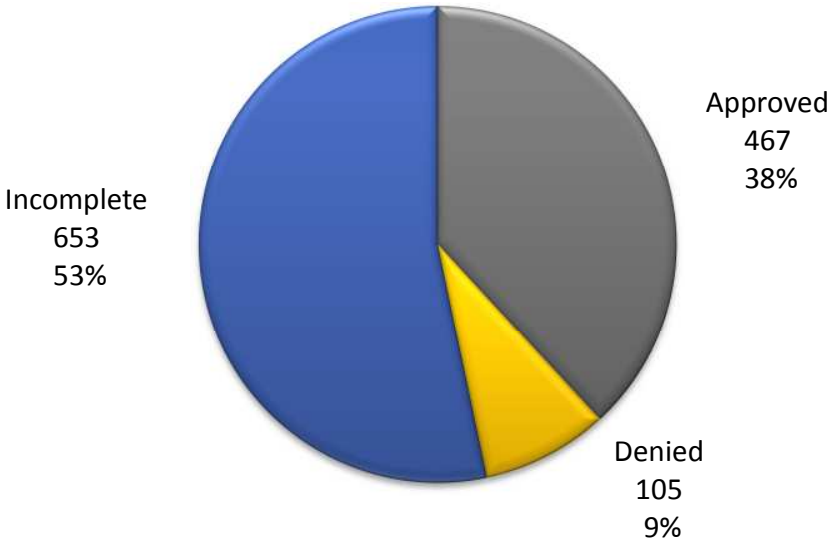
Prescribers of Testosterone Products by Number of Claims: CY 2012



Prior Authorization of Testosterone Products

There were a total of 1,225 petitions submitted for this PBPA category during calendar year 2012. The following chart shows the status of the submitted petitions.

Status of Petitions for Testosterone Products: CY 2012



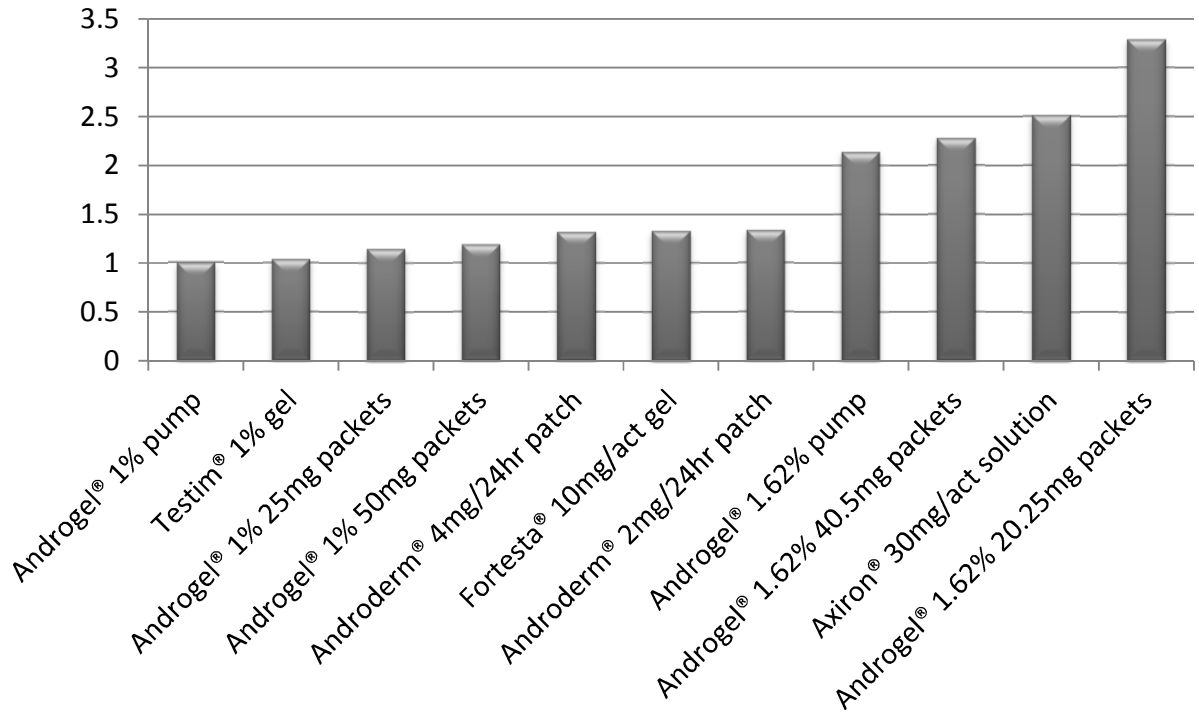
Market News and Update

Anticipated Patent Expirations:

- Androderm®: 10/2014
- Axiron®: 2017
- Fortesta® : 2018
- Striant® : 2019
- Androgel® : 2020
- Testim® : 2023

Androgel® 1.62% 2.5g (40.5mg testosterone) and 1.25g (20.25mg testosterone) packets are new to the market as of March 2013. The 1.25g packets are equivalent to one pump of the Androgel® 1.62% metered-dose pump.

The following is a cost comparison ratio of the topical testosterone products:



Conclusion and Recommendations

The College of Pharmacy recommends the addition of the Testosterone class of medications to the Product Based Prior Authorization program. The following tier-1 drug list has been reviewed and determined to be an acceptable combination for use as initial therapy for the majority of members. The College of Pharmacy recommends this list to the Drug Utilization Review Board based on cost and clinical effectiveness for approval before referral to the Oklahoma Healthcare Authority. The following is the proposed tier list and approval criteria.

Testosterone Products		
TIER-1	**TIER-2**	**Special PA**
Methyltestosterone powder	Testosterone patch (**Androderm®**)	Fluoxymesterone oral tablet (**Androxy®**)
Testosterone cypionate injection **(Depo-Testosterone®)**	Testosterone topical gel **(Androgel 1.62%, Fortesta®)**	Methyltestosterone oral tablet/capsule (**Android®, Methitest®, Testred®**)
Testosterone enanthate injection	Testosterone topical solution (**Axiron®**)	Testosterone buccal tablet (**Striant®**)
Testosterone topical gel **(Androgel® 1%, Testim®)**		

*Brand products are subject to the Brand Name Override where generics are available

All testosterone replacement products will require a prior authorization with the following approval criteria:

1. FDA approved diagnosis:
    a) Testicular failure due to cryptorchidism, bilateral torsions, orchitis, vanishing testis syndrome, or orchidectomy; or
    b) Idiopathic gonadotropin or luteinizing-hormone-releasing hormone (LHRH) deficiency, or pituitary hypothalamic injury from tumors, trauma, or radiation ; or
    c) Delayed puberty; or
    d) Advanced inoperable metastatic mammary cancer in females 1 to 5 years postmenopausal, or premenopausal women with breast cancer benefitting from oophorectomy and have been determined to have a hormone-responsive tumor; and
2. Must include two labs showing pre-medication testosterone levels below 300ng/dL or other labs necessary to demonstrate diagnosis

Tier-2 Prior Authorization Criteria:

1. A trial of at least two tier-1 products (must include at least one injectable and one topical formulation) at least 12 weeks in duration, or
2. A patient-specific, clinically significant reason why member cannot use all available tier-1 medications, or
3. Prior stabilization on a tier-2 medication (within the past 180 days)
4. Approval will be for one year

Special Prior Authorization Criteria:

1. Must provide a patient-specific, clinically significant reason why member cannot use all other available formulations of testosterone
2. Approval will be for one year

Utilization Details of Testosterone Products: Calendar Year 2012

BRAND NAME	CLAIMS	MEMBERS	COST	COST/ DAY	% COST
TESTOST CYP INJ 200MG/ML	311	127	$21,757.32	$1.08	9.20%
TESTOST ENAN INJ 200MG/ML	40	14	$2,470.97	$1.19	1.04%
DEPO-TESTOST® INJ 200MG/ML	37	15	$2,189.34	$1.11	0.93%
TESTOST CYP INJ 100MG/ML	21	14	$887.03	$0.47	0.37%
DEPO-TESTOST® INJ 100MG/ML	7	7	$476.50	$0.72	0.20%
SUBTOTAL	**416**	**177**	**$27,781.16**	**$1.04**	**11.74%**
ANDROGEL® GEL 1.62%	170	56	$71,091.23	$14.21	30.05%
ANDROGEL® GEL PUMP 1%	129	39	$46,531.86	$12.51	19.67%
ANDROGEL® GEL 1%(50MG)	116	21	$41,022.22	$11.79	17.34%
AXIRON® SOL 30MG/ACT	47	13	$17,306.19	$11.77	7.32%
TESTIM® GEL 1%(50MG)	43	18	$14,971.69	$11.70	6.33%
FORTESTA® GEL 10MG/ACT	13	2	$4,034.23	$10.34	1.71%
ANDROGEL® GEL 1%(25MG)	3	2	$1,023.33	$11.37	0.43%
SUBTOTAL	**521**	**151**	**$195,980.75**	**$12.70**	**82.85%**
ANDRODERM® DIS 4MG/24HR	21	7	$7,030.97	$11.16	2.97%
ANDRODERM® DIS 2MG/24HR	14	4	$4,650.64	$6.74	1.97%
ANDRODERM® DIS 2.5MG/24	4	3	$763.87	$6.37	0.32%
ANDRODERM® DIS 5MG/24HR	1	1	$310.43	$10.35	0.13%
SUBTOTAL	**40**	**15**	**$12,755.91**	**$8.68**	**5.39%**
TESTOSTERONE POW	5	5	$35.49	$0.32	0.02%
SUBTOTAL	**5**	**5**	**$35.49**	**$0.32**	**0.02%**
TOTAL	**982**	**298***	**$236,553.31**	**$5.41**	**100.00%**

***Total number of unduplicated members**

Appendix G

Calendar Year 2012 Annual Review of Multiple Sclerosis Medications And 30 Day Notice to Prior Authorize Aubagio® (Teriflunomide) and Tecfidera™ (Dimethyl Fumarate)

Oklahoma Health Care Authority
June 2013

Background and Current Prior Authorization of Multiple Sclerosis Medications

A prior authorization was first placed on Ampyra® (dalfampridine) in the fall of 2010, followed by a review of the entire category and prior authorization in January of 2012 of the interferon class of medications, Copaxone® (glatiramer acetate) and Gilenya™ (fingolimod). This is the first annual review of these medications, which will include Ampyra®. The following are the current prior authorization criteria:

Ampyra® (dalfampridine) Approval Criteria

1. Member must have a diagnosis of Multiple Sclerosis
2. Kurtzke Expanded Disability Status Scale (EDSS) score between 3 and 7.5
3. A 90 day trial will be approved. If member has responded well to treatment and physician states that the member has shown improvement or the drug was effective, member may receive authorization for one year
4. Quantity limit of 60 tabs for 30 days apply
5. May be used with other therapies and vice versa

Interferon PA 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 treatment therapies
4. Compliance will be checked for continued approval every 6 months

Tier 1	Tier 2
Interferon β - 1a (Rebif®)	Interferon β - 1a (Avonex®)
Interferon β - 1b (Betaseron®)	Interferon β - 1b (Extavia®)

Copaxone® (Glatiramer Acetate) Prior Authorization Criteria:

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

Gilenya™ (Fingolimod) 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. The first dose should be observed in the doctor's office for signs and symptoms of bradycardia for 6 hours after first dose
4. Compliance will be checked for continued approval every 6 months

Quantity limits apply based on FDA approved dosing.

Utilization of Multiple Sclerosis Medications

Utilization Trends

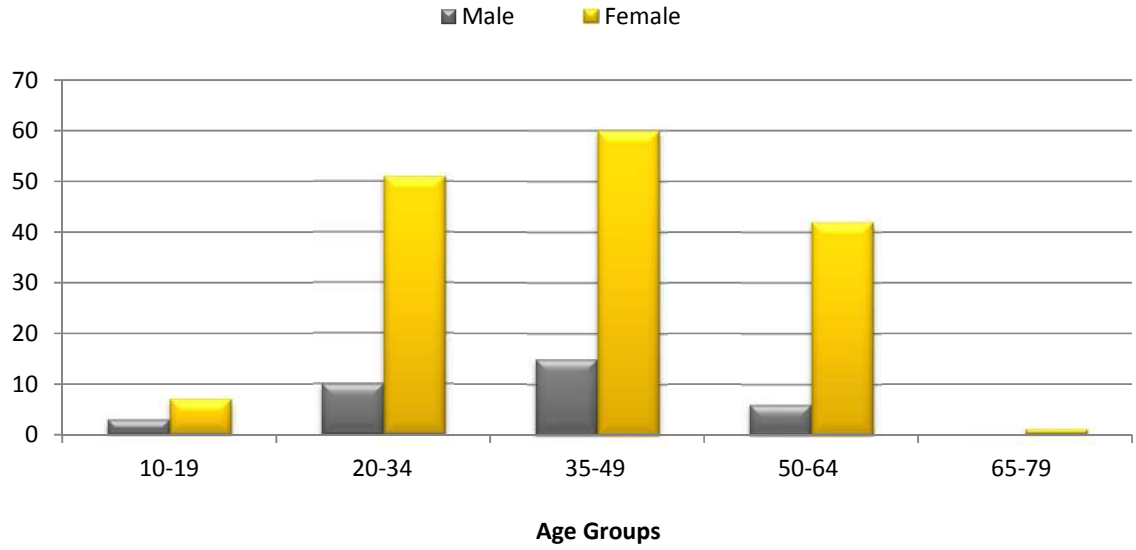
Calendar Year	Members	Claims	Cost	Cost/ Claim	Cost/ Day	Units	Days
2011	186	1,292	$4,358,073.18	$3,373.12	$113.71	9,248	38,326
2012	195	1,395	$5,408,041.25	$3,876.73	$131.99	13,305	40,973
% Change	**4.80%**	**8.00%**	**24.10%**	**14.90%**	**16.10%**	**43.90%**	**6.90%**
Change	**9**	**103**	**$1,049,968.07**	**$503.61**	**$18.28**	**4,057**	**2,647**

Utilization Details: CY 2012

CHEMICAL NAME	BRAND NAME	CLAIMS	UNITS	DAYS	MEMBERS	COST	CLAIMS/ MEMBER	COST/ DAY
Glatiramer	COPAXONE KIT 20MG/ML	535	535	16,050	87	$2,271,577.77	6.15	$141.53
Interferon Beta-1a	REBIF INJ 44/0.5	288	1,716	8,102	42	$1,042,673.85	6.86	$128.69
Interferon Beta-1a	AVONEX PREFL KIT 30MCG	151	561	4,582	32	$599,911.25	4.72	$130.93
Fingolimod	GILENYA CAP 0.5MG	138	3,864	3,868	25	$599,127.09	5.52	$154.89
Interferon Beta-1b	BETASERON INJ 0.3MG	113	1,691	3,558	20	$459,747.09	5.65	$129.22
Dalfampridine	AMPYRA TAB 10MG	69	4,140	2,070	15	$94,362.18	4.6	$45.59
Natalizumab	TYSABRI INJ	38	570	929	6	$133,305.99	6.33	$143.49
Interferon Beta-1a	AVONEX PEN KIT 30MCG	21	21	588	5	$82,310.54	4.2	$139.98
Interferon Beta-1a	AVONEX KIT 30MCG	12	48	336	3	$43,868.32	4	$130.56
Interferon Beta-1a	REBIF TITRTN SOL PACK	12	50	360	11	$40,562.38	1.09	$112.67
Interferon Beta-1b	EXTAVIA INJ 0.3MG	11	67	330	1	$16,136.85	11	$48.90
Interferon Beta-1a	REBIF INJ 22/0.5	7	42	200	4	$24,457.94	1.75	$122.29
	TOTAL	**1,395**	**13,305**	**40,973**	**195**	**$5,408,041.25**	**7.15**	**$131.99**

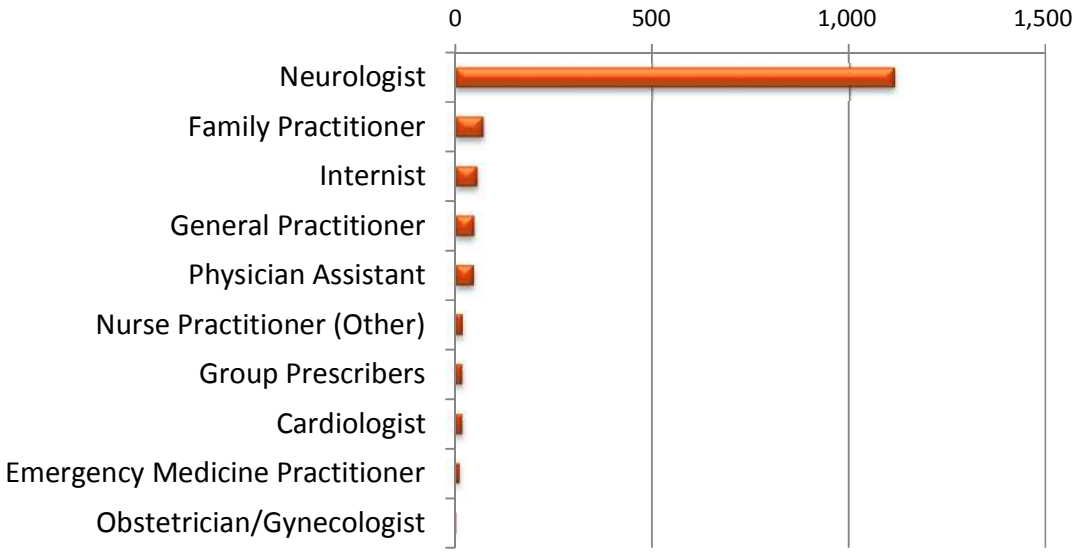
*Total number of unduplicated members.

Demographics of Members Utilizing Multiple Sclerosis Medications



All members under the age of 21 were verified to have the diagnosis of Multiple Sclerosis in their diagnosis history and their MS therapies were prescribed by a specialist in psychiatry/neurology, or neurologist.

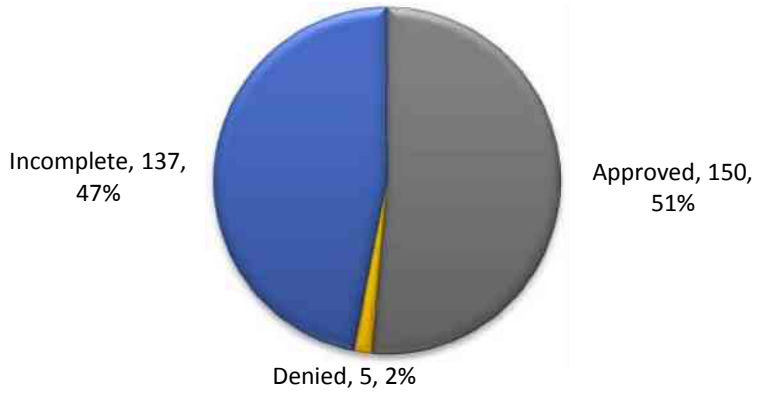
Top Prescriber Specialties of Multiple Sclerosis Medications by Number of Claims



Prior Authorization of Multiple Sclerosis Medications

There were 212 petitions received during calendar year 2012 for this category of medications. The following graph shows the status of the petitions submitted.

Status of Petitions Submitted: CY 2012



Market News and Updates

Anticipated Patent Expirations:

- Ampyra® (dalfampridine) – 2026
- Copaxone® (glatiramer) – 2014

Aubagio® (teriflunomide) was approved by the FDA during the fall of 2012 for the treatment of relapsing forms of multiple sclerosis. It is available as 7mg and 14mg tablets that can be taken once daily with or without food. Aubagio® is an immunomodulatory agent with anti-inflammatory properties that inhibits dihydro-orotate dehydrogenase, a mitochondrial enzyme involved in de novo pyrimidine synthesis. The exact mechanism by which Aubagio® exerts its therapeutic effect in multiple sclerosis is unknown but may involve a reduction in the number of activated lymphocytes in the central nervous system. Aubagio® is a pregnancy category X medication with the following contraindications:

1. Severe hepatic impairment.
2. Patients who are pregnant or women of childbearing potential not using reliable contraception.
3. Current treatment with leflunomide (Arava®).

Teriflunomide is the principal active metabolite of leflunomide and is responsible for leflunomide's activity in vivo. At recommended doses, teriflunomide and leflunomide result in a similar range of plasma concentrations of teriflunomide. As such, Aubagio® (teriflunomide) has similar warnings and precautions as Arava® (leflunomide). Monitoring during therapy with Aubagio® consists of:

1. Pregnancy test prior to treatment and during treatment when pregnancy is suspected.
2. CBC with differential; within 6 months prior to treatment initiation and during therapy if clinically indicated (due to decrease of white blood cell counts).

3. Serum transaminases and bilirubin; within 6 months prior to treatment initiation and then ALT (SGPT) at least monthly for the first 6 months of therapy. (Black box warning regarding risk of severe liver injury/dysfunction with leflunomide.)
4. Blood pressure before initiating therapy and periodically thereafter. (4% in clinical trial experienced an increase in blood pressure.)
5. Check serum potassium levels periodically (Patients with symptoms of hyperkalemia or acute renal failure.)
6. Checking for symptoms of peripheral neuropathy. (If patient develops symptoms consistent with peripheral neuropathy consider discontinuation of treatment.)

On average, Aubagio® can remain in the body between 8 months to 2 years after discontinuation. If necessary, accelerated elimination of teriflunomide via administration of cholestyramine or activated charcoal for 11 days may be used at time of discontinuation to decrease plasma concentrations of teriflunomide rapidly.

The efficacy of Aubagio® was demonstrated in a double-blind, placebo-controlled study with 1,088 patients diagnosed with relapsing forms of MS. These patients were randomized to receive Aubagio® 14 mg (n=359) or 7 mg (n=366) or placebo (n=363) for 108 weeks. The results are on the following table:

Trial Results: Clinical Endpoints	Aubagio® 14mg	Aubagio® 7mg	Placebo
Annualized Relapse Rate (ARR)	0.369 (p=0.0005)	0.370 (p=0.0002)	0.539
Relative Risk Reduction	31%	31%	
% of Patients Relapse Free at 108 weeks	56.5%	53.7%	45.6%
% Disability Progression at 108 weeks	20.2% (p=0.028)	21.7% (p=0.084)	27.3%
Hazard Ratio	0.70	0.76	
Median Δ in total lesion vol (mL) at wk 108	0.345 (p=0.0003)	0.755 (p=0.0317)	1.127
Mean # of Gd-enhancing T1-lesions per scan	0.261 (p=0.0001)	0.570 (p=0.0001)	1.331

*Total lesion volume = sum of T2 and hypointense T1 lesion volume in mL.

Tecfidera™ (dimethyl fumarate) was approved by the FDA in the spring of 2013 for the treatment of relapsing forms of multiple sclerosis. It is available as 120mg and 240mg delayed release tablets that can be taken twice daily with or without food. The mechanism by which dimethyl fumarate (DMF) exerts its therapeutic effect in multiple sclerosis is unknown.

There are no known contraindications listed; however, Tecfidera™ may cause lymphopenia. As a result, a complete blood cell count (CBC) should be performed before initiating treatment with Tecfidera™. A CBC is recommended annually and as clinically indicated. In patients with serious infections, withholding Tecfidera™ should be considered. The most common adverse reactions in clinical trials were flushing, abdominal pain, diarrhea, and nausea.

The efficacy of Tecfidera™ was demonstrated in two studies (Studies I and II) that evaluated Tecfidera™ taken either twice (BID) or three times (TID) a day, versus placebo, in patients with relapsing-remitting multiple sclerosis. Tecfidera™ had a statistically significant effect on all of the study endpoints, but the 240mg TID showed no additional benefit over the Tecfidera 240mg BID. The following are the results of Tecfidera™ 240mg BID vs. placebo from both studies:

	Study I Results			Study II Results		
Clinical Endpoints	**Tecfidera™ (N=410)**	**Placebo (N=408)**	**P-value**	**Tecfidera™ (N=359)**	**Placebo (N=363)**	**P-value**
Proportion relapsing	27%	46%	<0.0001	29%	41%	0.0020
Relative risk reduction	49%			34%		
Annualized relapse rate	0.172	0.364	<0.0001	0.224	0.401	<0.0001
Relative reduction	53%			44%		
Prop w disability prog.*	16%	27%	0.0050	13%	17%	0.25
Relative risk reduction	38%			21%		
MRI Endpoints	**(N=152)**	**(N=165)**		**(N=147)**	**(N=144)**	
Mean number of new or newly enlarging T2 lesions over 2 years	2.6	17	<0.0001	5.1	17.4	<0.0001
% with no new or newly enlarging lesions	45%	27%		27%	12%	
Mean (median)number of Gd+ lesions at 2 years	0.1 (0)	1.8 (0)		0.5 (0.0)	2.0 (0.0)	
% of subjects with:						
0 lesions	93%	62%		80%	61%	
1 lesion	5%	10%		11%	17%	
2 lesions	<1%	8%		3%	6%	
3 to 4 lesions	0	9%		3%	2%	
5 or more lesions	<1%	11%		3%	14%	
Relative odds reduction	90%		<0.0001	74%		<0.0001
Mean # of new T1 hypo-intense lesions over 2yrs	1.5	5.6	<0.0001	3.0	7.0	<0.0001

*Proportion of patients with disability progression.

Study II included glatiramer acetate as an active comparator arm. The annualized relapse rate at two years was 0.29 for glatiramer acetate compared with 0.224 for Tecfidera™, and 0.401 for placebo. However, this study was not designed to test the efficacy or superiority between these two products. The following table shows a cost comparison of the new therapies:

Medication	Cost/Unit	Cost/Day	Cost/Month
Aubagio® (teriflunomide)	$130.55 per tablet	$130.55	$3,916.50
Tecfidera™ (dimethyl fumarate)	$79.20 per tablet	$158.40	$4,752.00

Costs do not include dispensing fee.

There has been dynamic growth in the area of research and development for the treatment of multiple sclerosis, and currently, a number of pharmaceutical companies have products under review by the FDA. Novel treatments as well as improvements on existing therapies, such as a peginterferon β - 1a product that can be dosed once every two weeks, are expected to enter the market within the next few years.

Conclusions and Recommendations

Initiative has been taken to ensure appropriate and compliant use of medications for the management of multiple sclerosis in the SoonerCare population. However, this category of medications is anticipated to experience growth in the next few years, and increases in utilization and costs are expected to occur concurrently.

The College of Pharmacy recommends continued monitoring of the Multiple Sclerosis class of medications. The College of Pharmacy also recommends the prior authorization of the Aubagio® (teriflunomide) and Tecfidera™ (dimethyl fumarate) with the following criteria.

Aubagio® (Teriflunomide) Prior Authorization Criteria:

1. Documented diagnosis of relapsing remitting MS, and
2. Verification of all of the following:
    a. Female members are not pregnant and/or currently on a reliable contraceptive.
    b. No active infections and a normal CBC.
    c. Normal liver function via liver function test.
    d. Negative Tuberculin skin test, or completion of standard medical treatment for tuberculin positive patients.
3. No concurrent use with other disease modifying therapies.
4. Approval of Aubagio® will be initially for 6 months, after which time, all of the following will be required for further approval:
    a. Compliance on medication.
    b. Repeat CBC and verification of no bone marrow suppression.
    c. Repeat liver function tests and verification of no liver injury or failure.
    d. Verification that female members are not pregnant and/or still on reliable contraceptive.
    e. Verification of normal renal function.
5. Compliance will be checked every 6 months there-after for continuation of therapy.
6. Quantity limit of #30 tablets per 30 days applies.

Tecfidera (Dimethyl Fumarate) Prior Authorization Criteria:

1. FDA approved diagnosis of remitting/relapsing multiple sclerosis with at least one relapse in the previous 12 months, and
2. Verification of the following:
    a. No serious active infection, and
    b. CBC with normal lymphocyte counts.
3. No concurrent use with other disease modifying therapies.
4. Compliance will be checked every 6 months there-after for continuation of therapy.
5. Quantity limit of #60 tablets per 30 days applies.

PRODUCT DETAILS OF AUBAGIO® (TERIFLUNOMIDE) TABLETS

INDICATIONS: Treatment of relapsing forms of multiple sclerosis.

DOSAGE FORMS: Aubagio® is available as 7 mg and 14 mg tablets.

- The 14 mg tablet is a pale blue to pastel blue, pentagonal film-coated tablet with the dose strength, "14" imprinted on one side and engraved with the corporate logo on the other side. Each tablet contains 14 mg of teriflunomide.

- The 7 mg tablet is a very light greenish-bluish grey to pale greenish-blue, hexagonal film-coated tablet with dose strength "7" imprinted on one side and engraved with the corporate logo on other side. Each tablet contains 7 mg of teriflunomide.

ADMINISTRATION:

- Aubagio® can be taken with or without food once daily.
- Obtain transaminase and bilirubin levels within 6 months before initiation of Aubagio® therapy. Monitor ALT levels at least monthly for six months after starting Aubagio®.
- Obtain a complete blood cell count (CBC) within 6 months before the initiation of treatment with Aubagio®. Further monitoring should be based on signs and symptoms of infection.
- Prior to initiating Aubagio®, screen patients for latent tuberculosis infection with a tuberculin skin test.
- Check blood pressure before start of Aubagio® treatment and periodically thereafter.

CONTRAINDICATIONS:

- **Severe hepatic impairment**
- **Current treatment with leflunomide**
- **Patients who are pregnant or women of childbearing potential not using reliable contraception**: Aubagio® may cause fetal harm when administered to a pregnant woman. In animal studies, teriflunomide has been shown to be selectively teratogenic and embryolethal in multiple species when administered during pregnancy at doses less than those used clinically. Nonclinical studies indicate further that the intended pharmacologic action of the drug is involved in the mechanism of developmental toxicity. Aubagio® is contraindicated in women who are pregnant or women of child bearing potential not using reliable contraception. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus. If pregnancy does occur during treatment, the drug should be immediately discontinued and an accelerated elimination procedure should be initiated. Under these conditions, the patient should be referred to an obstetrician/gynecologist, preferably experienced in reproductive toxicity, for further evaluation and counseling.

SPECIAL POPULATIONS:

- **Pregnancy:** Pregnancy Category X. When teriflunomide (oral doses of 1, 3, or 10 mg/kg/day) was administered to pregnant rats throughout the period of organogenesis, high incidences of fetal malformation (primarily craniofacial, and axial and appendicular skeletal defects) and embryofetal death were observed at doses not associated with maternal toxicity. *Use in Males:* Aubagio® is detected in human semen. Animal studies to specifically evaluate the risk of male-

mediated fetal toxicity have not been conducted. To minimize any possible risk, men not wishing to father a child and their female partners should use reliable contraception. Men wishing to father a child should discontinue use of Aubagio® and undergo an accelerated elimination procedure to decrease the plasma concentration of teriflunomide to less than 0.02 mg/L (0.02 mg/mL). *Pregnancy Registry:* Although Aubagio® is contraindicated in pregnancy, a pregnancy registry has been established to monitor fetal outcomes of pregnant women exposed to Aubagio®. Physicians are encouraged to enroll pregnant women in the Aubagio® pregnancy registry, or pregnant women may enroll themselves, by calling 1-800-745-4447, option 2.

- **Nursing Mothers:** Teriflunomide was detected in rat milk following a single oral dose of teriflunomide. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from Aubagio® a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.
- **Pediatrics**: Safety and effectiveness in pediatric patients have not been established.
- **Geriatrics:** Clinical studies of Aubagio® did not include patients over 65 years old.
- **Hepatic Impairment:** No dosage adjustment is necessary for patients with mild and moderate hepatic impairment. The pharmacokinetics of teriflunomide in severe hepatic impairment has not been evaluated. Teriflunomide is contraindicated in patients with severe hepatic impairment.
- **Renal Impairment:** No dosage adjustment is necessary for patients with mild, moderate, and severe renal impairment.

WARNINGS AND PRECAUTIONS:

- **Hepatotoxicity:** Severe liver injury including fatal liver failure and dysfunction has been reported in some patients treated with leflunomide, which is indicated for rheumatoid arthritis. A similar risk would be expected for teriflunomide because recommended doses of teriflunomide and leflunomide result in a similar range of plasma concentrations of teriflunomide. Patients with pre-existing liver disease may be at increased risk of developing elevated serum transaminases when taking Aubagio®. Patients with pre-existing acute or chronic liver disease, or those with serum alanine aminotransferase (ALT) greater than two times the upper limit of normal (ULN) before initiating treatment, should not normally be treated with Aubagio®. **Aubagio® is contraindicated in patients with severe hepatic impairment.** Monitor ALT levels at least monthly for six months after starting Aubagio®. Consider additional monitoring when Aubagio® is given with other potentially hepatotoxic drugs. Consider discontinuing Aubagio® if serum transaminase increase (greater than three times the ULN) is confirmed. Monitor serum transaminase and bilirubin on Aubagio® therapy, particularly in patients who develop symptoms suggestive of hepatic dysfunction, such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine. If liver injury is suspected to be Aubagio®-induced, discontinue teriflunomide and start an accelerated elimination procedure and monitor liver tests weekly until normalized. If teriflunomide-induced liver injury is unlikely because some other probable cause has been found, resumption of teriflunomide therapy may be considered.
- **Use in Women of Childbearing Potential:** There are no adequate and well-controlled studies evaluating Aubagio® in pregnant women. However, based on animal studies, teriflunomide may increase the risk of teratogenic effects or fetal death when administered to a pregnant woman. **Women of childbearing potential must not be started on Aubagio® until pregnancy is excluded and it has been confirmed that they are using reliable contraception.** Before starting treatment with Aubagio®, patients must be fully counseled on the potential for serious risk to the fetus.

The patient must be advised that if there is any delay in onset of menses or any other reason to suspect pregnancy, they must notify the physician immediately for pregnancy testing and, if positive, the physician and patient must discuss the risk to the fetus. It is possible that rapidly lowering the plasma concentration of teriflunomide by instituting an accelerated elimination procedure may decrease the risk to the fetus from Aubagio®. Upon discontinuing Aubagio®, it is recommended that all women of childbearing potential undergo an accelerated elimination procedure. Women receiving Aubagio® treatment who wish to become pregnant must discontinue Aubagio® and undergo an accelerated elimination procedure, which includes verification of teriflunomide plasma concentrations less than 0.02 mg/L (0.02 mcg/mL). Human plasma concentrations of teriflunomide less than 0.02 mg/L (0.02 mcg/mL) are expected to have minimal risk.

- **Procedure for Accelerated Elimination of Teriflunomide:** Teriflunomide is eliminated slowly from the plasma. Without an accelerated elimination procedure, it takes on average 8 months to reach plasma concentrations less than 0.02 mg/L, although because of individual variations in drug clearance it may take as long as 2 years. An accelerated elimination procedure could be used at any time after discontinuation of Aubagio®. Elimination can be accelerated by either of the following procedures:
    - Administration of cholestyramine 8 g every 8 hours for 11 days. If cholestyramine 8 g three times a day is not well tolerated, cholestyramine 4 g three times a day can be used.
    - Administration of 50 g oral activated charcoal powder every 12 hours for 11 days. If either elimination procedure is poorly tolerated, treatment days do not need to be consecutive unless there is a need to lower teriflunomide plasma concentration rapidly. At the end of 11 days, both regimens successfully accelerated teriflunomide elimination, leading to more than 98% decrease in teriflunomide plasma concentrations. Use of the accelerated elimination procedure may potentially result in return of disease activity if the patient had been responding to Aubagio® treatment.

- **Bone Marrow Effects/Immunosuppression Potential/Infections:** *White Blood Cell (WBC) count decrease:* A mean decrease in white blood cell (WBC) count of approximately 15% (mainly neutrophils and lymphocytes) and in platelet count of approximately 10% was observed in placebo-controlled trials with 7 mg and 14 mg of Aubagio®. The decrease in mean WBC count occurred during the first 6 weeks and WBC count remained low during treatment. In placebo-controlled studies, neutrophil count < $1.5x10^9$/L was observed in 10% and 15% of patients on Aubagio® 7 mg and 14 mg, respectively, compared with 5% of patients on placebo; lymphocyte count <$0.8x10^9$/L was observed in 7% and 10% of patients on Aubagio® 7 mg and 14 mg, respectively, compared with 5% of patients on placebo. No cases of serious pancytopenia were reported in premarketing clinical trials of Aubagio® but rare cases of pancytopenia, agranulocytosis, and thrombocytopenia have been reported in the postmarketing setting with leflunomide. A similar risk would be expected for teriflunomide. Obtain a complete blood cell count (CBC) within 6 months before the initiation of treatment with Aubagio®. Further monitoring should be based on signs and symptoms suggestive of bone marrow suppression. *Risk of Infection / Tuberculosis Screening:* Patients with active acute or chronic infections should not start treatment until the infection(s) is resolved. If a patient develops a serious infection consider suspending treatment with Aubagio® and using an accelerated elimination procedure. Reassess the benefits and risks prior to resumption of therapy. Instruct patients receiving Aubagio® to report symptoms of infections to a physician. Aubagio® is not recommended for

patients with severe immunodeficiency, bone marrow disease, or severe, uncontrolled infections. Medications like teriflunomide that have immunosuppression potential may cause patients to be more susceptible to infections, including opportunistic infections. In placebo-controlled studies of Aubagio®, no overall increase in the risk of serious infections was observed with teriflunomide 7 mg (1.4%) or 14 mg (2.2%) compared to placebo (2.1%). However, one fatal case of klebsiella pneumonia sepsis occurred in a patient taking teriflunomide 14 mg for 1.7 years. Fatal infections have been reported in the post-marketing setting, in patients receiving leflunomide, especially *Pneumocystis jiroveci* pneumonia and aspergillosis. Most of the reports were confounded by concomitant immunosuppressant therapy and/or comorbid illness which, in addition to rheumatoid disease, may predispose patients to infection. **In clinical studies with Aubagio®, cytomegalovirus hepatitis reactivation has been observed. In clinical studies with Aubagio®, cases of tuberculosis have been observed.** Prior to initiating Aubagio®, screen patients for latent tuberculosis infection with a tuberculin skin test. Aubagio® has not been studied in patients with a positive tuberculosis screen, and the safety of Aubagio® in individuals with latent tuberculosis infection is unknown. For patients testing positive in tuberculosis screening, treat by standard medical practice prior to therapy with Aubagio®. *Vaccination*: No clinical data are available on the efficacy and safety of vaccinations in patients taking Aubagio®. Vaccination with live vaccines is, however, not recommended. The long half-life of Aubagio® should be considered when contemplating administration of a live vaccine after stopping Aubagio®. No clinical data are available on the efficacy and safety of vaccinations in patients taking Aubagio®. **Vaccination with live vaccines is, however, not recommended.** The long half-life of Aubagio® should be considered when contemplating administration of a live vaccine after stopping Aubagio®. *Malignancy:* The risk of malignancy, particularly lymphoproliferative disorders, is increased with the use of some immunosuppressive medications. There is a potential for immunosuppression with teriflunomide. No apparent increase in the incidence of malignancies and lymphoproliferative disorders was reported in the Aubagio® clinical trials, but larger and longer-term studies would be needed to determine whether there is an increased risk of malignancy or lymphoproliferative disorders with Aubagio®.

- **Peripheral Neuropathy:** In placebo-controlled studies, peripheral neuropathy, including both polyneuropathy and mononeuropathy (e.g., carpal tunnel syndrome), was reported more frequently in patients taking Aubagio® than in patients taking placebo. In one 108-week placebo-controlled study in 1086 patients with multiple sclerosis, the incidence of peripheral neuropathy confirmed by nerve conduction studies was 1.2% (4 patients) and 1.9% (6 patients) on 7 mg and 14 mg of Aubagio®, respectively, compared with 0% on placebo. Treatment was discontinued in 2 patients with polyneuropathy, one on each dose; one of them recovered following treatment discontinuation. The other cases of peripheral neuropathy did not resolve with continued treatment. There have also been reports of peripheral neuropathy in patients receiving leflunomide. Age older than 60 years, concomitant neurotoxic medications, and diabetes may increase the risk for peripheral neuropathy. If a patient taking Aubagio® develops symptoms consistent with peripheral neuropathy, such as bilateral numbness or tingling of hands or feet, consider discontinuing Aubagio® therapy and performing an accelerated elimination procedure

- **Acute Renal Failure:** In placebo-controlled trials, 10 of 844 (1.2%) of Aubagio®-treated subjects had transient acute renal failure with a creatinine measurement increased by 100% or more of

their baseline serum creatinine value, compared to 0 of 421 placebo-treated subjects. Seven of the 10 subjects had a nadir creatinine clearance less than 30 cc/minute. In each of the 10 subjects, the serum creatinine level was normal on the next reported measurement (6-48 days from the increase in creatinine) with continued teriflunomide use. These increased creatinine measurements occurred between 12 weeks and 2 years after first dose of teriflunomide. Of the 6 subjects with available serum potassium measurements, 3 (50%) had hyperkalemia (measurements of 6.7, >7.3, and >7.3 mmol/L). No associated symptoms were documented. Aubagio® causes increases in renal uric acid clearance with mean decreases in serum uric acid of 20-30%. Acute uric acid nephropathy is a likely explanation for the cases of transient acute renal failure seen with teriflunomide. Although symptoms associated with acute uric acid nephropathy, such as loin pain or flank pain, were not reported, this information was not systematically collected. No inciting factors, such as dehydration, exercise, or increase in physical activity in the 30 days prior to the adverse event were reported, but this information was not systematically collected.

- **Hyperkalemia:** In placebo-controlled trials, treatment-emergent hyperkalemia >7.0 mmol/L occurred in 8/829 (1.0%) of teriflunomide-treated subjects, compared to 1/414 (0.2%) of placebo-treated subjects. Two teriflunomide-treated subjects had hyperkalemia >7.0 mmol/L with acute renal failure. Possible causes in other cases were not documented. Check serum potassium level in Aubagio®-treated patients with symptoms of hyperkalemia or with acute renal failure.

- **Skin Reactions:** Rare cases of Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported in patients with rheumatoid arthritis receiving leflunomide. A similar risk would be expected for teriflunomide. If a patient taking Aubagio® develops any of these conditions, stop Aubagio® therapy and perform an accelerated elimination procedure.

- **Blood Pressure Increase:** In placebo-controlled studies, mean change from baseline in systolic blood pressure was 2.9 mmHg and 2.7 mmHg for AUBAGIO 7 mg and 14 mg, respectively, and -1.3 mmHg for placebo. The change from baseline in diastolic blood pressure was 1.4 mmHg and 1.3 mmHg for Aubagio® 7 mg and 14 mg, respectively, and -0.9 mmHg for placebo. Hypertension was reported as an adverse reaction in 4% of patients treated with 7 mg or 14 mg of Aubagio®, compared with 2% on placebo. Check blood pressure before start of Aubagio® treatment and periodically thereafter. Elevated blood pressure should be appropriately managed during treatment with Aubagio®.

- **Respiratory Effects:** Interstitial lung disease and worsening of pre-existing interstitial lung disease have been reported during treatment with leflunomide. A similar risk would be expected for teriflunomide. Interstitial lung disease may be fatal. Interstitial lung disease may occur acutely at any time during therapy and has a variable clinical presentation. New onset or worsening pulmonary symptoms, such as cough and dyspnea, with or without associated fever, may be a reason for discontinuation of the therapy and for further investigation as appropriate. If discontinuation of the drug is necessary, consider initiation of an accelerated elimination procedure.

- **Concomitant Use with Immunosuppressive or Immunomodulating Therapies:** Co-administration with antineoplastic, or immunosuppressive therapies used for treatment of

multiple sclerosis has not been evaluated. Safety studies in which teriflunomide was concomitantly administered with other immune modulating therapies for up to one year (interferon beta, glatiramer acetate) did not reveal any specific safety concerns. The long term safety of these combinations in the treatment of multiple sclerosis has not been established. In any situation in which the decision is made to switch from Aubagio® to another agent with a known potential for hematologic suppression, it would be prudent to monitor for hematologic toxicity, because there will be overlap of systemic exposure to both compounds. Use of an accelerated elimination procedure may decrease this risk, but may also potentially result in return of disease activity if the patient had been responding to Aubagio® treatment.

ADVERSE REACTIONS:

- **Serious adverse reactions:** Hepatotoxicity, bone marrow effects/immunosuppression potential/infection, peripheral neuropathy, acute renal failure, hyperkalemia, serious skin reactions, blood pressure effects, respiratory effects.

- **Other adverse reactions in clinical trials:** The most frequent adverse reactions for Aubagio® (incidence ≥10% and ≥2% greater than placebo) in the placebo-controlled studies were ALT increased, alopecia, diarrhea, influenza, nausea, and paresthesia. Alopecia was the most common cause of discontinuation because of adverse events in controlled clinical studies as compared to placebo (0.5% and 1.4% of patients on Aubagio® 7 mg and 14 mg, respectively, and 0% on placebo). Four cardiovascular deaths, including three sudden deaths, and one myocardial infarction in a patient with a history of hyperlipidemia and hypertension were reported among approximately 2600 patients exposed to teriflunomide in the premarketing database. These cardiovascular deaths occurred during uncontrolled extension studies, one to nine years after initiation of treatment. A relationship between teriflunomide and cardiovascular death has not been established. In clinical trials, 18% of teriflunomide-treated subjects had mild hypophosphatemia (≥ 0.6 mmol/L and < lower limit of normal), compared to 9% of placebo-treated subjects; 5% of teriflunomide-treated subjects had moderate hypophosphatemia (≥0.3 mmol/L and <0.6 mmol/L), compared to 1% of placebo-treated subjects. No subject in either treatment group had a serum phosphorus <0.3 mmol/L.

DRUG INTERACTIONS:

- Teriflunomide on CYP2C8 substrates: There was an increase in mean repaglinide Cmax and AUC (1.7- and 2.4-fold, respectively), following repeated doses of teriflunomide and a single dose of 0.25 mg repaglinide, suggesting that teriflunomide is an inhibitor of CYP2C8 in vivo. The magnitude of interaction could be higher at the recommended repaglinide dose. Therefore, monitoring patients with concomitant use of drugs metabolized by CYP2C8, such as repaglinide, paclitaxel, pioglitazone, or rosiglitazone is recommended as they may have higher exposure.
- Teriflunomide and warfarin: A 25% decrease in peak international normalized ratio (INR) was observed when teriflunomide was coadministered with warfarin as compared with warfarin alone. Therefore, when warfarin is coadministered with teriflunomide, close INR follow-up and monitoring is recommended.
- Teriflunomide and oral contraceptives: There was an increase in mean ethinylestradiol Cmax and AUC0-24 (1.58- and 1.54-fold, respectively) and levonorgestrel Cmax and AUC0-24 (1.33- and 1.41-fold, respectively) following repeated doses of teriflunomide. Consideration should be given to the type or dose of oral contraceptives used in combination with teriflunomide.

- Teriflunomide and CYP1A2 substrates: Repeated doses of teriflunomide decreased mean Cmax and AUC of caffeine (CYP1A2 substrate) by 18% and 55% respectively, suggesting that teriflunomide may be *in vivo* a weak inducer of CYP1A2. Therefore, patients should be monitored when teriflunomide is coadministered with drugs metabolized by CYP1A2 (such as duloxetine, alosetron, theophylline, and tizanidine), as the efficacy of such drugs could be reduced.

PATIENT COUNSELING INFORMATION:

- A Medication Guide is required for distribution with Aubagio®. Encourage patients to read the Aubagio® Medication Guide. The complete text of the Medication Guide is reprinted at the end of this document. Summarize for patients the benefits and potential risks of treatment with Aubagio®. Tell patients to take Aubagio® once daily as prescribed. Tell patients not to discontinue Aubagio® without first discussing with the prescribing physician.
- Inform patients that Aubagio® may increase liver enzymes and that their liver enzymes will be checked before starting Aubagio® and for at least 6 months while they are taking Aubagio®. Advise patients that they should contact their physician if they have any unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine.
- Inform patients that based on animal studies, Aubagio® may cause fetal harm. Advise women of childbearing potential of the need for effective contraception during Aubagio® treatment and until completion of an accelerated elimination procedure. Advise them that an accelerated elimination procedure can be used at any time after the discontinuation of Aubagio®. Instruct the patient that if she suspects or confirms pregnancy, she should immediately inform her physician. Inform the patients that an Aubagio® pregnancy registry is available. Instruct men who are taking Aubagio® and wish to father a child to discontinue Aubagio® and use an accelerated elimination procedure. Instruct men taking Aubagio® who do not wish to father a child that they and their female partners should use reliable contraception.
- Advise patients that Aubagio® may stay in the blood for up to 2 years after the last dose and that an accelerated elimination procedure may be used if needed.
- Inform patients that they may develop peripheral neuropathy. Advise patients that they should contact their physician if they develop symptoms of peripheral neuropathy, such as numbness or tingling of hands or feet.
- Inform patients that they may develop a lowering of their white blood cell counts and that their blood counts will be checked before starting Aubagio®. Inform patients that they may be more likely to get infections when taking Aubagio® and that they should contact their physician if they develop symptoms of infection, particularly in case of fever. Advise patients that the use of some vaccines should be avoided during treatment with Aubagio® and for at least 6 months after discontinuation.
- Inform patients that they may develop peripheral neuropathy. Advise patients that they should contact their physician if they develop symptoms of peripheral neuropathy, such as numbness or tingling of hands or feet.
- Inform patients that Aubagio® may increase blood pressure.
- Inform patients that it is not known whether this drug is present in human milk. Advise patients to discontinue breastfeeding or discontinue the drug.

PRODUCT DETAILS OF TECFIDERA™ (DIMETHYL FUMARATE)

INDICATIONS: Treatment of relapsing forms of multiple sclerosis.

DOSAGE FORMS: Tecfidera™ is available as 120mg and 240mg delayed release capsules.

ADMINISTRATION:

- Starting dose: 120mg orally twice a day for 7 days.
- Maintenance dose after 7 days: 240mg orally twice a day.
- Swallow Tecfidera™ capsules whole and intact. Do not crush, chew, or sprinkle capsule contents on food.
- Take Tecfidera™ with or without food.

CONTRAINDICATIONS: none listed

SPECIAL POPULATIONS:

- **Pregnancy:** Pregnancy Category C. There are no adequate and well-controlled studies in pregnant women. In animals, adverse effects on offspring survival, growth, sexual maturation, and neurobehavioral function were observed when dimethyl fumarate (DMF) was administered during pregnancy and lactation at clinically relevant doses. Tecfidera™ should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
- **Nursing Mothers:** It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Tecfidera™ is administered to a nursing woman.
- **Pediatrics**: Safety and effectiveness in pediatric patients have not been established.
- **Geriatrics:** Clinical studies of Tecfidera™ did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently from younger patients.

WARNINGS AND PRECAUTIONS:

Lymphopenia

- Tecfidera™ may cause decreased lymphocyte counts. A recent CBC should be available before initiating treatment with Tecfidera™. A CBC is recommended annually, and as clinically indicated. Consider withholding treatment in patients with serious infections.
- In the MS placebo controlled trials, mean lymphocyte counts decreased by approximately 30% during the first year of treatment with Tecfidera™ and then remained stable. Four weeks after stopping Tecfidera™, mean lymphocyte counts increased but did not return to baseline. Six percent (6%) of Tecfidera™ patients and <1% of placebo patients experienced lymphocyte counts <0.5x109/L (lower limit of normal 0.91x109/L). The incidence of infections (60% vs 58%) and serious infections (2% vs 2%) was similar in patients treated with Tecfidera™ or placebo, respectively. There was no increased incidence of serious infections observed in patients with lymphocyte counts <0.8x109/L or 0.5x109/L.

Flushing

- Tecfidera™ may cause flushing (e.g., warmth, redness, itching, and/or burning sensation).
- In clinical trials, 40% of Tecfidera™ treated patients experienced flushing. Flushing symptoms generally began soon after initiating Tecfidera™ and usually improved or resolved over time. In the majority of patients who experienced flushing, it was mild or moderate in severity. Three percent (3%) of patients discontinued Tecfidera™ for flushing and <1% had serious flushing

symptoms that were not life-threatening but led to hospitalization. Administration of Tecfidera™ with food may reduce the incidence of flushing.

ADVERSE REACTIONS: Most common adverse reactions (incidence ≥10% and ≥2% placebo) were flushing, abdominal pain, diarrhea, and nausea.

DRUG INTERACTIONS: No drug interaction studies were included in the product information.

PATIENT COUNSELING INFORMATION:

- Patients should be counseled regarding the expected adverse effects of Tecfidera such as flushing and lymphopenia.
- Patients should be instructed to take Tecfidera capsules whole, twice daily.
- Patients should be instructed to store Tecfidera in the original container and throw away opened containers after 90 days.

REFERENCES:

1. Aubagio® Prescribing Information. Pillar5 Pharma Inc. Available on line at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/202992s000lbll.pdf. Last revised: September 2012; Last accessed 11/12/2012
2. Tecfidera™ Prescribing Information. Biogen Idec, Inc. Available on line at: http://www.tecfidera.com/pdfs/full-prescribing-information.pdf Last revised: March 2013; Last accessed 5/17/2013.

Appendix H

Calendar Year 2012 Annual Review of Leukotriene Modifiers: Singulair® (Montelukast) and Zyflo CR® (Zileuton)

Oklahoma Health Care Authority
June 2013

Current Prior Authorization Criteria

The prior authorization criteria for Singulair® (montelukast) are listed below:

Asthma Approval Criteria:

Children age 11 and under:

- Diagnosis of asthma; or
- A claim for inhaled corticosteroid; or
- Use of 3 or more rescue medications.
- All claims should be within the member's previous year's history.

Children age 12 and older and adults:

- Diagnosis of mild or moderate persistent asthma, and/or exercise induced asthma; and
- Trial of inhaled corticosteroid and corticosteroid/LAB_2A therapy within the previous 6 months and reason for trial failure.

Allergic Rhinitis Approval Criteria:

- For members 2 years of age or older - Trial of an antihistamine and nasal corticosteroid, each 14 days in duration, that has failed to relieve allergic rhinitis symptoms. Agents may be used concomitantly or consecutively within the past 30 days.
- For members less than 2 years of age - Trial of an oral antihistamine, 14 days in duration, that has failed to relieve allergic rhinitis symptoms within the past 30 days.

The prior authorization criteria for Zyflo CR® (zileuton) are listed below:

Children age 12 and older and adults only with:

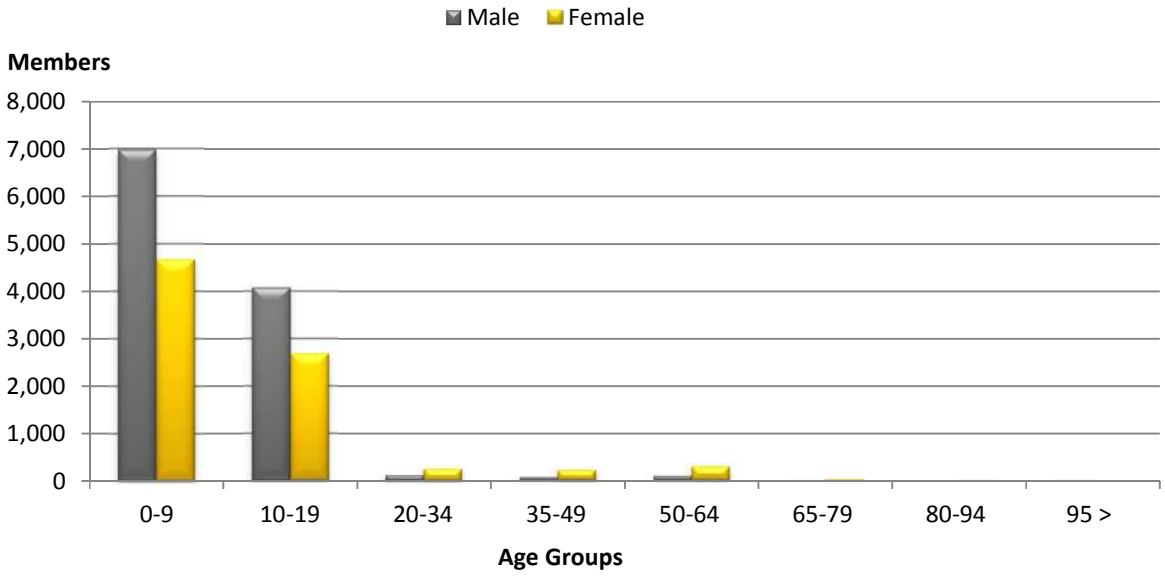
- Diagnosis of mild or moderate persistent asthma; and
- Trial of inhaled corticosteroid and corticosteroid/LAB_2A therapy within the previous 6 months and reason for trial failure; and
- Recent trial with at least one other available leukotriene modifier that did not yield adequate response.

Singulair® was FDA approved in 1998 as adjunctive therapy for asthma. After receiving additional indications for use in allergic rhinitis in 2004, Singulair® utilization rose dramatically to become one of the top reimbursed medications in the SoonerCare pharmacy program, totaling over $13 million dollars in fiscal year 2007, and $16 million in 2008. The prior authorization of Singulair® was implemented in January of 2009. The patent on Singulair® expired in the spring of 2012 and by August 2012 a state maximum allowable cost was applied.

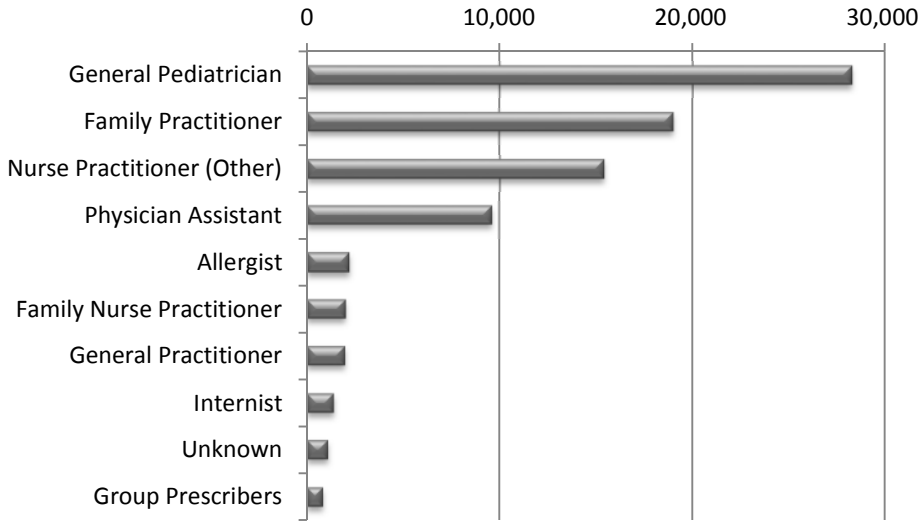
Utilization of Leukotriene Modifiers

Calendar Year	Members	Claims	Cost	Cost/Claim	Cost/ Day	Units	Days
2011	19,415	84,027	$12,061,088.18	$143.54	$4.79	2,531,072	2,517,955
2012	19,527	85,183	$9,576,341.63	$112.42	$3.75	2,569,600	2,552,666
% Change	**0.60%**	**1.40%**	**-20.60%**	**-21.70%**	**-21.70%**	**1.50%**	**1.40%**
Change	**111**	**1,155**	**-$2,484,746.55**	**-$31.12**	**-$1.04**	**38,528**	**34,711**

Demographics of Members Utilizing Leukotriene Modifiers

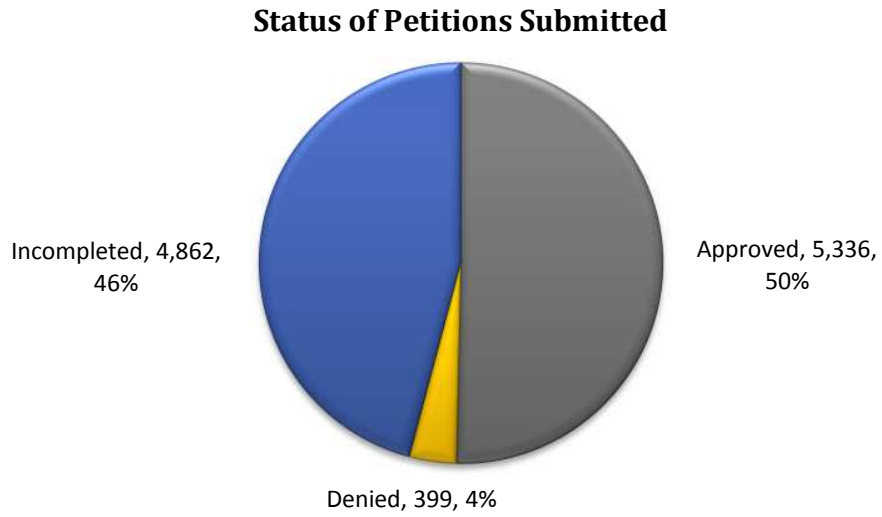


Top Prescriber Specialties of Leukotriene Modifiers



Prior Authorization of Leukotriene Modifiers

There were a total of 10,597 petitions submitted for this category during calendar year 2012. Computer edits are in place to automatically detect asthma diagnoses from member's medical or hospital claims within the previous 12 months to generate automated prior authorizations at the point of sale where applicable. The following chart shows the status of the submitted petitions.



Market News and Updates

Currently all formulations of Singulair® are available in a generic equivalent. However, the granules are available from only one manufacturer; hence it does not have a maximum allowable cost applied. The following are the prices of the available generic montelukast formulations:

- 10mg tabs – $0.39 per tab
- 5mg chewable tabs - $0.44 per chewtab
- 4mg chewable tabs - $0.42 per chewtab
- Granules packet – $5.53 per packet

The patent for Zyflo CR® (zileuton extended release tablets) is anticipated to expire this fall.

Conclusion and Recommendations

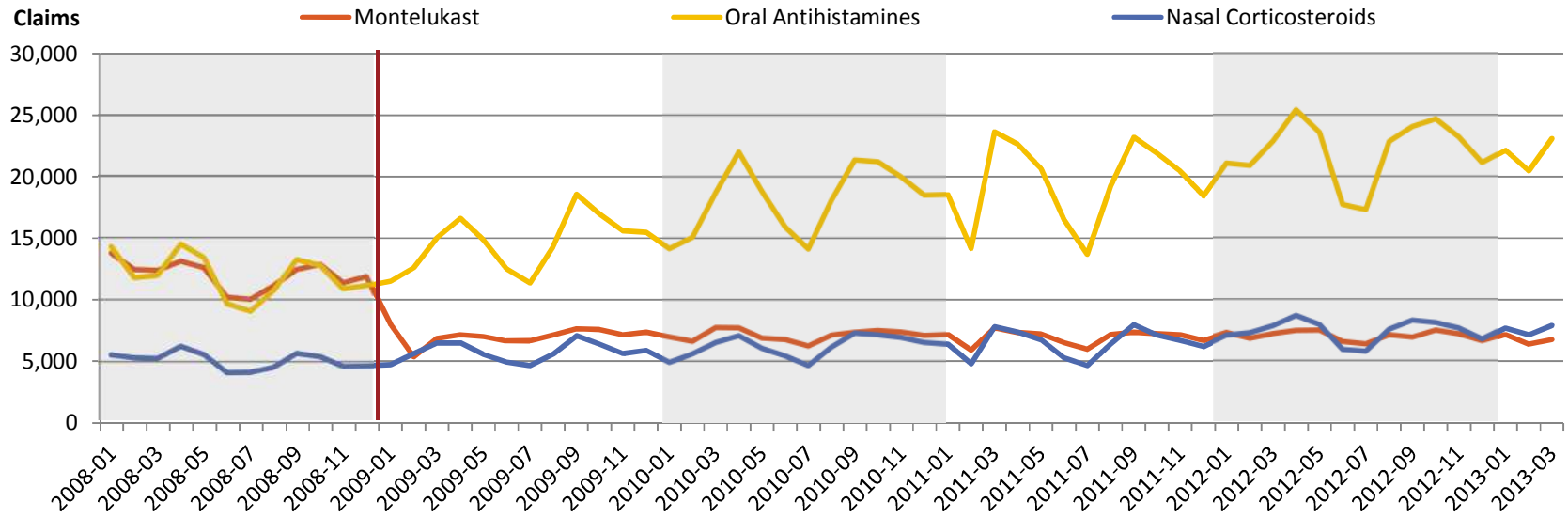
The College of Pharmacy recommends the removal of the prior authorization on all formulations of Singulair®, except the granules, for pediatric SoonerCare members aged 0-20. The asthma prior authorization criteria will remain effective for adult members aged 21 and above. The College of Pharmacy recommends the following changes to the allergic rhinitis criteria:

For members 21 years of age or older – Recent trial of an oral antihistamine, 14 days in duration, that has failed to relieve allergic rhinitis symptoms.

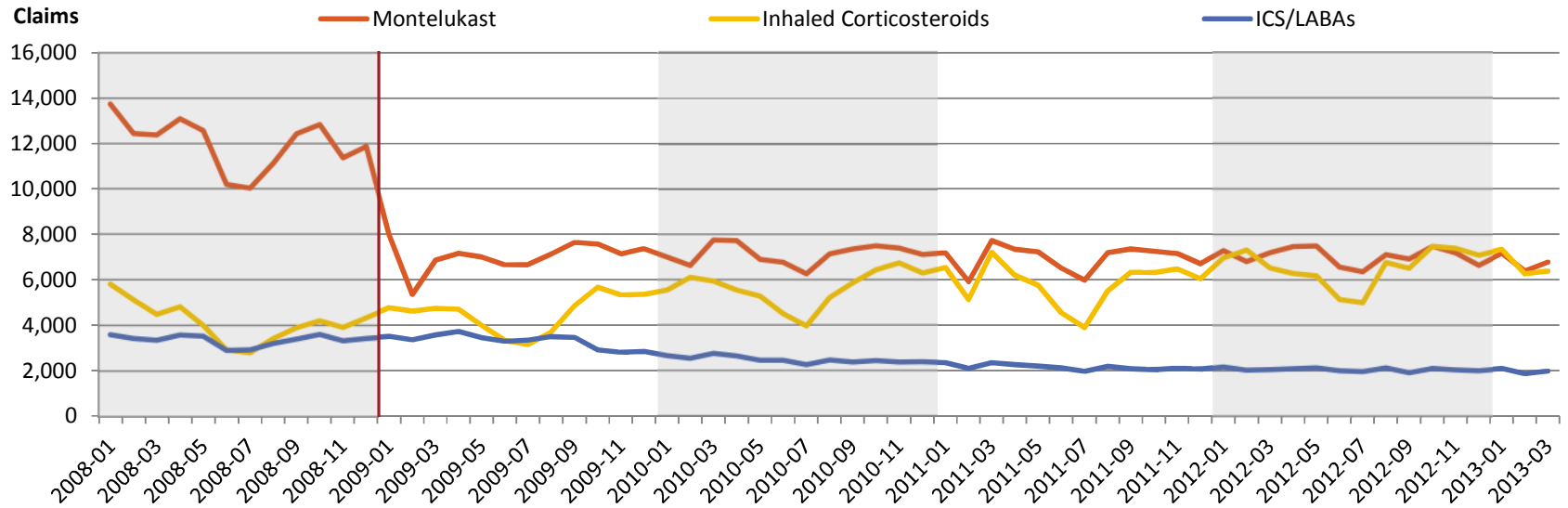
Utilization Details of Leukotriene Modifiers

CHEMICAL NAME	BRAND NAME	CLAIMS	MEMBERS	COST	CLAIMS/ MEMBER	PERDIEM	% COST
Montelukast	SINGULAIR CHW 5MG	23,026	7,099	$3,755,193.53	3.24	$5.44	39.21%
Montelukast	SINGULAIR CHW 4MG	14,632	4,757	$2,371,482.76	3.08	$5.41	24.76%
Montelukast	MONTELUKAST CHW 5MG	14,202	6,303	$335,980.36	2.25	$0.79	3.51%
Montelukast	SINGULAIR TAB 10MG	13,115	3,741	$2,141,384.69	3.51	$5.45	22.36%
Montelukast	MONTELUKAST CHW 4MG	8,830	4,058	$207,224.40	2.18	$0.78	2.16%
Montelukast	MONTELUKAST TAB 10MG	7,642	3,211	$176,947.49	2.38	$0.77	1.85%
Montelukast	SINGULAIR GRA 4MG	2,622	1,080	$429,321.85	2.43	$5.45	4.48%
Zafirlukast	ZAFIRLUKAST TAB 20MG	489	109	$37,062.12	4.49	$2.59	0.39%
Montelukast	MONTELUKAST GRA 4MG	467	339	$66,483.56	1.38	$4.73	0.69%
Zafirlukast	ZAFIRLUKAST TAB 10MG	109	53	$8,080.65	2.06	$2.35	0.08%
Zileuton	ZYFLO CR TAB 600MG	34	9	$41,832.01	3.78	$41.01	0.44%
Zafirlukast	ACCOLATE TAB 20MG	9	4	$743.91	2.25	$2.76	0.01%
Zafirlukast	ACCOLATE TAB 10MG	3	2	$252.38	1.5	$2.80	0.00%
Zileuton	ZYFLO TAB 600MG	3	2	$4,374.29	1.5	$48.60	0.05%
	TOTAL	**85,183**	**19,527**	**$9,576,364.00**	**1.01**	**4.36**	**100.01%**

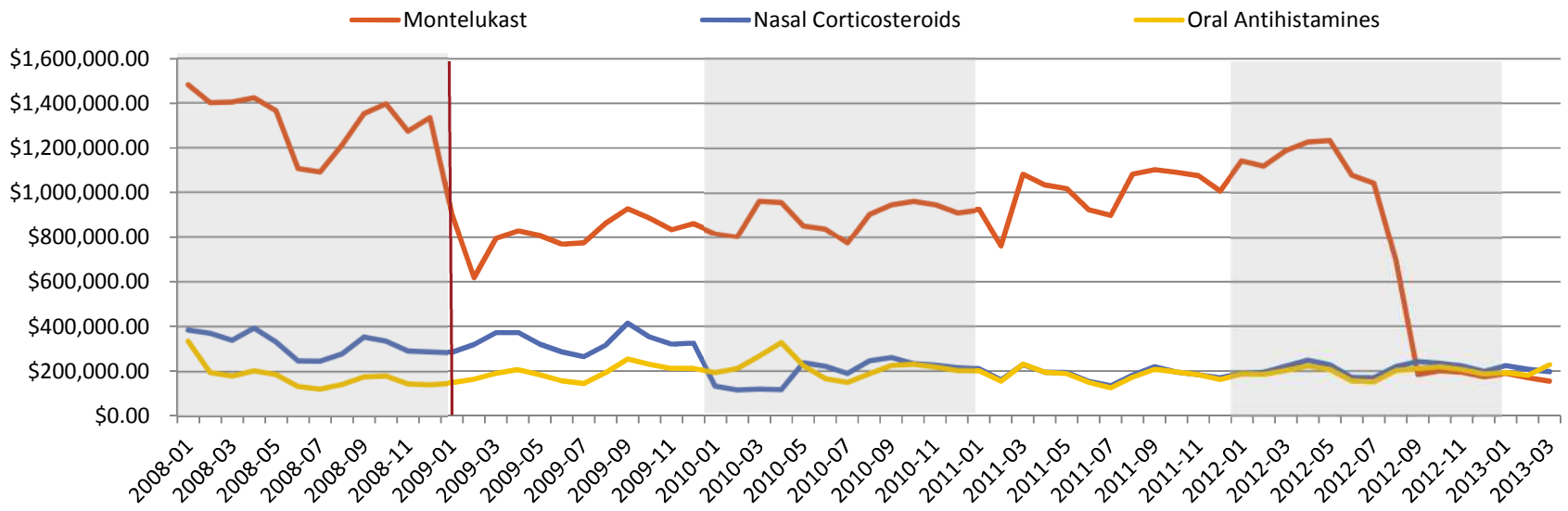
Utilization by Total Claims per Month of Singulair® vs. Allergic Rhinitis Medications



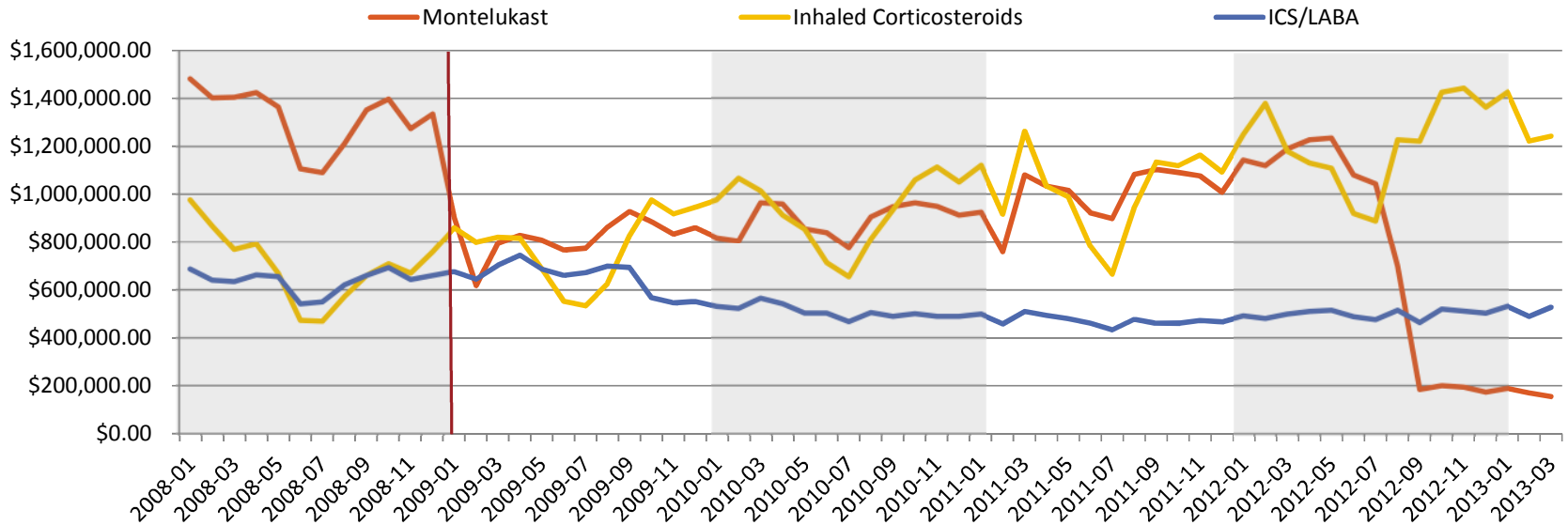
Utilization by Total Claims per Month of Singulair® vs. Asthma Daily Controller Medications



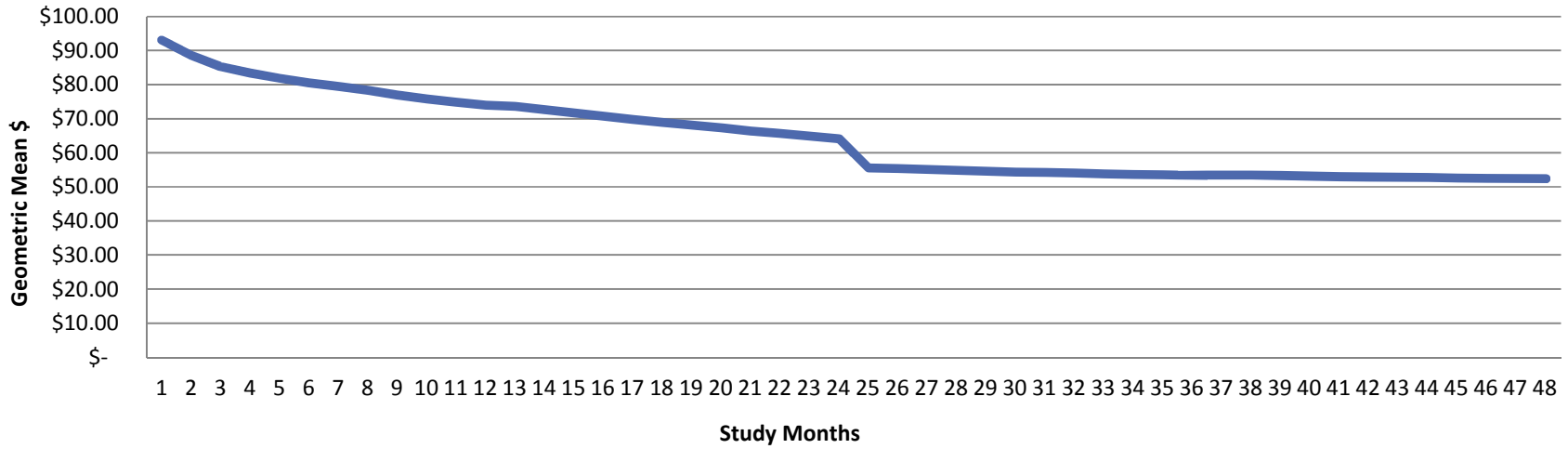
Utilization by Total Cost per Month of Singulair® vs. Allergic Rhinitis Medications



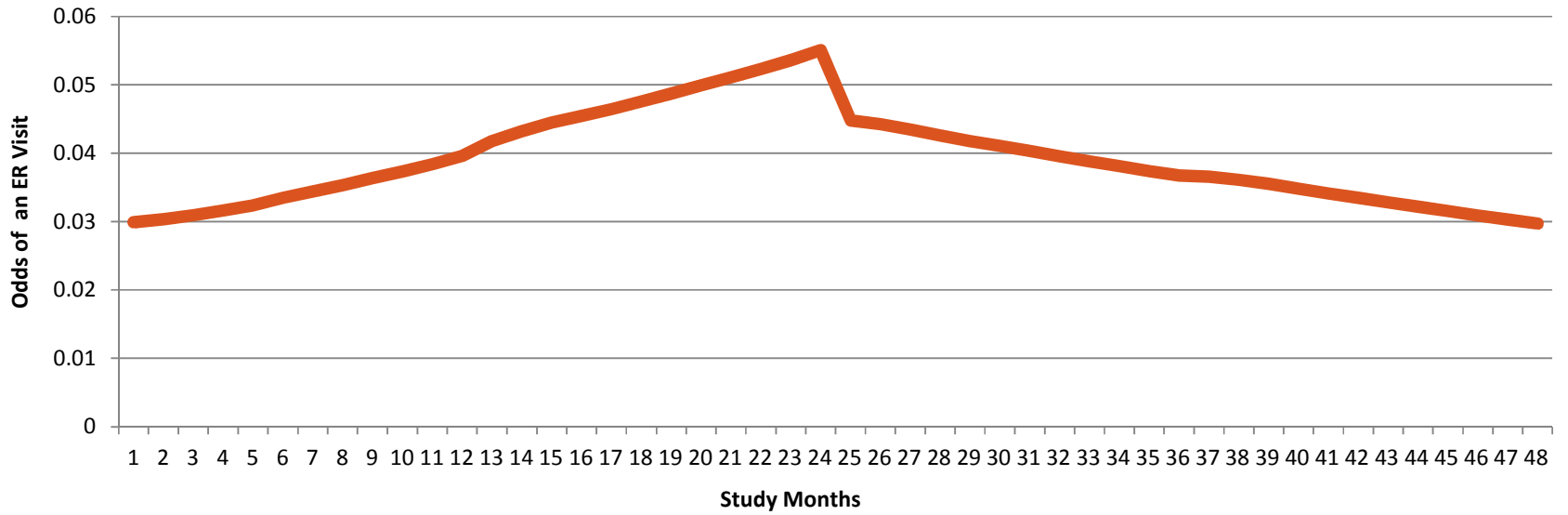
Utilization by Total Cost per Month of Singulair® vs. Asthma Daily Controller Medications



Disease Related (Allergies and Asthma) Healthcare Costs Before and After Singulair PA*



Probability of Disease Related ER Visit Before and After Singulair PA*



*Research results used with permission from Dr. Shellie Keast.

Appendix I

Calendar Year 2012 Annual Review of Horizant® and Gralise™ (Gabapentin Extended-Release)

Oklahoma Health Care Authority
June 2013

Prior Authorization of Horizant® and Gralise™

Horizant® Prior Authorization Criteria:

1. Restless Legs Syndrome
    a. Must be 18 years or older.
    b. Must provide documented treatment attempts at recommended dose with at least two of the following that did not yield adequate relief:
        i. carbidopo/levodopa
        ii. pramipexole
        iii. ropinirole
    c. Reason why immediate release gabapentin cannot be used.
2. Postherpetic Neuralgia
    a. Provide documented treatment attempts at recommended dosing or contraindication to at least one agent from two of the following drug classes:
        i. Tricyclic antidepressants
        ii. Anticonvulsants
        iii. Topical or Oral Analgesics
    b. Reason why immediate release gabapentin cannot be used.

Gralise™ Prior Authorization 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.

Utilization of Horizant® and Gralise™

There has been no use of Horizant® during calendar years 2011 and 2012.

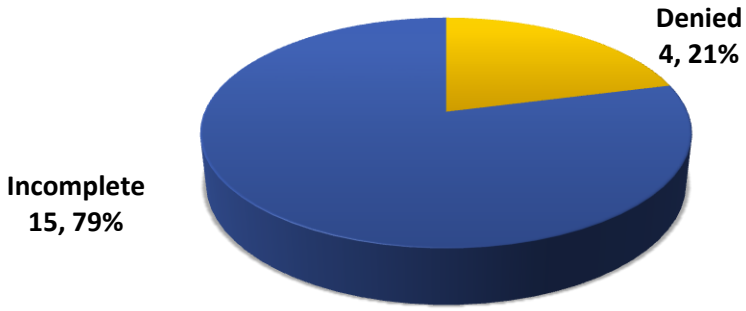
The following is the utilization data for Gralise™ during calendar year 2012:

CLAIMS	UNITS	DAYS	MEMBERS	COST	UNITS/DAY	COST/ DAY
2	180	60	1	$428.72	3	$7.15

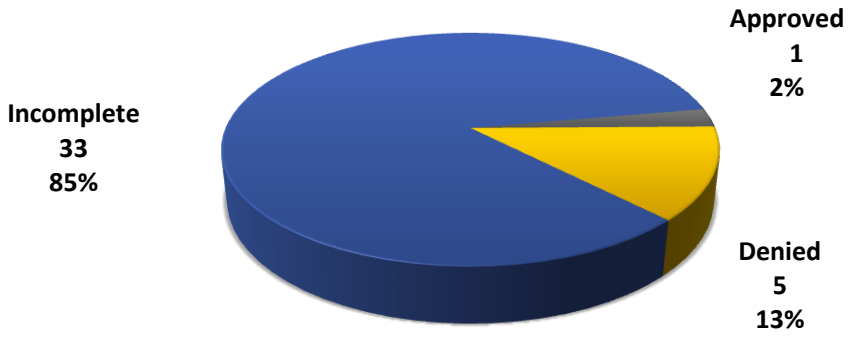
*no use of Gralise™ during CY 2011

Status of Petitions for Extended-Release Gabapentin Products

Nineteen petitions were submitted for consideration of Horizant®. The following chart shows the status of the submitted petitions:



Thirty-nine petitions were submitted for consideration of Gralise™. The following chart shows the status of the submitted petitions:



Market News and Updates

Anticipated Patent Expirations:

- Gralise™ - September 2016
- Horizant® - November 2022

Recommendations

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

Appendix J

FDA & DEA Updates (additional information can be found at http://www.fda.gov/Drugs/default.htm)

FDA NEWS RELEASE

For Immediate Release: May 29, 2013
FDA approves two drugs, companion diagnostic test for advanced skin cancer

The U.S. Food and Drug Administration today approved two new drugs, Tafinlar (dabrafenib) and Mekinist (trametinib), for patients with advanced (metastatic) or unresectable (cannot be removed by surgery) melanoma, the most dangerous type of skin cancer.

Melanoma is the leading cause of death from skin disease. The National Cancer Institute estimates 76,690 Americans will be diagnosed with melanoma and 9,480 will die from the disease in 2013.

Tafinlar, a BRAF inhibitor, is approved to treat patients with melanoma whose tumors express the BRAF V600E gene mutation. Mekinist, a MEK inhibitor, is approved to treat patients whose tumors express the BRAF V600E or V600K gene mutations. Approximately half of melanomas arising in the skin have a BRAF gene mutation. Tafinlar and Mekinist are being approved as single agents, not as a combination treatment.

The FDA approved Tafinlar and Mekinist with a genetic test called the THxID BRAF test, a companion diagnostic that will help determine if a patient's melanoma cells have the V600E or V600K mutation in the BRAF gene.

Zelboraf (vemurafenib) and Yervoy (ipilimumab) were approved in 2011 for the treatment of metastatic or unresectable melanoma.

The FDA's approval of the THxID BRAF test is based on data from clinical studies that support the Tafinlar and Mekinist approvals. Samples of patients' melanoma tissue were collected to test for the mutation.

Tafinlar was studied in 250 patients with BRAF V600E gene mutation-positive metastatic or unresectable melanoma. Patients were randomly assigned to receive Tafinlar or the chemotherapy drug dacarbazine. Patients who took Tafinlar had a delay in tumor growth that was 2.4 months later than those receiving dacarbazine.

The most serious side effects reported in patients receiving Tafinlar included an increased risk of skin cancer (cutaneous squamous cell carcinoma), fevers that may be complicated by hypotension (low blood pressure), severe rigors (shaking chills), dehydration, kidney failure and increased blood sugar levels requiring changes in diabetes medication or the need to start medicines to control diabetes.

The most common side effects reported in patients receiving Tafinlar included thickening of the skin (hyperkeratosis), headache, fever, joint pain, non-cancerous skin tumors, hair loss and hand-foot syndrome.

Mekinist was studied in 322 patients with metastatic or unresectable melanoma with the BRAF V600E or V600K gene mutation. Patients were randomly assigned to receive either Mekinist or chemotherapy. Patients receiving Mekinist had a delay in tumor growth that was 3.3 months later than those on chemotherapy. Patients who previously used Tafinlar or other inhibitors of BRAF did not appear to benefit from Mekinist.

The most serious side effects reported in patients receiving Mekinist included heart failure, lung inflammation, skin infections and loss of vision. Common side effects included rash, diarrhea, tissue swelling (peripheral edema) and skin breakouts that resemble acne.

Women of child bearing years should be advised that Tafinlar and Mekinist carry the potential to cause fetal harm. Men and women should also be advised that Tafinlar and Mekinist carry the potential to cause infertility.

Tafinlar and Mekinist are marketed by GlaxoSmithKline, based in Research Triangle Park, N.C. The THxID BRAF Kit is manufactured by bioMérieux of Grenoble, France. Yervoy is marketed by New York City-based Bristol-Myers Squibb, and Zelboraf is marketed by South San Francisco-based Genentech, a member of the Roche Group.

FDA NEWS RELEASE

For Immediate Release: May 29, 2013

FDA announces import of injectable nutrition drugs

Action addresses shortages of drugs needed to treat premature infants, patients unable to eat or drink by mouth

The U.S. Food and Drug Administration announced today that injectable drugs used in total parenteral nutrition (TPN) in critical shortage will be imported into the United States and available to patients this week. TPN is an intravenous food solution containing several drugs that have been in short supply, including trace elements, potassium phosphate, and sodium phosphate. Hospitals nationwide rely on TPN, which is primarily used to treat premature infants who are unable to eat or drink by mouth or who are experiencing other deficiencies. Cancer patients and those who have had gastrointestinal surgeries who are also unable to eat or drink by mouth have been affected by these shortages.

The FDA is exercising regulatory discretion for Fresenius Kabi USA, LLC, based in Lake Zurich, Ill., to import trace elements and phosphate injection from its Norway plant so the drugs can reach Americans in need.

The shortages are largely the result of a decision by American Regent/Luitpold, a large manufacturer of TPN products, to temporarily shut down at the end of 2012. The FDA worked with American Regent in an effort to avoid a shutdown. The company, however, ultimately decided that it had to cease operations temporarily in order to address quality issues that included particulate matter in its injectable products. The FDA continues to work with the company to prioritize the most critical drugs in shortage as it restarts production, and on the quality issues, to protect patient health.

Upon learning of American Regent's decision to temporarily shut down, the FDA looked for ways to increase supply and ultimately sought foreign companies willing and able to help the United States resolve these shortages. When the FDA looks for a foreign source to bolster supply in the U.S., the agency evaluates the foreign drug to ensure that it is of adequate quality and does not pose undue risks for U.S. patients.

The FDA's exercise of enforcement discretion for these TPN components is temporary, and applied to address this critical shortage. While the FDA cannot force a manufacturer to make a product, the agency will continue to provide expedited regulatory review and advice to manufacturers of TPN components and other drugs most in need.

Other manufacturers of TPN components, including Hospira, Inc. of Lake Forest, Ill., are also working to increase supplies of these critical drugs.

Since 2010, the FDA has used its regulatory discretion for the importation of 14 drugs. With the addition of these injectable nutrition drugs, the total will be at 17.

FDA NEWS RELEASE

For Immediate Release: May 15, 2013

FDA approves Simponi to treat ulcerative colitis

The U.S. Food and Drug Administration today approved a new use for Simponi (golimumab) injection to treat adults with moderate to severe ulcerative colitis.

Simponi works by blocking tumor necrosis factor (TNF), which plays an important role in causing abnormal inflammatory and immune responses. Previously approved to treat rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis (arthritis affecting the joints in the spine and the pelvis), Simponi is now approved to treat adults with moderate to severe ulcerative colitis that is resistant (refractory) to prior treatment or requires continuous steroid therapy.

Ulcerative colitis is a chronic disease that affects about 620,000 Americans. It causes inflammation and ulcers

in the inner lining of the large intestine and is one of two main forms of chronic inflammatory bowel disease. The inflammation can lead to abdominal discomfort, gastrointestinal bleeding, production of pus and diarrhea.
The safety and effectiveness of Simponi for ulcerative colitis were established in two clinical studies. Evaluations of patients included measures of stool frequency, rectal bleeding, endoscopic findings and a physician's overall assessment.
In the first study, 513 patients with moderate to severe ulcerative colitis who could not tolerate or failed to respond to other therapies were randomly assigned to receive Simponi or a placebo. Results showed that a greater proportion of Simponi-treated patients achieved clinical response, clinical remission and, as seen during endoscopy, had improved appearance of the colon after six weeks compared with the placebo group.
In the second study, 310 patients with moderate to severe ulcerative colitis who were responders to Simponi were randomly assigned to receive Simponi or placebo. A greater proportion of Simponi-treated patients maintained clinical response through week 54 and had clinical remission at both weeks 30 and 54.
The most common side effects in patients treated with Simponi are upper respiratory infection and redness at the site of injection. Patients treated with Simponi are at increased risk of developing serious infections, invasive fungal infections, reactivation of Hepatitis B infection, lymphoma, heart failure, nervous system disorders and allergic reactions.
Simponi is marketed by Horsham, Penn.-based Janssen Biotech, Inc.

FDA NEWS RELEASE

For Immediate Release: May 14, 2013
FDA approves Nymalize– first nimodipine oral solution for use in certain brain hemorrhage patients

New oral formulation may help reduce potentially fatal medication errors
On May 10, the U.S. Food and Drug Administration approved Nymalize, a new nimodipine oral solution, to treat patients experiencing symptoms resulting from ruptured blood vessels in the brain (subarachnoid hemorrhage). Nimodipine previously was available only as a liquid-filled gel capsule.
Subarachnoid hemorrhage is serious, life threatening bleeding that occurs in the subarachnoid space – the area between the brain and the thin tissues that cover the brain. Nimodipine is a medication given in a critical care setting to treat neurologic complications from subarachnoid hemorrhage.
Over the years, the FDA has received reports of serious and sometimes fatal consequences from intravenous (IV) injection of the liquid contents of oral nimodipine capsules. IV administration of nimodipine meant for oral use can result in death, cardiac arrest, severe decreases in blood pressure and other heart-related complications. In August 2010, the agency reminded health care1 professionals about the risks of IV administration of nimodipine from oral capsules and in 2006 a Boxed Warning was added to the drug to warn against such use.
Based on the potential of the oral formulation, Nymalize, to decrease or eliminate medication errors, the application received fast track designation and priority review2. Fast track and priority review are two programs the FDA uses to make drugs rapidly available.
The approval of Nymalize is based on clinical studies evaluating the use of nimodipine oral capsules in patients with subarachnoid hemorrhage. The most common adverse event observed in the studies was decreased blood pressure. A patient's blood pressure should be carefully monitored during treatment.
Nymalize is made by Atlanta-based Arbor Pharmaceuticals Inc.

Safety Announcements

FDA Drug Safety Communication: Valproate Anti-seizure Products Contraindicated for Migraine Prevention in Pregnant Women due to Decreased IQ Scores in Exposed Children

Safety Announcement

[05-06-2013] The U.S. Food and Drug Administration (FDA) is advising health care professionals and women that the anti-seizure medication valproate sodium and related products, valproic acid and divalproex sodium, are contraindicated and should not be taken by pregnant women for the prevention of migraine headaches. Based on information from a recent study, there is evidence that these medications can cause decreased IQ scores in children whose mothers took them while pregnant. Stronger warnings about use during pregnancy will be added to the drug labels, and valproate's pregnancy category for migraine use will be changed from "D" (the potential benefit of the drug in pregnant women may be acceptable despite its potential risks) to "X" (the risk of use in pregnant women clearly outweighs any possible benefit of the drug).

With regard to valproate use in pregnant women with epilepsy or bipolar disorder, valproate products should only be prescribed if other medications are not effective in treating the condition or are otherwise unacceptable. Valproate products will remain in pregnancy category D for treating epilepsy and manic episodes associated with bipolar disorder.

With regard to women of childbearing age who are not pregnant, valproate should not be taken for any condition unless the drug is essential to the management of the woman's medical condition. All non-pregnant women of childbearing age taking valproate products should use effective birth control.

Valproate products include: valproate sodium (Depacon), divalproex sodium (Depakote, Depakote CP, and Depakote ER), valproic acid (Depakene and Stavzor), and their generics.

This alert is based on the final results of the Neurodevelopmental Effects of Antiepileptic Drugs (NEAD) study showing that children exposed to valproate products while their mothers were pregnant had decreased IQs at age 6 compared to children exposed to other anti-epileptic drugs. The difference in average IQ between the children who had been exposed to valproate and the children who had been exposed to other antiepileptic drugs varied between 8 and 11 points depending on the drug to which valproate was compared.

FDA previously communicated initial findings about this risk in a June 2011 Drug Safety Communication. At that time, FDA also worked with valproate manufacturers to revise the drug labels after interim results from the NEAD study showed lower cognitive test scores at age 3 in children exposed to valproate compared to children exposed to other antiepileptic drugs.[2]

Women who are pregnant and taking a valproate medication should not stop their medication but should talk to their health care professionals immediately. Stopping valproate treatment suddenly can cause serious and life-threatening medical problems to the woman or her baby.

It is not known whether there is a specific time period during pregnancy when valproate exposure can result in negative cognitive effects. Similarly, there is no known time during pregnancy in which exposure may be considered to have less risk for decreased IQ in children. Because the women in the NEAD study were exposed to antiepileptic drugs throughout pregnancy, whether the risk for decreased IQ was related to a particular time period during pregnancy could not be assessed.

FDA is working with manufacturers to change the drug labels for valproate products with this updated risk information. FDA continues to evaluate information about the potential risks of valproate use during pregnancy and will update the public as more information becomes available.

Pregnancy Category X means that studies in animals or humans have shown positive evidence of fetal risk, and the risk of the use of the drug in pregnant women clearly outweighs any possible benefits. Category D means there is positive evidence of risk to a baby based on data from studies or other experience in humans, but the potential benefits from the use of the drug in pregnant women may be acceptable despite its potential risks.

Safety Announcements

FDA Drug Safety Communication: FDA Recommends Against Prolonged Use of Magnesium Sulfate to Stop Pre-term Labor Due to Bone Changes in Exposed Babies

Safety Announcement

[5-30-2013] The U.S. Food and Drug Administration (FDA) is advising health care professionals against using magnesium sulfate injection for more than 5-7 days to stop pre-term labor in pregnant women. This use of the drug is off-label, which means that it is not an FDA-approved use of the drug. Administration of magnesium sulfate injection to pregnant women longer than 5-7 days may lead to low calcium levels and bone problems in the developing baby or fetus, including thin bones, called osteopenia, and bone breaks, called fractures. The shortest duration of treatment that can result in harm to the baby is not known.

Magnesium sulfate is approved to prevent seizures in preeclampsia, a condition in which the pregnant woman develops high blood pressure and protein in the urine, and for control of seizures in eclampsia. Both preeclampsia and eclampsia are life-threatening complications that can occur during pregnancy. Preeclampsia can lead to eclampsia, seizures, stroke, multiple organ failure, and death of the woman and/or baby.

In light of this new safety information about low calcium levels and bone problems in the developing baby, the following information is being added to the drug label for Magnesium Sulfate Injection, USP 50%:

- A new Warning stating that continuous administration of magnesium sulfate injection beyond 5-7 days in pregnancy for the treatment of pre-term labor can cause low calcium levels and bone changes in the baby.
- A new Teratogenic Effects section conveying the potential harm to developing babies by changing the Pregnancy Category to D from A. This section also includes the concerns described under the new Warning.
    - Pregnancy Category D means there is positive evidence of human fetal risk, but the potential benefits from using the drug in pregnant women may be acceptable in certain situations despite its risks.
    - Pregnancy Category A means that adequate and well-controlled studies have failed to demonstrate a risk to the fetus in the first trimester of pregnancy, and there is no evidence of risk in later trimesters.
- A new Labor and Delivery section emphasizing that continuous administration of magnesium sulfate injection to treat pre-term labor is not approved and that the safety and efficacy of use for this indication are not established.

The manufacturers of other magnesium sulfate injection products have made similar changes to their drug labels.

Safety Announcements

Public Notification:

"Vicerex" Contains Hidden Drug Ingredient

[05-07-2013] The Food and Drug Administration (FDA) is advising consumers not to purchase or use "Vicerex," a product promoted and sold for sexual enhancement on various websites and in some retail stores.

FDA laboratory analysis confirmed that "Vicerex" contains tadalafil, the active ingredient in the FDA-approved prescription drug Cialis, used to treat Erectile Dysfunction (ED). This undeclared ingredient may interact with nitrates found in some prescription drugs, such as nitroglycerin, and may lower blood pressure to dangerous levels. Men with diabetes, high blood pressure, high cholesterol, or heart disease often take nitrates.

Consumers should stop using this product immediately and throw it away. Consumers who have experienced any negative side effects should consult a health care professional as soon as possible.

Note: This notification is to inform the public of a growing trend of dietary supplements or conventional foods with hidden drugs and chemicals. These products are typically promoted for sexual enhancement, weight loss, and body building, and are often represented as being "all natural." FDA is unable to test and identify all products marketed as dietary supplements on the market that have potentially harmful hidden ingredients. Consumers should exercise caution before purchasing any product in the above categories.

"Bullet Proof" Contains Hidden Drug Ingredient

[05-07-2013] The Food and Drug Administration (FDA) is advising consumers not to purchase or use "Bullet Proof," a product promoted and sold for sexual enhancement on various websites and in some retail stores. FDA laboratory analysis confirmed that "Bullet Proof" contains tadalafil, the active ingredient in Cialis, an FDA-approved prescription drug for Erectile Dysfunction (ED). This undeclared ingredient may interact with nitrates found in some prescription drugs, such as nitroglycerin, and may lower blood pressure to dangerous levels. Men with diabetes, high blood pressure, high cholesterol, or heart disease often take nitrates.
Consumers should stop using this product immediately and throw it away. Consumers who have experienced any negative side effects should consult a health care professional as soon as possible.

"Lightning ROD" Contains Hidden Drug Ingredient

[05-07-2013] The Food and Drug Administration (FDA) is advising consumers not to purchase or use "Lightning ROD," a product promoted and sold for sexual enhancement on various websites and in some retail stores. FDA laboratory analysis confirmed that "Lightning ROD" contains hydroxythiohomosildenafil. Hydroxythiohomosildenafil is structurally similar to sildenafil, the active ingredient in Viagra, an FDA-approved prescription drug for Erectile Dysfunction (ED). This undeclared ingredient may interact with nitrates found in some prescription drugs, such as nitroglycerin, and may lower blood pressure to dangerous levels. Men with diabetes, high blood pressure, high cholesterol, or heart disease often take nitrates.
Consumers should stop using this product immediately and throw it away. Consumers who have experienced any negative side effects should consult a health care professional as soon as possible.

Current Drug Shortages Index (as of June 5, 2013):

The information provided in this section is provided voluntarily by manufacturers.

Acetylcysteine Inhalation Solution UPDATED 6/4/2013
Acyclovir Sodium Injection (initial posting 11/13/2012)
Alfentanil Hydrochloride (Alfenta) (initial posting 1/23/2012)
Alteplase (Cathflo Activase) (initial posting 1/27/2012)
Amikacin Injection
Amino Acid Products (initial posting 2/14/2012)
Aminocaproic Acid Injection (initial posting 3/8/2013) UPDATED 6/4/2013
Aminophylline (initial posting 12/10/2012) UPDATED 6/4/2013
Ammonium Chloride Injection (initial posting 3/8/2013)
Amytal Sodium Injection (initial posting date 1/31/2013)
Argatroban Injection (initial posting date 2/11/2013)
Atracurium besylate (initial posting 2/27/2012) UPDATED 6/4/2013
Atropine Sulfate Injection UPDATED 6/4/2013
Bacteriostatic 0.9% Sodium Chloride (initial posting 9/10/2012)
Barium Sulfate for Suspension (initial posting 10/12/2012)
Bismuth Subsalicylate; Metronidazole; Tetracycline Hydrochloride (Helidac) (initial posting 3/8/2012)

Bumetanide Injection (initial posting 6/21/2012) UPDATED 6/4/2013
Bupivacaine Hydrochloride (Marcaine, Sensorcaine) Injection UPDATED 6/4/2013
Buprenorphine hydrochloride (Buprenex) Injection
Caffeine, anhydrous (125 mg/mL) and Sodium benzoate (125 mg/mL) UPDATED 6/4/2013
Caffeine and Ergotamine Tartrate Tablet (Cafergot) (initial posting 3/8/2012)
Calcium Chloride Injection (initial posting 12/11/2012) UPDATED 6/4/2013
Calcium Gluconate Injection (initial posting 1/10/2013)
Chromic Chloride Injection UPDATED 6/4/2013
Cidofovir Injection (initial posting 2/15/2013)
Citric Acid; Gluconolactone; Magnesium Carbonate Solution (Renacidin); Irrigation (initial posting 6/30/2012)
Copper Injection (Cupric Chloride) (initial posting 4/25/2013) UPDATED 6/4/2013
Cyanocobalamin Injection (initial posting 1/25/2013)
Daunorubicin Hydrochloride Solution for Injection
Denileukin diftitox (Ontak) (initial posting 9/22/2012)
Desmopressin Acetate Injection (DDAVP) (initial posting 5/7/2013)
Dexamethasone Sodium Phosphate Injection (initial posting 1/15/2013)
Dexrazoxane Injection (Zinecard)
Dextrose Injection (initial posting 5/23/2012) UPDATED 6/4/2013
Diazepam Injection UPDATED 6/4/2013
Dipyridamole Injection (initial posting 7/24/2012)
Dobutamine Hydrochloride Injection (initial posting 4/26/2013) UPDATED 6/4/2013
Doxorubicin (adriamycin) lyophilized powder (initial posting 12/2/2011)
Doxorubicin Liposomal Injection UPDATED 5/31/2013
Doxycycline Hyclate (initial posting 1/18/2013)
Edetate Calcium Disodium (Calcium Disodium Versenate) Injection (initial posting 10/12/2012)
Epinephrine Injection (initial posting 4/27/2012) UPDATED 6/5/2013
Epinephrine 1mg/mL (Preservative Free) (initial posting 6/21/2012)
Ethiodol (ETHIODIZED OIL) ampules
Etomidate (Amidate) Injection (initial posting 2/9/2012) UPDATED 6/5/2013
Fentanyl Citrate (Sublimaze) Injection UPDATED 6/5/2013
Fluphenazine Decanoate Injection 4/25/2013
Fluphenazine Hydrochloride Injection 4/29/2013
Fluticasone Propionate and Salmeterol (Advair HFA) Inhalation Aerosol (initial posting date) - 10/17/2012)
Fosphenytoin Sodium (Cerebyx) Injection (initial posting 3/30/2012)
Furosemide Injection (initial posting 6/20/2012) UPDATED 6/5/2013
Gabapentin Enacarbil (Horizant) ER Tablet (initial posting 4/16/2013)
Gallium Nitrate Injection (Ganite) (initial posting 4/4/2012)
Heparin Sodium Premixes (initial posting 7/5/2012) UPDATED 6/5/2013
Hydromorphone Hydrochloride (Dilaudid) Injection (initial posting 3/7/2012)
Hydromorphone Hydrochloride Tablets (initial posting 2/19/2013)
Ibandronate sodium (Boniva) injection (initial posting 6/6/2012)
Intravenous Fat Emulsion
Isoniazid; Rifampin (Rifamate) Capsules 3/15/2013 UPDATED 5/30/2013
Ketorolac Tromethamine Injection UPDATED 6/5/2013
Leucovorin Calcium Lyophilized Powder for Injection
Leuprolide Acetate Injection
Levothyroxine sodium (Levoxyl) Tablets (initial posting date - 3/15/2013)
Lidocaine HCl, 4% Topical Solution (initial posting date - 2/12/2013)
Lidocaine (Xylocaine) Hydrochloride Injection (initial posting date - 2/22/2012)
Liotrix (Thyrolar) Tablets
Lomustine Capsules (initial posting date - 5/9/2013)

Lorazepam (Ativan) Injection
Magnesium Sulfate Injection
Mannitol Injection (Osmitrol, Resectisol) Injection (initial posting date - 12/21/2011)
Mecasermin [rDNA origin] (Increlex) Injection (initial posting date - 4/26/2013)
Methazolamide (Glauctabs, Neptazane) Tablets
Methoxsalen (Oxsoralen) 1% topical lotion
Methyldopate HCL Injection
Methylphenidate Hydrochloride Tablets (initial posting date - 2/19/2013)
Methylphenidate Hydrochloride ER Tablets (initial posting date - 2/19/2013)
Methylin Chewable Tablets (initial posting date - 2 /19/2013)
Metoclopramide (Reglan) Injection
Midazolam HCL (Versed) Injection
Morphine Sulfate Injection
Morphine Sulfate (Astramorph PF, Duramorph, Infumorph) Injection (Preservative Free)
Multi-Vitamin Infusion (Adult and pediatric)
Nalbuphine HCl (Nubain) Injection (initial posting 5/15/2012)
Naloxone (Narcan) Injection (initial posting 2/22/2012)
Neostigmine Methylsulfate Injection (initial posting 1/14/2013)
Nitroglycerin Ointment USP, 2% (Nitro-Bid) (Initial posting 10/23/2012)
Norethindrone and Ethinyl Estradiol Tablets, USP (Ovcon 50 Tablets) (initial posting 4/16/2012)
Ondansetron (Zofran) Injection 2 mg/mL UPDATED 6/5/2013
Oseltamivir Phosphate (Tamiflu) for Oral Suspension (6mg/mL 60 mL) (Initial posting 1/10/2013)
Pancuronium Bromide Injection
Papaverine Hydrochloride Injection (initial posting 12/17/2012)
Peginterferon Alfa-2a (Pegasys) Injection-Prefilled Syringes (initial posting 3/26/2012)
Pentamidine isethionate inhalant (NebuPent) (initial posting 8/27/2012)
Pentamidine isethionate for injection (Pentam 300) (initial posting 8/27/2012)
Phosphate Injection (Glycophos) (initial posting 5/29/2013)
Pilocarpine HCL Opthalmic Gel 4% (Pilopine HS) (initial posting 6/1/2012)
Potassium Acetate Injection, USP 2 mEq/mL UPDATED 6/5/2013
Potassium Chloride Injection (initial posting 5/15/2012) UPDATED 6/5/2013
Potassium Phosphate Injection
Procainamide HCL Injection UPDATED 6/5/2013
Prochlorperazine Injection (initial posting 1/30/2012)
Promethazine Injection (initial posting 2/10/2012)
Reserpine Tablets (initial posting 4/17/2013)
Rifampin for Injection (initial posting 3/22/2013)
Secretin Synthetic Human (ChiRhoStim) Injection (ChiRhoStim) (initial posting 6/15/2012)
Selenium Injection
Sodium Acetate Injection (initial posting 1/31/2012)
Sodium benzoate and Sodium phenylacetate (Ammonul) Injection
Sodium Bicarbonate Injection (initial posting 3/20/2012)
Sodium Chloride 0.9% (5.8mL and 20mL) (initial posting 5/4/2012)
Sodium Chloride 23.4%
Sodium Phosphate Injection
Succinylcholine (Anectine, Quelicin) Injection (initial posting 8/17/2012)
Sufentanil Citrate (Sufenta) Injection
Sulfamethoxazole 80mg/trimethoprim 160mg/ml injection (SMX/TMP) Bactrim)
Technetium Tc99m Bicisate for Injection (Neurolite) (initial posting 5/4/2012)
Technetium Tc99m Sestamibi Kit for Injection (Cardiolite) (initial posting 2/14/2012)
Telavancin (Vibativ) Injection

Tetracycline Capsules
Thiotepa (Thioplex) for Injection
Ticarcillin disodium/Clavulanic Potassium Injection (Timentin) (initial posting 8/16/12)
Ticlopidine (Ticlid) Tablets
Tobramycin Solution for Injection
Trace Elements (initial posting 1/24/2013) UPDATED 6/4/2013
Tromethamine (Tham) Injection (initial posting 5/2/2012)
Verapamil Hydrochloride Injection, USP (initial posting 4/17/2013)
Vinblastine Sulfate Injection (initial posting 1/31/2012)
Vitamin A Palmitate (Aquasol A)
Vitamin K1 (Phytonadione) Injection (initial posting 2/12/2013)
Zinc Injection (initial posting 2/15/2012)