Drug Utilization Review Board

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

Wednesday
August 14, 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 – August 14, 2013**

DATE: August 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.

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

Action Item – Vote to Prior Authorize Fulyzaq™ – See Appendix C.

Action Item – Vote to Prior Authorize Vecamyl ™ – See Appendix D.

Action Item – Annual Review of ADHD Medications and 30 Day Notice to PA Quillivant XR™ – See Appendix E.

Action Item – Annual Review of Atypical Antipsychotics – See Appendix F.

30 Day Notice to Prior Authorize Tysabri® – See Appendix G.

30 Day Notice to Prior Authorize Diclegis® – See Appendix H.

Questions Regarding Annual Reviews of Synagis® – See Appendix I.

FDA and DEA Updates – See Appendix J.

Future Business

Adjournment

Oklahoma Health Care Authority
Drug Utilization Review Board
(DUR Board)
Meeting – August 14, 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. July 10, 2013 DUR Minutes – Vote
   B. July 10, 2013 DUR Recommendation Memorandum

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

4. Update on DUR / Medication Coverage Authorization Unit – See Appendix B.
   A. Medication Coverage Activity for July 2013
   B. Pharmacy Help Desk Activity for July 2013
   C. SoonerCare Atypical Rx Program Update

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

5. Action Item – Authorize Fulyzaq™ – See Appendix C.
   A. COP Recommendations

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

6. Action Item – Vote to Prior Authorize Vecamyl™ – See Appendix D.
   A. COP Recommendations

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

7. Action Item – Annual Review of ADHD Medications and 30 Day Notice to PA Quillivant XR™ – See Appendix E.
   A. Current Authorization Criteria
   B. Utilization of Stimulants
   C. Prior Authorization Review
   D. Market News and Updates
   E. Product Summary
   F. COP Recommendations
   G. Utilization Details
   H. Product Details

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

8. Action Item – Annual Review of Atypical Antipsychotics Appendix F.

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

Items to be presented by Kori Hammon, Dr. Muchmore, Chairman

9. 30 Day Notice to Prior Authorize Tysabri® – See Appendix G.

A. Summary
B. Utilization of Tysabri®
C. COP Recommendations
D. Product Details

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

10. 30 Day Notice to Prior Authorize Diclegis® – See Appendix H.

A. Summary
B. COP Recommendations
C. Product Details

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

11. Questions Regarding Annual Review of Synagis® – See Appendix I.

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

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

13. FDA and DEA Updates – See Appendix J.

14. Future Business

A. Annual Reviews
B. New Product Reviews

15. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF JULY 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, Ph.D.; Clinical Assistant Professor	x	
Bethany Holderread, Pharm. D.; Clinical Pharmacist	x	
Chris Le, Pharm.D.; Assistant 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	
Ashley Teel, Pharm.D.; Clinical Pharmacist		x
Jo'Nel Weber, Pharm.D.; Clinical Pharmacist		x
Michyla Adams, Pharm.D..; Clinical Pharmacist	x	
Graduate Students: Manish Mittal	x	
Visiting Pharmacy Student(s): Kori Hamman, Kelsey Gose	x	

OKLAHOMA HEALTH CARE AUTHORITY STAFF:	PRESENT	ABSENT
Nico Gomez, Chief Executive Officer		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	
Allison 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, Drug Rebate Manager	x	

OTHERS PRESENT:		
Crystal Henderson, Otsuka	Bridget Jones, Hyperion	Anna Super, Medimmune
Bob Gustafon, Lundbeck	Toby Thompson, Pfizer	Sam Smothers, Medimmune
Audray Rattan, Otsuka	Ron Cain, Pfizer	Laura Walker, Lundbeck
John Jackimiec, Lundbeck	Mark DeClerk, Lilly	Charlene Kaiser, Amgen
Don Kempin, Novo Nordisk	Patrick Moty, Supernus	Roger Grotzinger, BMS
Chet Steckler, Purdue	Mai Duong, Novartis	Brieana Buckley, Biogen
Deron Grothe, Teva		

PRESENT FOR PUBLIC COMMENT:	
David Tworek, MS, MBA	Lundbeck, US

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 NO 5: Speaker: David Tworek

ACTION: NONE REQUIRED

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

3A: June 12, 2013 DUR Minutes

3B: June 12, 2013 DUR Recommendation Memorandum

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

ACTION: MOTION CARRIED

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

4A: Medication Coverage Activity: June 2013

4B: Pharmacy Help Desk Activity: June 2013

4C: Retrospective Drug Evaluation: Focusing on Safety

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

Dr. Kuhls and Dr. Muchmore recommend that letters be sent to patients that are on valproate and women who are of child bearing years as well as doctors.

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: **VOTE TO PRIOR AUTHORIZE OXTELLAR XR™ AND SABRIL®**

5A: COP Recommendations

Materials included in agenda packet; presented by Dr. Holderread

Dr. Kuhls moved to approve; seconded by Ms. Varalli-Claypool

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE AUBAGIO® AND TECFIDERA™**

6A: COP Recommendations

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

Dr. Kuhls moved to approve; seconded by Dr. Bell.

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: **CALENDAR YEAR 2012 ANNUAL REVIEW OF TOPICAL CORTICOSTEROIDS**

7A: Current Authorization Criteria

7B: Utilization Review

7C: Prior Authorization Review

7D: Market News and Update

7E: COP Recommendations

7F: Utilization Details
Materials included in agenda packet; presented by Dr. Moore and Dr. Egesdal.
Dr. Bell moved to approve; seconded by Dr. Harrell.
ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: 30 DAY NOTICE TO PRIOR AUTHORIZE FULYZAQ™
8A: Introduction
8B: Product Summary
8C: COP Recommendations
8D: Product Details
Materials included in agenda packet; presented by Dr. Holderread.
Dr. Kuhls recommends *"define non-infectious diarrhea."*
ACTION: NONE REQUIRED

AGENDA ITEM NO. 9: 30 DAY NOTICE TO PRIOR AUTHORIZE VECAMYL™
9A: Product Summary
9B: COP Recommendations
9C: Product Details
Materials included in agenda packet; presented by Dr. Adams.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 10: OPIOID PRESCRIBING INITIATIVE FOR APPROPRIATE TREATMENT AND EDUCATION
10A: Survey Responses
10B: COP Recommendations
Materials included in agenda packet; presented by Dr. Le.
Dr. Kuhls states *"take a deeper look into dentist prescribers- speak to dentist and recommendations on prescribers for wisdom tooth extractions*." Dr. Kuhls recommends *"sending letters to all Medicaid prescribers."*
ACTION: NONE REQUIRED

AGENDA ITEM NO. 11: PRESENTATION OF SINGULAIR® PA IN THE SOONERCARE POPULATION
Slides Only; Presented by Dr. Keast.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 12: ANNUAL REVIEW OF ULORIC® AND COLCRYS®
12A: Current Authorization Criteria
12B: Utilization Review
12C: Prior Authorization Review
12D: Market News and Update
12E: COP Recommendations
Materials included in agenda packet
ACTION: NONE REQUIRED

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

AGENDA ITEM NO. 14: FUTURE BUSINESS
A: Annual Reviews
B: New Product Reviews
ACTION: NONE REQUIRED

AGENDA ITEM NO. 15: ADJOURNMENT
The meeting was adjourned at 7:25pm

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

Memorandum

Date: August 5, 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 August 14, 2013

Recommendation 1: Retrospective Drug Evaluation: Focusing on Safety

The DUR Board recommended sending prescribers of valproate in female members a letter detailing the drug safety communication by the FDA regarding increased risk of lower IQ scores in children born to women who took valproate during pregnancy for the prevention of migraines. The DUR Board also recommended sending educational materials to women on valproate to encourage them to speak to their healthcare providers.

Recommendation 2: Vote to Prior Authorize Oxtellar XR™ (Oxcarbazepine ER) and Sabril® (Vigabatrin)

MOTION CARRIED by unanimous approval.

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) with the following criteria:
    a. FDA approved diagnosis of refractory complex seizures in adults, OR infantile spasms in children ages 1 month to 2 years of age.
    b. Members with refractory complex seizures must have previous trials of at least three other antiepileptic medications.
    c. Members with infantile spasms must have had a previous trial with adrenocorticotropic hormone (ACTH) OR have a diagnosis of infantile spasms with tuberous sclerosis.
    d. Prescription must be written by a neurologist.
    e. Member, prescriber, and pharmacy must all register in the SHARE program and maintain enrollment throughout therapy.

Recommendation 3: Vote to Prior Authorize Aubagio® (Teriflunomide) and Tecfidera™ (Dimethyl Fumarate)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Aubagio® (teriflunomide) and Tecfidera™ (dimethyl fumarate) with the following criteria:

Aubagio® (Teriflunomide) Prior Authorization Criteria:

1. Documented diagnosis of relapsing forms of Multiple Sclerosis.
2. All of the following will be required for initiation of treatment:
    a. No concurrent use with other disease modifying therapies.
    b. Verification that female members are not pregnant and currently on a reliable contraceptive.
    c. Verification that member has no active infection(s).
    d. CBC counts and verification that levels are acceptable to the prescriber.
    e. Liver function tests and verification that levels are acceptable to the prescriber.
    f. Blood pressure measurement and verification that blood pressure is being monitored.
    g. Verification that members do not have tuberculosis, or completion of standard medical treatment for patients with tuberculosis.
3. Approval of Aubagio® will be initially for 6 months, after which time, all of the following will be required for further approval:
    a. Medication compliance.
    b. Repeat CBC counts and verification that counts are acceptable to the prescriber.

a. Repeat liver function tests and verification that levels are acceptable to the prescriber.
b. Verification that female members are not pregnant and still on reliable contraceptive.
c. Verification that blood pressure and symptoms of renal failure are being monitored.

4. Compliance will be checked every 6 months there-after for continuation of therapy.
5. Quantity limit of #30 tablets per 30 days applies.

Tecfidera™ (Dimethyl Fumarate) Prior Authorization Criteria:

1. Documented diagnosis of relapsing forms of Multiple Sclerosis.
2. All of the following will be required for initiation of treatment:
    a. No concurrent use with other disease modifying therapies
    b. Verification from the prescriber that member has no active infection(s).
    c. CBC counts and verification that levels are acceptable to the prescriber.
3. Compliance will be checked every 6 months there-after for continuation of therapy.
4. Quantity limit of #60 tablets per 30 days applies.

Recommendation 4: Calendar Year 2012 Annual Review of Topical Corticosteroids

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends moving selected products with significant price increases to Tier-2 as indicated in red on the Tier chart. Additionally, products may be moved throughout the year in response to price increases as necessary. The existing criteria will apply.

Tier 2 Approval Criteria

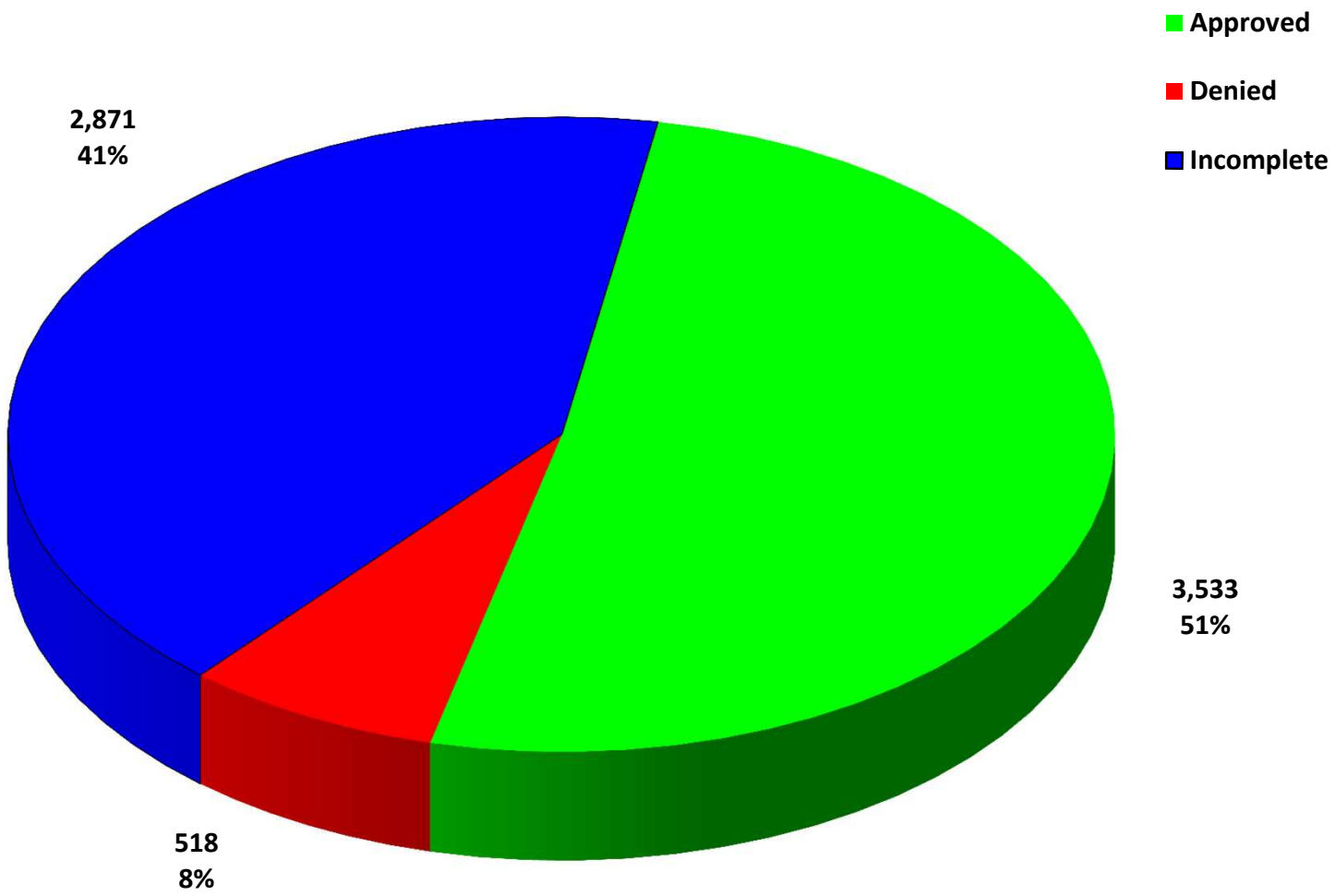
1. Documented trials of all Tier 1 topical corticosteroids of similar potency in the past 30 days that did not yield adequate relief.
    a. If Tier 1 trials are completed and do not yield adequate relief, the member must also provide a clinical reason for requesting a Tier 2 in the same potency instead of trying a higher potency.
2. When the same medication is available in Tier 1, a clinical reason must be provided for using a special dosage form of that medication in Tier 2 (foams, shampoos, kits, etc.).

Topical Corticosteroids	
Tier 1	Tier 2
Ultra high to high potency	
Augmented betamethasone dipropionate (C)	Betamethasone dipropionate (C,O)
Clobetasol propionate 0.05% (C,G,O,So)	Fluocinonide 0.05% (G,So)
Fluocinonide 0.05% (C,O)	Diflorasone diacetate 0.05% (C, ApexiCon E® C, O)
Halobetasol propionate (Ultravate® C, O)	Amcinonide (C,O,L)
	Augmented betamethasone dipropionate (Diprolene® O,G,L)
	Clobetasol propionate 0.05% (Clobex® L,Sh,Spr; Olux® F, Olux-E™ F)
	Desoximetasone 0.25% (Topicort® C,O,) 0.05% (G)
	Fluocinonide 0.1% (Vanos® C)
	Halobetasol propionate (Halonate™, F)
	Halobetasol propionate/lactic acid (Ultravate® X C)
	Halcinonide (Halog® C,O)
Med/high to medium potency	
Betamethasone dipropionate (L)	Mometasone furoate 0.1% (O)
Betamethasone valerate 0.1% (C)	Betamethasone valerate 0.1% (O,L)
Fluocinonide emollient (C)	Fluocinolone acetonide 0.025% (Synalar® C,O)
Fluticasone propionate (Cutivate® C,O)	Hydrocortisone valerate 0.2% (O)
Mometasone furoate 0.1% (Elocon® C,L)	Betamethasone dipropionate/calcipotriene (Taclonex® O, Sus, Spr)
Triamcinolone acetonide (Pediaderm™, Trianex™ C,O,L)	Betamethasone valerate 0.12% (Luxiq® Foam)
Hydrocortisone valerate 0.2% (C)	Desoximetasone 0.05% (Topicort LP ® C)
	Flurandrenolide tape (Cordran®)
	Fluticasone propionate (Cutivate® L)
	Hydrocortisone butyrate 0.1% So
	Hydrocortisone probutate (Pandel® C)
	Hydrocortisone valerate (Westcort® C,O)
	Prednicarbate (Dermatop® O,C)
	Triamcinolone acetonide (Kenalog® Spray)
Low potency	
Alclometasone dipropionate (Aclovate® C,O)	Fluocinolone acetonide 0.01% (C, So, Synalar® So)
Fluocinolone acetonide 0.01% (Synalar So, C; Derma-Smooth®; Derma-Smooth FS® oil)	Coclortolone pivalate (Cloderm® C)
Hydrocortisone acetate 2.5% (C,O,L)	Desonide 0.05% (Desonate® G, Verdeso® F, L, C, O)
Hydrocortisone/urea (U-Cort® C)	Desonide/emollient (Desowen® kit C,O)
	Fluocinolone acetonide 0.01% (Capex® Sh)
	Hydrocortisone/lidocaine (C)

C= Cream, O = Ointment, L = Lotion, G = Gel, Sh = Shampoo, So – Solution, Spr = Spray, Sus = Suspension, F = Foam

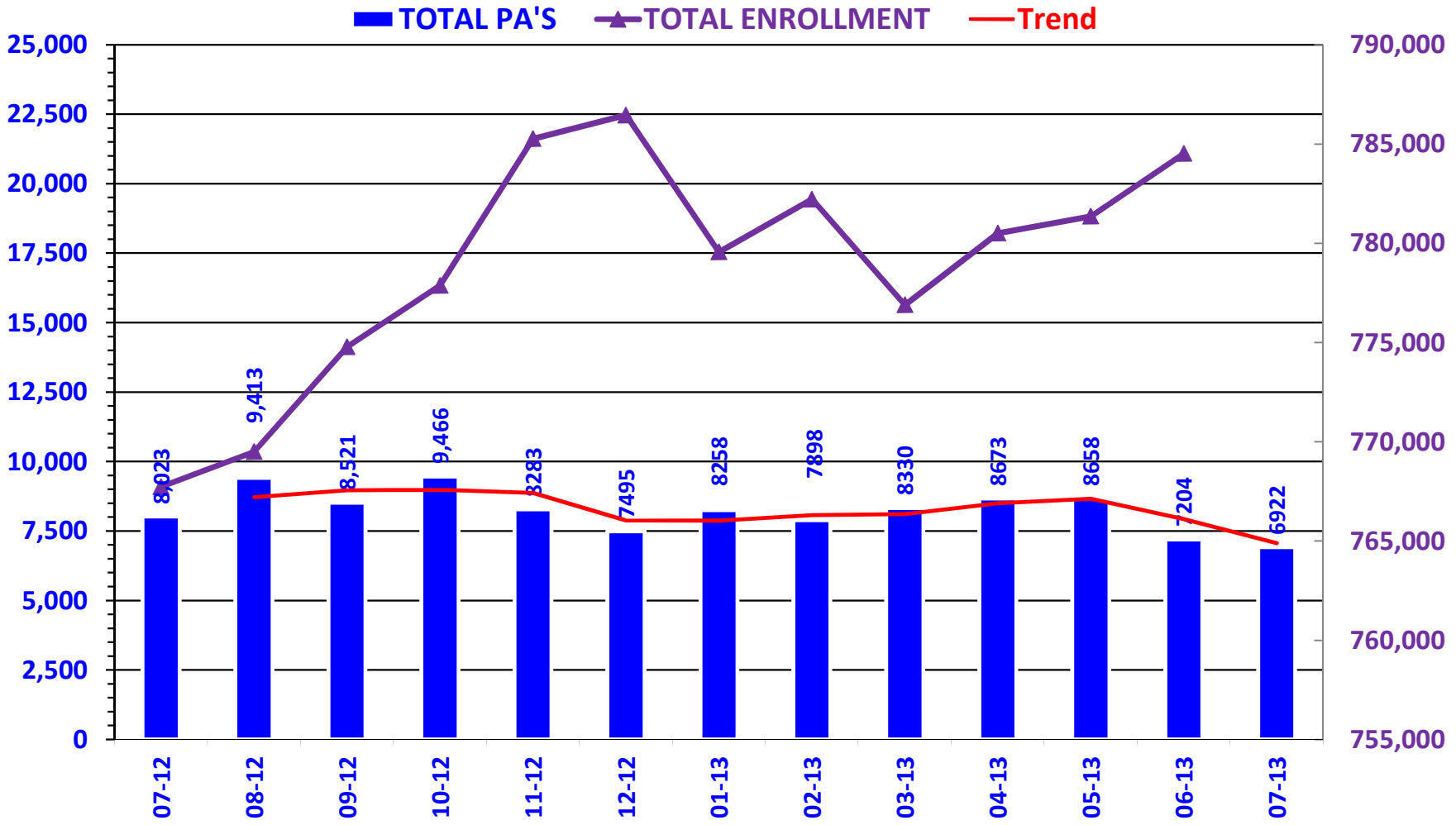
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: JULY 2013



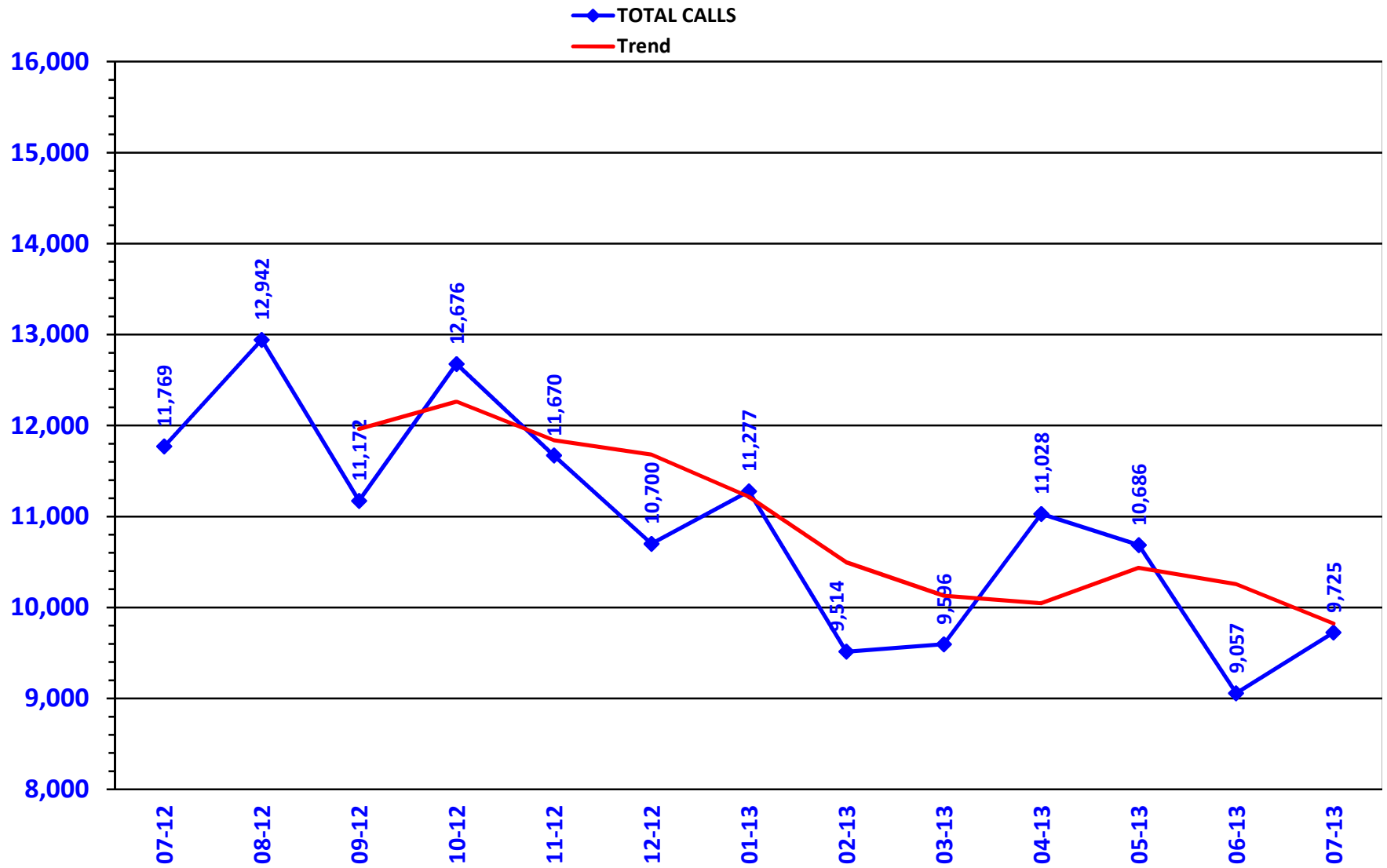
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: JULY 2012- JULY 2013



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
JULY 2012-JULY 2013



Prior Authorization Activity

7/1/2013 Through 7/31/2013

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	336	132	9	195	359
Analgesic, Narcotic	365	194	14	157	250
Angiotensin Receptor Antagonist	50	12	10	28	359
Antiasthma	294	159	11	124	292
Antibiotic	25	4	2	19	7
Anticoagulant	55	32	2	21	330
Anticonvulsant	46	23	0	23	328
Antidepressant	231	73	13	145	333
Antidiabetic	130	61	6	63	327
Antifungal	10	3	0	7	62
Antigout	10	3	0	7	298
Antihistamine	190	141	4	45	351
Antihyperlipidemic	19	11	1	7	351
Antimigraine	68	21	8	39	349
Antiplatelet	11	7	0	4	331
Antiulcers	268	66	61	141	119
Anxiolytic	96	69	7	20	226
Atypical Antipsychotics	390	254	7	129	329
Benign Prostatic Hypertrophy	10	2	3	5	357
Biologics	28	20	1	7	304
Bladder Control	48	3	8	37	299
Botox	31	27	0	4	347
Calcium Channel Blockers	12	6	1	5	172
Cardiovascular	25	14	0	11	289
Dermatological	143	35	45	63	107
Endocrine & Metabolic Drugs	159	100	6	53	208
Erythropoietin Stimulating Agents	39	25	1	13	113
Fibromyalgia	158	37	22	99	340
Gastrointestinal Agents	109	29	11	69	130
Glaucoma	13	2	0	11	357
Growth Hormones	80	56	5	19	152
HFA Rescue Inhalers	57	17	1	39	332
Insomnia	60	12	6	42	186
Multiple Sclerosis	31	20	1	10	232
Muscle Relaxant	112	37	35	40	44
Nasal Allergy	87	9	18	60	97
Neurological Agents	51	35	0	16	357
Nsaids	190	30	25	135	295
Ocular Allergy	47	10	2	35	98
Ophthalmic	34	5	5	24	77
Osteoporosis	30	9	2	19	340
Other*	124	32	16	76	114
Otic Antibiotic	59	7	3	49	23
Pediculicide	125	51	14	60	14
Prenatal Vitamins	11	0	0	11	0
Smoking Cess.	10	2	0	8	87
Statins	82	20	9	53	337
Stimulant	458	270	12	176	326
Suboxone/Subutex	129	101	4	24	80

* 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	45	0	12	33	0
Topical Corticosteroids	30	0	2	28	0
Vitamin	47	10	29	8	317
Pharmacotherapy	165	108	11	46	101
Emergency PAs	0	0	0	0	
Total	**5,446**	**2,407**	**467**	**2,572**	
Overrides					
Brand	42	28	1	13	299
Dosage Change	356	331	3	22	6
High Dose	3	3	0	0	131
Ingredient Duplication	15	9	0	6	4
Lost/Broken Rx	120	111	2	7	4
NDC vs Age	9	6	1	2	117
Nursing Home Issue	76	74	1	1	4
Other	24	21	0	3	4
Quantity vs. Days Supply	747	481	34	232	244
Stolen	9	9	0	0	6
Temporary Unlock	31	28	1	2	23
Third Brand Request	44	25	8	11	40
Overrides Total	**1,476**	**1,126**	**51**	**299**	
Total Regular PAs + Overrides	**6,922**	**3,533**	**518**	**2,871**	

Denial Reasons	
Unable to verify required trials.	2,209
Lack required information to process request.	640
Does not meet established criteria.	525

Other PA Activity	
Duplicate Requests	428
Letters	3,401
No Process	46
Changes to existing PAs	461
Partials	902

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

SoonerCare Atypical Rx Program Update

Oklahoma Health Care Authority
August 2013

Physician Response to Mailing Regarding Metabolic Monitoring

Approximately 2,700 prescribers for adults and children were listed on paid pharmacy claims for atypical antipsychotics in the 12 months prior to each report date. A total of 27,074 unduplicated members were reviewed for metabolic monitoring while receiving an atypical antipsychotic. Members receiving atypical antipsychotic medications who had a medication possession ratio (MPR) of ≥0.6 were included in the metabolic monitoring review. In general the MPR is calculated by the sum of the day supply for all fills in the period divided by the number of total days in the period. Metabolic monitoring was determined by the presence of a CPT code for metabolic panels, glucose testing, A1cs, lipid panels, cholesterol or triglycerides during the 12 month review period. Members were eligible for inclusion in the mailing if they did not have any metabolic or glucose testing during the year. Members with a diagnosis of hyperlipidemia were included if they did not have any lipid testing during the year.

There were 2,095 adult members and 3,099 pediatric members who were flagged for not having appropriate metabolic monitoring. 664 adult members and 1,344 pediatric members were included in the mailings. Packets were mailed to 200 prescribers for each mailing in February and March 2013. The packets included information regarding recommended metabolic monitoring and patient specific prescription claim information. The packets also included an optional individual member response page which allows the prescriber to provide feedback. Because some prescribers had multiple members, the maximum number of members included in a single packet was 10 in order to keep the volume manageable for the individual prescriber. We received responses for 191 adult members and 515 pediatric members.

Summary of Mailings

Adult Mailing

Letters/Physicians	#
Total Letters Mailed	200
Members	
Total Members Included	664
Total Responses Received	191

Pediatric Mailing

Letters/Physicians	#
Total Letters Mailed	200
Members	
Total Members Included	1,344
Total Responses Received	515

Member Response Summary

Q#	Adult Response	Total*
Q1	Possible billing error – Not my patient.	0
Q2	I am no longer seeing this patient.	26
Q3	Medication has been discontinued prior to date of review letter.	2
Q4	I was unaware of this situation and will consider ordering appropriate labs.	37
Q5	I am aware of this situation and will plan to order monitoring labs.	68
Q6	I am aware of this situation but do not plan to order labs.	3
Q7	Other, comments.	98
	I am placing the Patient Detail Report in the patient's medical record	26

*Members can be included in multiple categories.

Q#	Pediatric Response	Total*
Q1	Possible billing error – Not my patient.	0
Q2	I am no longer seeing this patient.	50
Q3	Medication has been discontinued prior to date of review letter.	19
Q4	I was unaware of this situation and will consider ordering appropriate labs.	75
Q5	I am aware of this situation and will plan to order monitoring labs.	280
Q6	I am aware of this situation but do not plan to order labs.	7
Q7	Other, comments.	196
	I am placing the Patient Detail Report in the patient's medical record	126

*Members can be included in multiple categories.

Summary of Additional Comments Provided

Adult Members	Total*
Labs taken prior to date of review letter	23
Labs taken while inpatient or at an IHS facility	17
Labs being followed by another prescriber	17
Patient has missed appointments/reports non-compliance/dropped out of treatment	13
Doctor no longer seeing patient/admitted to inpatient	11
Labs have been monitored appropriately	11
Will begin metabolic monitoring	9
Not my patient	6
Continuing medications from previous prescriber	3
Patient specific information provided	2
No longer my patient	1

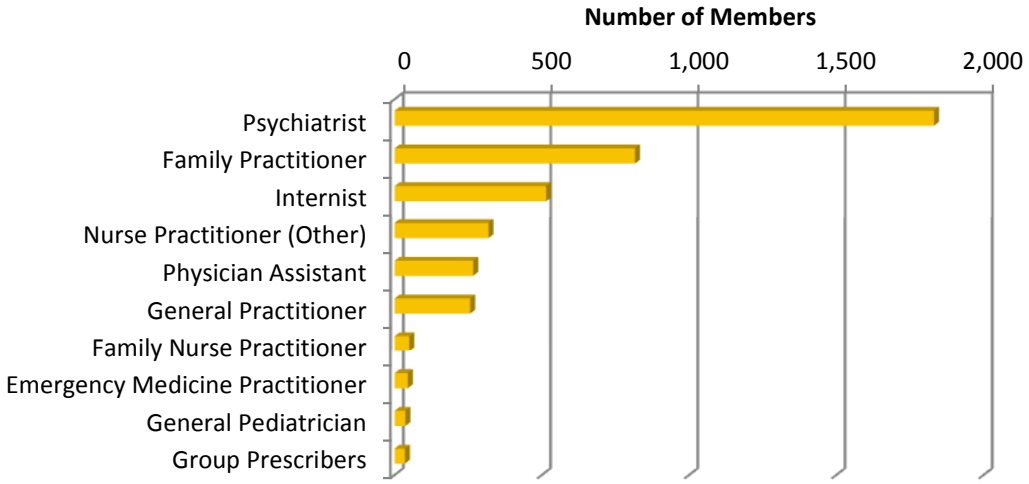
*Members can be included in multiple categories, not all responses listed.

Pediatric Members	Total*
Labs have been monitored appropriately	62
Will begin metabolic monitoring	49
Labs being followed by another prescriber	23
Patient has missed appointments/reports non-compliance/dropped out of treatment	24
Labs taken prior to date of review letter	19
The medication has been discontinued	19
Patient specific information provided	19
Doctor no longer seeing patient/admitted to inpatient	9
Member has been referred to another provider	9
Continuing medications from previous prescriber	6
Labs taken while inpatient or at an IHS facility	6

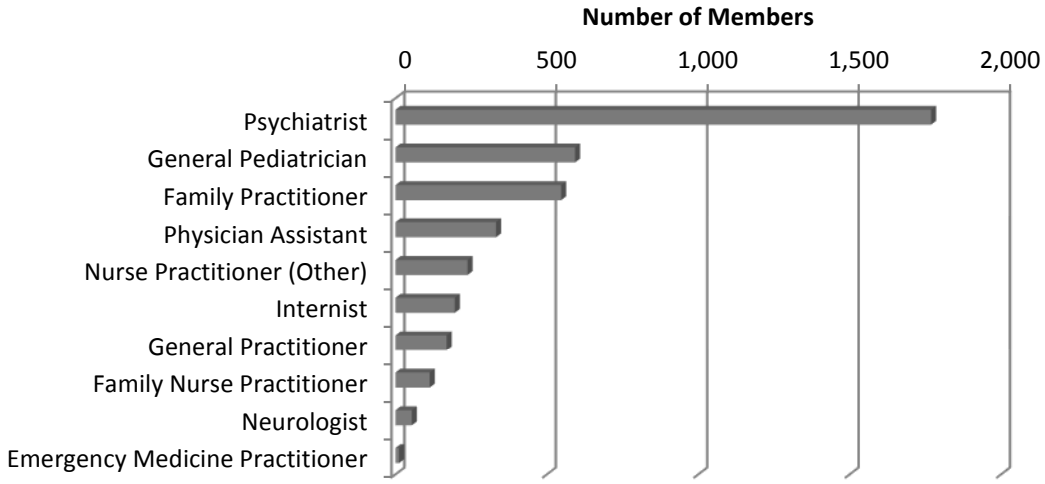
*Members can be included in multiple categories, not all responses listed

Top Ten Prescriber Specialties by Number of Members Included in Final Review

Adult Mailing

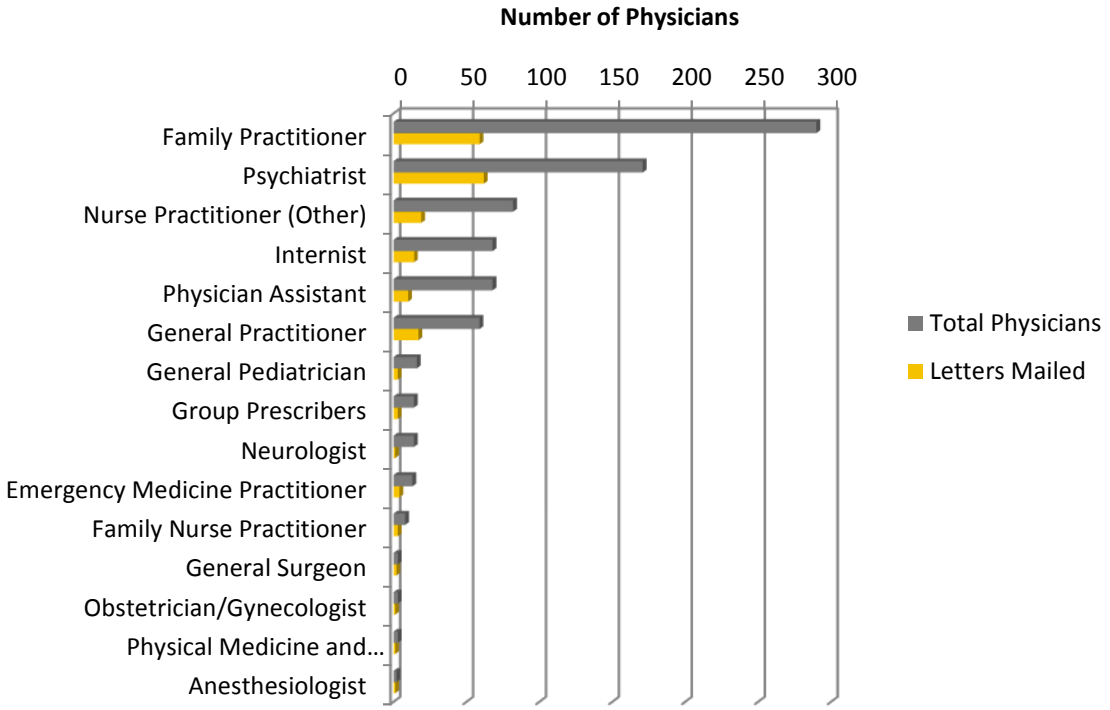


Pediatric Mailing

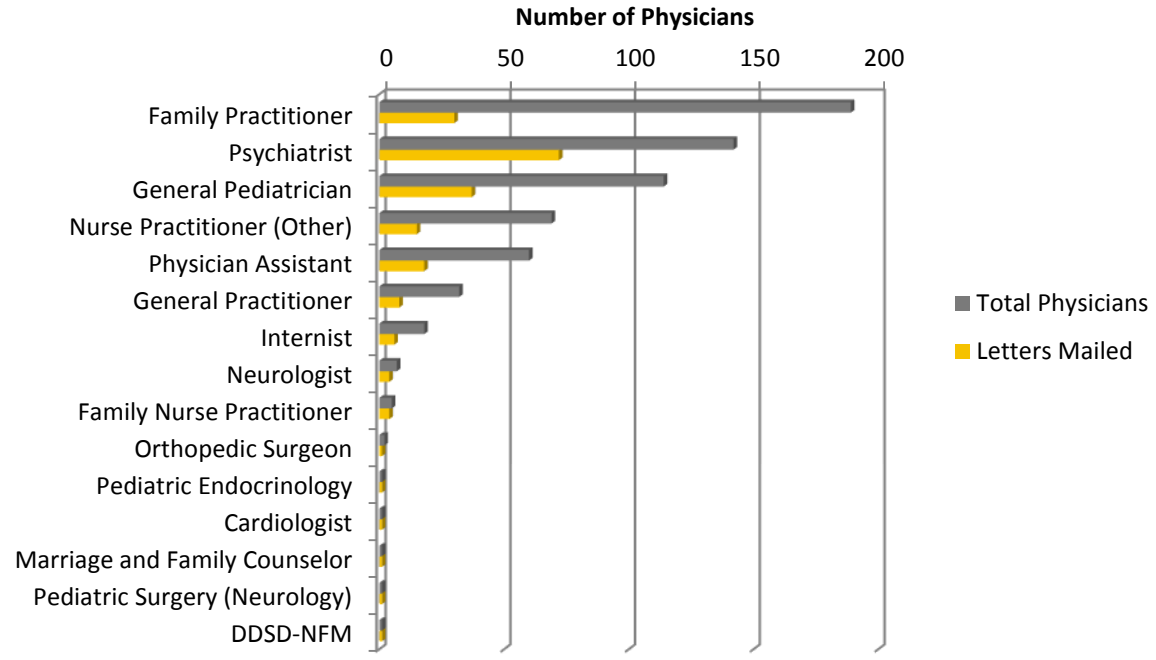


Total Physicians Versus Letters Mailed by Prescriber Specialty

Adult Mailing



Pediatric Mailing



Last Mailing- June 2013

The last mailing was processed in June and addressed dose and diagnosis for members age 5-14 years. For this project, nonstandard dosing was determined by atypical antipsychotic claims with dosing greater than or equal to 1.5 times the FDA maximum dose. Inclusion based on diagnosis was determined by the absence of a diagnosis with a strong indication for prescribing an antipsychotic medication. The review period was for one year and was prevalent in nature (not based on a new start of an atypical antipsychotic). Members were eligible for inclusion in the mailing if claims history indicates dosing greater than or equal to 1.5 times the FDA maximum. Members lacking a diagnosis with a strong indication for prescribing an antipsychotic medication in member's recent twelve month medical claims history were included. A total of 553 members where included in this mailing.

Appendix C

Vote to Prior Authorize Fulyzaq™ (Crofelemer)

Oklahoma Health Care Authority
August 2013

Recommendations

The College of Pharmacy recommends the prior authorization of Fulyzaq™ (crofelemer) with the following criteria:

1. FDA approved diagnosis of non-infectious diarrhea in adult patients with HIV/AIDS currently on anti-retroviral therapy.
2. Duration of diarrhea has been ≥4 weeks.
3. Dietary modifications have failed.
4. Prescribers must verify that infectious diarrhea has been ruled out via confirmation of all of the following:
    a. CD4 count has been measured and possible opportunistic infections have been ruled out; and
    b. Member does not have fever; and
    c. Stool studies for pathogens are negative including:
        i. Bacterial cultures
        ii. Ova and parasites
        iii. *Clostridium difficile* (*Clostridium difficile* testing should include a glutamate dehydrogenase screen and if positive followed by a confirmatory test OR nucleic acid amplification test in patients with documented diarrhea. A toxin enzyme immunoassay should not be used as a stand-alone test.)
5. If stool study results are negative and the patient has severe symptoms, particularly in the case of advanced immunodeficiency, an endoscopy with biopsy is recommended, at the doctor's discretion, to rule out inflammatory bowel disease, cancer, cytomegalovirus (CMV) infection, microsporidium, or mycobacterium avium complex (MAC).
6. A quantity limit of 60 tablets per 30 days will apply.
7. Initial approval will be for 4 weeks of therapy. An additional 6 month approval may be granted if physician documents member is responding well to treatment.

Appendix D

Vote to Prior Authorize Vecamyl™ (Mecamylamine)

Oklahoma Health Care Authority
August 2013

Recommendations[1,2,3]

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

Vecamyl™ (Mecamylamine) Prior Authorization Criteria:

1. FDA approved diagnosis of moderately severe to severe essential hypertension or uncomplicated malignant hypertension.
2. Use of at least 6 classes of medications, in the past 12 months, that did not yield adequate blood pressure control. Treatment must have included combination therapy with a diuretic, and therapy with at least a four-drug regimen. Medications can be from, but not limited to, the following classes: ACE inhibitors, ARBs, CCBs, DRIs, beta blockers, alpha blockers, alpha agonists, diuretics, etc.
3. Prescriber must verify member does not have any of the following contraindications:
    a. Coronary insufficiency
    b. Recent myocardial infarction
    c. Rising or elevated BUN, or known renal insufficiency
    d. Uremia
    e. Glaucoma
    f. Organic pyloric stenosis
    g. Currently receiving sulfonamides or antibiotics
    h. Known sensitivity to Vecamyl™ (mecamylamine)

[1] "Mecamylamine" Drug Information. Micromedex 2.0. Available online at: http://www.micromedexsolutions.com/micromedex2/librarian/ND_T/evidencexpert/ND_PR/evidencexpert/CS/2B2ECF/ND_AppProduct/evidencexpert/DUPLICATIONSHIELDSYNC/AD6DC3/ND_PG/evidencexpert/ND_B/evidencexpert/ND_P/evidencexpert/PFActionId/evidencexpert.IntermediateToDocumentLink?docId=2507&contentSetId=31&title=MECAMYLAMINE&servicesTitle=MECAMYLAMINE. Last revised: April 2013; Last accessed 6/24/2013.

[2] Vecamyl™ Package Insert. Med Library.org. Available online at: http://medlibrary.org/lib/rx/meds/vecamyl/. Last revised: February 2012; Last accessed 6/24/2013.

[3] Vecamyl™ Prescribing Information. Manchester Pharmaceuticals, Inc. Available online at: http://manchesterpharma.com/assets/files/100ct%20Vecamyl%20(Mecamylamine%20HCl%20Tablets%20USP)%202%205%20mg%20Rev12b.pdf. Last revised: September 2012; Last accessed 6/24/2013.

Appendix E

Fiscal Year 2013 Annual Review of ADHD Medications and 30 Day Notice to Prior Authorize Quillivant XR™ (Methylphenidate Extended Release) Oral Suspension

Oklahoma Health Care Authority
August 2013

Current Prior Authorization Criteria

Tier 1	Tier 2	Tier 3
Amphetamine	**Amphetamine**	**Amphetamine**
Adderall®	Amphetamine/	Desoxyn®
Adderall XR® (Brand)	Dextroamphetamine ER	Dexedrine®
Vyvanse®	(Generic Adderall XR®)	Dexedrine Spansules®
Methylphenidate	**Methylphenidate**	ProCentra™
Ritalin®	Metadate ER®	**Non-Stimulant**
Methylin®	Metadate CD®	Provigil® (modafinil)
Ritalin SR®	Ritalin LA®	Nuvigil® (armodafinil)
Concerta®	**Daytrana™**	Xyrem® (sodium oxybate)
Focalin XR®	**Non-Stimulant**	
Non-Stimulant	Kapvay® (clonidine ER)	
Strattera® (atomoxetine)		
Intuniv® (guanfacine ER)		

Blue color indicates supplemental rebate program participation.

Tier 2 Authorization Criteria:

1. FDA approved diagnosis.
2. Trials of long acting medications from both the amphetamine and methylphenidate category.
   a. Trials should have been within the last 30-60 days.
   b. Dosed up to maximum recommended dose or provide information regarding side effects at higher dose.
   c. If trials are not in member's claim history, the pharmacy profile should be submitted or detailed information regarding dates and doses should be included along with the signature from the physician.
3. Use of Kapvay® requires recent 14 day trial with immediate release clonidine and clinically significant reason why member cannot use immediate release products.

Tier 3 Authorization Criteria:

1. FDA approved diagnosis.

2. Trials with at least three lower tiered long acting medications, each from different chemical categories, unless contraindicated, that did not yield adequate response.
   a. Trials should have been within the last 60-90 days.
   b. Dosed up to maximum recommended dose or provide information regarding side effects at higher dose.
   c. If trials are not in member's claim history, the pharmacy profile should be submitted or detailed information regarding dates and doses should be included along with the signature from the physician.

Additional Criteria:

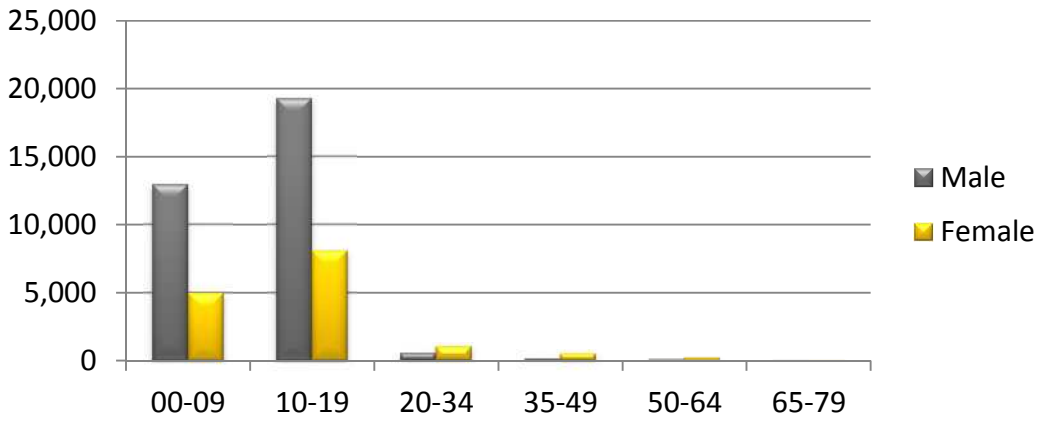
1. Dose exceeding 1.5 times the FDA maximum is not covered.
2. Prior Authorization is required for all tiers for members greater than 20 years of age and for members 0-4 years of age. All prior authorization requests for members under the age of 5 years must be reviewed by an OHCA contracted psychiatrist.
3. Use of Xyrem® requires recent trials with Tier 1 and Tier 2 stimulants from different chemical categories, and trials with both Provigil® and Nuvigil® within the past 6 months, unless contraindicated, that did not yield adequate results.
4. The diagnosis of obstructive sleep apnea requires concurrent treatment for the obstructive sleep apnea.
5. The diagnosis of shift work sleep disorder requires the member's work schedule to be included with the petition.

Utilization of ADHD Medications

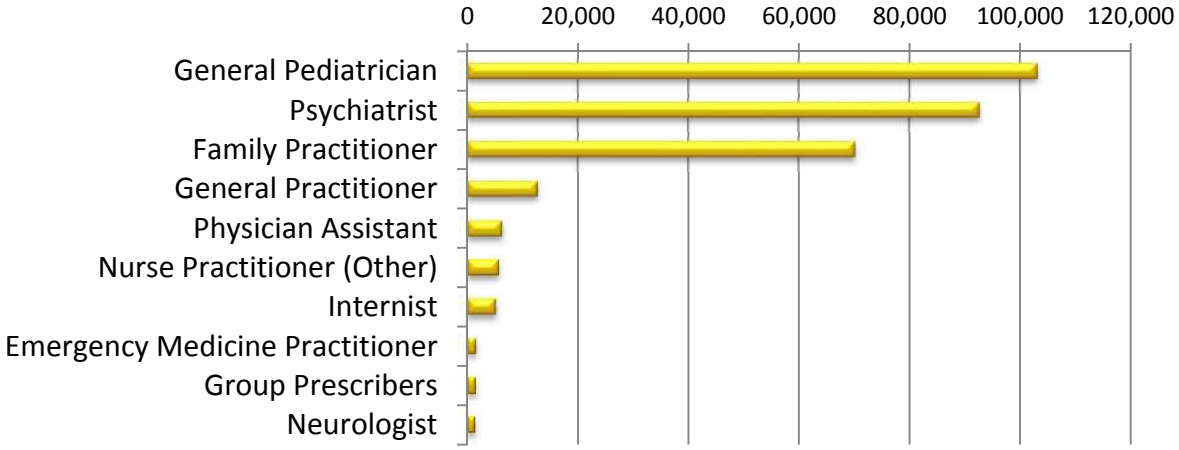
Comparison of Fiscal Years

Fiscal Year	Members	Claims	Cost	Cost/Claim	Perdiem	Units	Days
2012	42,742	265,423	$38,920,998.29	$146.64	$4.94	9,267,803	7,881,771
2013	47,793	305,037	$50,069,077.71	$164.14	$5.53	10,606,819	9,057,710
% Change	**11.82%**	**14.92%**	**28.64%**	**11.94%**	**11.94%**	**14.45%**	**14.92%**
Change	**5,051**	**39,614**	**$11,148,079.42**	**$17.50**	**$0.59**	**1,339,016**	**1,175,939**

Demographics of Members Utilizing ADHD Medications: FY 2013



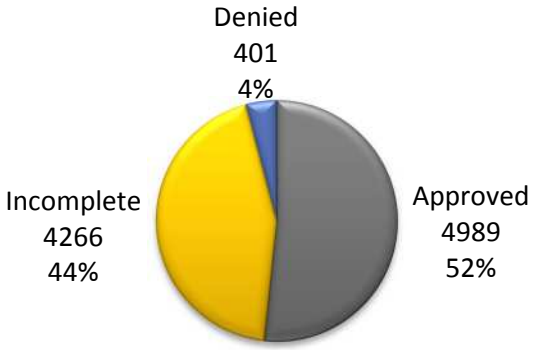
Prescribers of ADHD Medications by Number of Claims: FY 2013



Prior Authorization of Stimulants

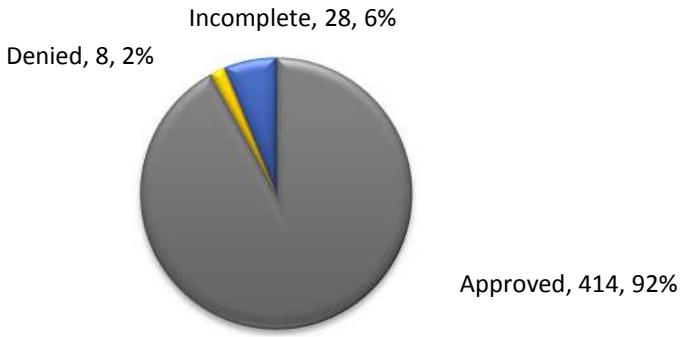
There were a total of 9,656 petitions submitted for this PBPA category during fiscal year 2013. The following chart shows the status of the submitted petitions.

Status of Petitions for ADHD Medications: FY 2013



There were a total of 450 petitions submitted for a total of 327unique members that were referred for a psychiatric consultation. Most requests were for children between the ages of 0 and 4 years old. The following shows the status of these petitions.

Status of Psychiatric Consultations: Fiscal Year 2013



Market News and Update

- Anticipated Patent Expirations:
  - Kapvay® (clonidine ER)- 10/2013
  - Nuvigil® (armodafinil)- 10/2014
  - Intuniv® (guanfacine ER)- 9/2015
  - Ritalin LA® (methylphenidate ER)- 12/2015
  - Focalin XR® (dexmethylphenidate ER)- 12/2015
  - Strattera® (atomoxetine)- 10/2018
  - Xyrem® (sodium oxybate)- 12/2019
  - Metadate CD® (methylphenidate ER)- 10/2020
  - Vyvanse® (lisdexamfetamine)- 2/2023
  - Methylin® (methylphenidate) oral solution- 10/2024

- Quillivant XR™ (methylphenidate extended release) oral suspension was approved by the FDA in September 2012. It became available on the market in January of 2013.

Quillivant XR™ (Methylphenidate ER) Summary[1,2,3]

Quillivant XR™ (methylphenidate ER) is an oral suspension approved by the FDA in September 2012. Quillivant XR™ (methylphenidate ER) oral suspension is a central nervous system (CNS) stimulant that is indicated in the treatment of Attention Deficit Hyperactivity Disorder (ADHD).

Quillivant XR™ is a powder for reconstitution for an extended-release methylphenidate 5mg/mL oral suspension. It is available in 60mL, 120mL, 150mL, and 180mL bottles for reconstitution. Quillivant XR™ should be dispensed in the original bottle and comes with a bottle adapter and oral dosing syringe. The suspension is stable for up to 4 months after reconstitution. The recommended starting dose of Quillivant XR™ for patients 6 years of age and older is 20mg (4mL) taken once daily in the morning with or without food. The dose may be titrated weekly in increments of 10mg to 20mg. Daily doses above 60mg have not been studied and are not recommended.

Quillivant XR™ is contraindicated in patients receiving concurrent treatment with a monoamine oxidase inhibitor (MAOI), with use of an MAOI within the preceding 14 days, and with known hypersensitivity to methylphenidate or other components of Quillivant XR™. Concomitant use of MAOIs and CNS stimulants may result in hypertensive crisis. Quillivant XR™ has a black box warning regarding the high potential of abuse and dependence associated with the use of CNS stimulants. The risk of abuse should be assessed prior to prescribing, and signs of abuse and dependence should be monitored while on therapy. Quillivant XR™ has similar warnings and precautions as other CNS stimulant medications, including serious cardiovascular reactions, increased blood pressure and heart rate, psychiatric adverse reactions, and long-term suppression of growth.

The efficacy of Quillivant XR™ was evaluated in a laboratory classroom study conducted in 45 pediatric patients (ages 6 to 12 years) with ADHD. The study began with an open-label dose

optimization period (4 to 6 weeks) with an initial Quillivant XR™ dose of 20mg once daily in the morning. The dose could be titrated weekly in increments of 10 or 20mg until an optimal dose or the maximum dose of 60mg/day was reached. Subjects then entered a 2-week randomized, double-blind, and crossover treatment with the individually optimized dose of Quillivant XR™ or placebo. At the end of each week, school teachers and raters evaluated the attention and behavior of the subjects in a laboratory classroom using the Swanson, Kotkin, Agler, M-Flynn, and Pelham (SKAMP) rating scale. SKAMP-Combined scores were statistically lower (improved) at all time points (0.75, 2, 4, 8, 10, 12 hours) post-dosing with Quillivant XR™ compared to placebo.

The cost per bottle (regardless of size) is $184.80. The monthly cost, based on a starting dose of 20mg per day and up to a maximum dose of 90mg per day (based on 1.5 times the FDA maximum dose), ranges from $184.80 to $1,663.20. The yearly cost ranges from $2,217.60 to $19,958.40.

Recommendations

The College of Pharmacy recommends the addition of Quillivant XR™ to Tier 3 of the ADHD Product Based Prior Authorization. The existing criteria for this category will apply. In addition, use of Quillivant XR will require a patient specific, clinically significant reason why member cannot use the oral solid formulation of extended release methylphenidate.

Tier 1	Tier 2	Tier 3
Amphetamine	**Amphetamine**	**Amphetamine**
Adderall®	Amphetamine/	Desoxyn®
Adderall XR® (Brand)	Dextroamphetamine ER	Dexedrine®
Vyvanse®	(Generic Adderall XR®)	Dexedrine Spansules®
Methylphenidate	**Methylphenidate**	ProCentra™
Ritalin®	Metadate ER®	**Methylphenidate**
Methylin®	Metadate CD®	**Quillivant XR™**
Ritalin SR®	Ritalin LA®	**Non-Stimulant**
Concerta®	**Daytrana™**	Provigil® (modafinil)
Focalin XR®	Kapvay® (clonidine ER)	Nuvigil® (armodafinil)
Non-Stimulant		Xyrem® (sodium oxybate)
Strattera® (atomoxetine)		
Intuniv® (guanfacine ER)		

Blue color indicates supplemental rebate program participation.

Tier 2 Authorization Criteria:

1. FDA approved diagnosis.
2. Trials of long acting medications from both the amphetamine and methylphenidate category.
   a. Trials should have been within the last 30-60 days.

b. Dosed up to maximum recommended dose or provide information regarding side effects at higher dose.
c. If trials are not in member's claim history, the pharmacy profile should be submitted or detailed information regarding dates and doses should be included along with the signature from the physician.

3. Use of Kapvay® requires recent 14 day trial with immediate release clonidine and clinically significant reason why member cannot use immediate release products.

Tier 3 Authorization Criteria:

1. FDA approved diagnosis.
2. Trials with at least three lower tiered long acting medications, each from different chemical categories, unless contraindicated, that did not yield adequate response.
    a. Trials should have been within the last 60-90 days.
    b. Dosed up to maximum recommended dose or provide information regarding side effects at higher dose.
    c. If trials are not in member's claim history, the pharmacy profile should be submitted or detailed information regarding dates and doses should be included along with the signature from the physician.

Additional Criteria:

1. Dose exceeding 1.5 times the FDA maximum is not covered.
2. Prior Authorization is required for all tiers for members greater than 20 years of age and for members 0-4 years of age. All prior authorization requests for members under the age of 5 years must be reviewed by an OHCA contracted psychiatrist.
3. Use of Xyrem® requires recent trials with Tier 1 and Tier 2 stimulants from different chemical categories, and trials with both Provigil® and Nuvigil® within the past 6 months, unless contraindicated, that did not yield adequate results.
4. The diagnosis of obstructive sleep apnea requires concurrent treatment for the obstructive sleep apnea.
5. The diagnosis of shift work sleep disorder requires the member's work schedule to be included with the petition.

Utilization Details of Stimulants: Fiscal Year 2013

CHEMICAL NAME	BRAND NAME	CLAIMS	MEMBERS	COST	COST/DAY	%COST
Lisdexamfetamine	Vyvanse®	38,264	8,822	$6,548,762.14	$5.75	13.08%
Amphetamine/Dextroamphetamine ER	Adderall XR®	36,810	9,705	$8,225,191.99	$7.52	16.43%
Amphetamine/Dextroamphetamine	Adderall®	29,533	7,359	$1,689,876.15	$1.92	3.38%
Dextroamphetamine ER	Dexedrine Spansules®	208	38	$49,505.19	$7.91	0.10%
Dextroamphetamine	Dexedrine®	77	15	$5,877.39	$2.57	0.01%
Methamphetamine	Desoxyn®	10	1	$5,464.15	$18.21	0.01%
Dextroamphetamine	ProCentra™	1	1	$146.34	$4.88	0.00%
AMPHETAMINE	**SUBTOTAL**	**104,903**		**$16,524,823.35**	**$5.29**	**33.00%**
Methylphenidate ER	Concerta®	68,901	16,160	$12,625,244.89	$6.16	25.22%
Dexmethylphenidate ER	Focalin XR®	34,638	9,382	$6,505,047.26	$6.33	12.99%
Methylphenidate	Ritalin®	16,774	4,530	$273,422.28	$0.55	0.55%
Dexmethylphenidate	Focalin®	11,808	2,831	$453,377.05	$1.29	0.91%
Methylphenidate ER	Metadate CD®	2,476	630	$405,797.93	$5.51	0.81%
Methylphenidate ER	Ritalin SR®	1,730	563	$55,764.59	$1.06	0.11%
Methylphenidate ER	Methylin®	1,602	501	$241,558.46	$5.22	0.48%
Methylphenidate ER	Daytrana™	1,304	302	$250,010.45	$6.41	0.50%
Methylphenidate ER	Ritalin LA®	231	76	$35,100.39	$5.09	0.07%
Methylphenidate ER	Metadate ER®	88	43	$4,372.91	$1.69	0.01%
Methylphenidate ER	Quillivant XR™	3	3	$566.46	$6.29	0.00%
METHYLPHENIDATE	**SUBTOTAL**	**139,555**		**$20,850,262.67**	**$5.02**	**41.64%**
Guanfacine ER	Intuniv®	33,799	9,136	$6,708,068.65	$6.75	13.40%
Atamoxetine	Strattera®	23,716	6,672	$5,085,792.55	$7.29	10.16%
Clonidine ER	Kapvay®	2,629	496	$568,732.48	$7.27	1.14%
Modafinil	Provigil®	341	65	$251,053.10	$25.54	0.50%
Armodafinil	Nuvigil®	145	31	$65,776.85	$14.73	0.13%
Sodium Oxybate	Xyrem®	3	1	$14,568.06	$173.43	0.03%
NON-STIMULANT	**SUBTOTAL**	**60,633**		**$12,693,991.69**	**$7.11**	**25.35%**
	TOTAL	**305,091**	**38,300***	**$50,069,077.71**	**$5.53**	**100.00%**

*Total number of unduplicated members

PRODUCT DETAILS OF QUILLIVANT XR™ (METHYLPHENIDATE EXTENDED RELEASE ORAL SUSPENSION)

INDICATIONS AND USE: Quillivant XR™ is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD).

DOSAGE FORMS: 5mg/mL methylphenidate extended-release oral suspension.

ADMINISTRATION:

- The recommended starting dose of Quillivant XR™ for patients 6 years of age and older is 20mg (4 mL) once daily in the morning.
- The dose may be titrated weekly in increments of 10mg to 20mg.
- Daily doses above 60mg have not been studied and are not recommended.
- Quillivant XR™ can be taken with or without food.
- Quillivant XR™ should be stored at room temperature, and is stable for up to 4 months after reconstitution.
- Before administering dose, vigorously shake the bottle for at least 10 seconds.
- Quillivant XR™ comes in a 60mL, 120mL, 150mL, and 180mL bottle that includes a bottle adapter and oral dosing syringe.

CONTRAINDICATIONS:

- Concurrent treatment with a Monoamine Oxidase Inhibitor (MAOI) or use of a MAOI within the preceding 14 days
- Hypersensitivity to methylphenidate or other components of Quillivant XR™

SPECIAL POPULATIONS:

- **Pregnancy:** There are no adequate or well-controlled studies with Quillivant XR™ in pregnant women. Stimulant medications, such as Quillivant XR™, cause vasoconstriction and thereby decrease placental perfusion. Adverse pregnancy outcomes, including premature delivery and low birth weight have been seen in mothers dependent on other stimulant products such as amphetamines. Methylphenidate showed some potential for teratogenicity when pregnant animals were treated during organogenesis, including an increased incidence of fetal spina bifida in rabbits and an increased incidence of fetal skeletal variations in rats. Quillivant XR™ should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. (Category C)
- **Nursing Mothers:** Quillivant XR™ is excreted in human milk. Long-term neurodevelopmental effects on infants from stimulant exposure are unknown. 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:** The safety and effectiveness of Quillivant XR™ have been established in pediatric patients ages 6 to 17 years. The long-term efficacy of methylphenidate in pediatric patients has not been established. Safety and efficacy in pediatric patients below the age of 6 years have not been established.
- **Geriatrics:** Quillivant XR™ has not been studied in patients over the age of 65 years.

- **Renal Impairment:** Quillivant XR™ has not been studied in patients with renal insufficiency.
- **Hepatic Impairment:** Quillivant XR™ has not been studied in patients with hepatic insufficiency.

WARNINGS AND PRECAUTIONS:

- **Potential for Abuse and Dependence:** Quillivant XR™ has a boxed warning regarding the high potential of CNS stimulants for abuse and dependence. The risk of abuse should be assessed prior to prescribing, and signs of abuse and dependence should be monitored while on therapy.
- **Serious Cardiovascular Reactions:** Avoid use in patients with known structural cardiac abnormalities, cardiomyopathy, serious cardiac arrhythmias, coronary artery disease, or other serious cardiac problems. Stroke and myocardial infarction have occurred in adults treated with CNS stimulants at recommended doses, and sudden death has occurred in adults taking CNS stimulants at recommended doses and in children and adolescents with structural cardiac abnormalities and other serious cardiac problems.
- **Blood Pressure and Heart Rate Increases:** Monitor all patients for hypertension and tachycardia. CNS stimulants can cause an increase in blood pressure and heart rate.
- **Psychiatric Adverse Reactions:** Patients taking Quillivant XR™ should be monitored for psychiatric adverse reactions. CNS stimulants, at recommended doses, may cause psychotic or manic symptoms in patients without a prior history of psychotic illness or mania. CNS stimulants may exacerbate symptoms of behavior disturbance and thought disorder in patients with a pre-existing psychotic disorder, or may induce a manic or mixed episode in patients with bipolar disorder.
- **Long-Term Suppression of Growth:** Growth (height and weight) should be closely monitored in pediatric patients treated with Quillivant XR™. CNS stimulants have been associated with weight loss and slowing of growth rate in pediatric patients.

ADVERSE REACTIONS:

- Adverse reactions reported in clinical trials in ≥ 2% of subjects on Quillivant XR™ and greater than placebo:
    - Affect lability (9%)
    - Excoriation (4%)
    - Insomnia (2%)
    - Tics (2%)
    - Decreased appetite (2%)
    - Vomiting (2%)
    - Motion sickness (2%)
    - Eye pain (2%)
    - Rash (2%)
- Adverse reactions reported in postmarketing experience:
    - **Blood and Lymphatic System Disorders:** pancytopenia, thrombocytopenia, thrombocytopenic purpura
    - **Cardiac Disorders:** angina pectoris, bradycardia, extrasystole, supraventricular tachycardia, ventricular extrasystole
    - **Eye Disorders:** diplopia, mydriasis, visual impairment
    - **General Disorders:** chest pain, chest discomfort, hyperpyrexia

- **Immune System Disorders:** hypersensitivity reactions such as angioedema, anaphylactic reactions, auricular swelling, bullous conditions, exfoliative conditions, urticarias, pruritus, necrotizing enterocolitis (NEC), rashes, eruptions, exanthemas NEC
- **Investigations:** increased alkaline phosphatase, increased bilirubin, increased hepatic enzymes, decreased platelet count, abnormal white blood cell count
- **Musculoskeletal, Connective Tissue, and Bone Disorders:** arthralgia, myalgia, muscle twitching
- **Nervous System Disorders:** convulsion, grand mal convulsion, dyskinesia
- **Psychiatric Disorders:** disorientation, hallucination, auditory hallucination, visual hallucination, mania
- **Urogenital System:** priapism
- **Skin and Subcutaneous Tissue Disorders:** alopecia, erythema
- **Vascular Disorders:** Raynaud's phenomenon

DRUG INTERACTIONS:

- Concomitant use of Monoamine Oxidase Inhibitors (MAOIs) and Quillivant XR™ (and use of a MAOI within the preceding 14 days) is contraindicated due to risk of hypertensive crisis. Potential outcomes include death, stroke, myocardial infarction, aortic dissection, ophthalmological complications, eclampsia, pulmonary edema, and renal failure.

PATIENT COUNSELING INFORMATION:

- Patients and their families and/or caregivers should be informed about the benefits and risks associated with treatment with Quillivant XR™ and counseled on its appropriate use. A patient Medication Guide is available for Quillivant XR™.
- Quillivant XR™ is a federally controlled substance (CII) and can be abused and lead to dependence. Store Quillivant XR™ in a safe place, preferably locked, to prevent abuse. Selling or giving away Quillivant XR™ may harm others and is against the law. Dispose of remaining, unused, or expired Quillivant XR™ through a medicine take-back program if available. Contact your pharmacist or healthcare provider for more information about proper disposal of this medication.
- There is a potential for serious cardiac risks with Quillivant XR™ use, including sudden death, heart attack, and stroke. Contact a healthcare provider immediately if you develop signs of heart problems, such as chest pain, shortness of breath, or fainting while taking Quillivant XR™.
- Quillivant XR™ can increase blood pressure and heart rate. Your healthcare provider should check your blood pressure and heart rate regularly during treatment with Quillivant XR™.
- Quillivant XR™ can cause psychotic or manic symptoms, even in patients without a prior history of psychotic symptoms or mania. Contact a healthcare provider immediately if you have new or worsening mental symptoms or problems while taking Quillivant XR™, especially seeing or hearing things that are not real, believing things that are not real, or are suspicious.
- Quillivant XR™ can cause slowing of growth and weight loss.
- Inform your healthcare provider if you become pregnant or intend to become pregnant during treatment with Quillivant XR™. Quillivant XR™ has potential adverse effects on the fetus if taken during pregnancy. Talk to your healthcare provider for more information and to discuss taking Quillivant XR™ during pregnancy.
- Inform your healthcare provider if you are breastfeeding. Quillivant XR™ is excreted in breast milk and should not be taken while breastfeeding. Nursing mothers should discontinue

Quillivant XR™ while breastfeeding or discontinue breastfeeding. Talk to your healthcare provider for more information about the potential risk to the infant of taking Quillivant XR™ while breastfeeding.

- Do not take Quillivant XR™ if you are also taking a Monoamine Oxidase Inhibitor (MAOI) or if you've taken a MAOI within the past 14 days. Talk to your pharmacist or healthcare provider for more information about this drug interaction.
- Do not take Quillivant XR™ if you are allergic to methylphenidate or any of the ingredients in Quillivant XR™. Please refer to the Medication Guide or talk to your pharmacist or healthcare provider for a complete list of inactive ingredients in Quillivant XR™.
- Quillivant XR™ should be stored at room temperature and is stable for up to 4 months after reconstitution.
- Quillivant XR™ should be taken once daily in the morning with or without food at the dose prescribed by your healthcare provider. Vigorously shake the bottle for at least 10 seconds before each dose, to ensure that the proper dose is administered.
- Remove the bottle cap and confirm that the bottle adapter has been inserted into the top of the bottle. Insert the tip of the oral dosing syringe provided into the bottle adapter and turn the bottle upside down to withdraw the prescribed amount of Quillivant XR™ into the oral dosing syringe. Remove the filled oral dosing syringe from the bottle and dispense medication directly into the mouth. Replace the bottle cap and store bottle at room temperature as directed. Wash the oral dosing syringe after each use.

[1] Quillivant XR™ Drug Information. Micromedex 2.0. Available online at: http://www.micromedexsolutions.com/micromedex2/librarian/ND_T/evidencexpert/ND_PR/evidencexpert/CS/12E0CC/ND_AppProduct/evidencexpert/DUPLICATIONSHIELDSYNC/391F66/ND_PG/evidencexpert/ND_B/evidencexpert/ND_P/evidencexpert/PFActionId/evidencexpert.IntermediateToDocumentLink?docId=372780&contentSetId=100&title=Methylphenidate+Hydrochloride&servicesTitle=Methylphenidate+Hydrochloride. Last revised: 7/16/13; Last accessed 7/19/13.

[2] Quillivant XR™ Package Insert. Med Library.org. Available online at: http://medlibrary.org/lib/rx/meds/quillivant-xr/. Last revised: 1/15/13; Last accessed 7/19/13.

[3] Quillivant XR™ Full Prescribing Information. Pfizer Inc. Available online at: http://labeling.pfizer.com/ShowLabeling.aspx?id=965. Last revised: 1/2013; Last accessed: 7/19/13.

Appendix F

Fiscal Year 2013 Annual Review of Atypical Antipsychotics

Oklahoma Health Care Authority
August 2013

Current Prior Authorization Criteria

Atypical Antipsychotics[a]		
Tier 1	**Tier 2[b]**	**Tier 3[c]**
risperidone **(Risperdal®)** quetiapine **(Seroquel®)**[d] olanzapine **(Zyprexa®)**[d] clozapine **(Clozaril®)**	aripiprazole **(Abilify®)** iloperidone **(Fanapt™)** quetiapine ER **(Seroquel XR®)** ziprasidone **(Geodon®)** asenapine **(Saphris®)** lurasidone **(Latuda®)**	paliperidone **(Invega®)** clozapine **(Fazaclo®)** olanzapine/fluoxetine **(Symbyax®)**

[a] **Mandatory Generic Plan Applies**
[b] **Suplemental rebate products**
[c] **May be rebated to Tier 2 status only**
[d] **Moved to Tier-1 when SMAC was applied.**

Approval Criteria for Tier 2 Medication:

1. A trial of one Tier 1 product, at least 14 days in duration, titrated to recommended dose, that did not yield adequate response or resulted in intolerable adverse effects.
2. Clozapine is available without prior authorization, but does not count towards a Tier 1 trial.

Approval Criteria for Tier 3 Medication:

1. A trial of one Tier 1 product (not including clozapine), at least 14 days in duration, titrated to recommended dose, that did not yield adequate response or resulted in intolerable adverse effects.
2. A trial of three Tier 2 medications, at least 14 days in duration, titrated to recommended dose, that did not yield adequate response or resulted in intolerable adverse effects.

Approval Criteria for Use as Adjunctive Treatment for Depression:

1. For aripiprazole, quetiapine extended release, or olanzapine/fluoxetine: a diagnosis of depression requires current use of an antidepressant, and previous trials with at least two other antidepressants from both categories (an SSRI and a dual acting antidepressant) that did not yield adequate response. Tier structure still applies.

Clinical Exceptions:

1. Members currently stabilized on a higher tiered medication defined by paid claim(s) for the higher tiered medication in the past 90 days will be approved.
2. Members being released from a hospital and stabilized on a higher tiered medication will be approved.
3. Approvals will be granted for members with clinical conditions for which lower tiered drugs are contraindicated.
4. Approvals will be granted for members whose current regimen includes drugs known to adversely interact with all lowered tiered drugs.

Second Opinion Process for Children 0 - 4 Years of Age

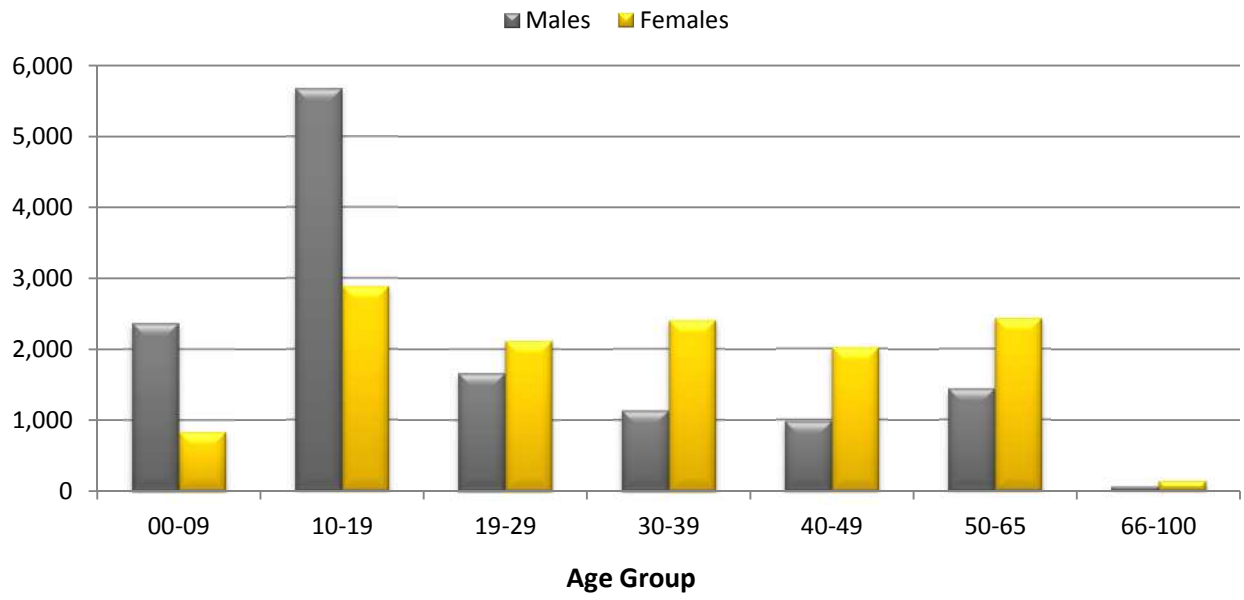
Children less than 5 years of age will require a "second opinion" prior authorization to be reviewed by an OHCA-contracted child psychiatrist.

Utilization of Atypical Antipsychotics

Trends in Utilization

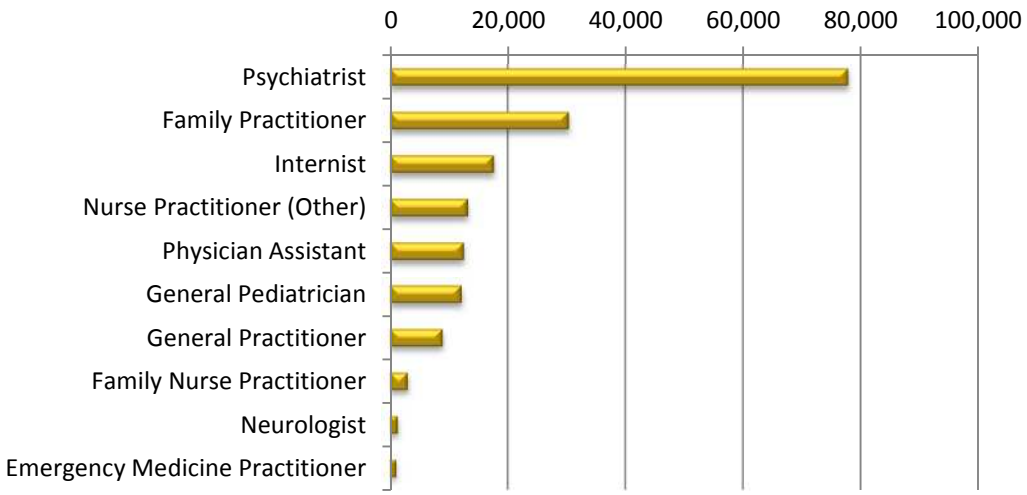
Fiscal Year	Members	Claims	Cost	Cost/Claim	Per-Diem	Units	Days
2012	25,187	177,748	$57,020,658.71	$320.79	$10.59	7,366,127	5,382,487
2013	26,133	181,755	$45,476,575.72	$250.21	$8.26	7,532,659	5,508,118
% Change	**3.80%**	**2.30%**	**-20.20%**	**-22.00%**	**-22.00%**	**2.30%**	**2.30%**
Change	**946**	**4,007**	**-$11,544,082.99**	**-$70.58**	**-$2.33**	**166,532**	**125,631**

Demographics



Age Groups	Total Members	Total Cost	Total Claims	Claims/ Member	Cost/ Member
00-09	3,196	$2,658,709.90	20,769	6.5	$831.89
10-19	8,562	$12,843,814.45	58,472	6.8	$1,500.10
19-29	3,774	$7,597,394.43	25,638	6.8	$2,013.09
30-39	3,533	$6,378,717.00	21,143	6.0	$1,805.47
40-49	2,996	$6,365,421.29	20,739	6.9	$2,124.64
50-65	3,870	$9,245,207.85	32,720	8.5	$2,388.94
66-100	199	$386,434.20	2,279	11.5	$1,941.88

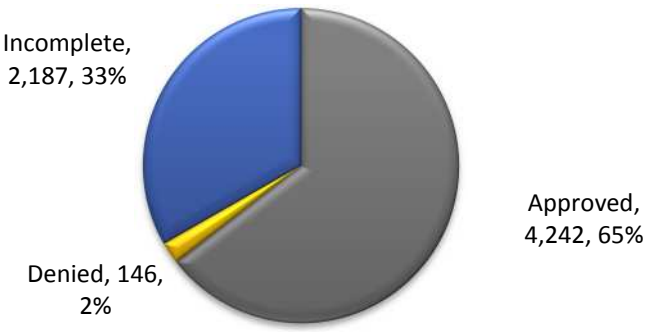
Top Prescriber Specialties by Total Claims: Fiscal Year 2013



Prior Authorization of Atypical Antipsychotics

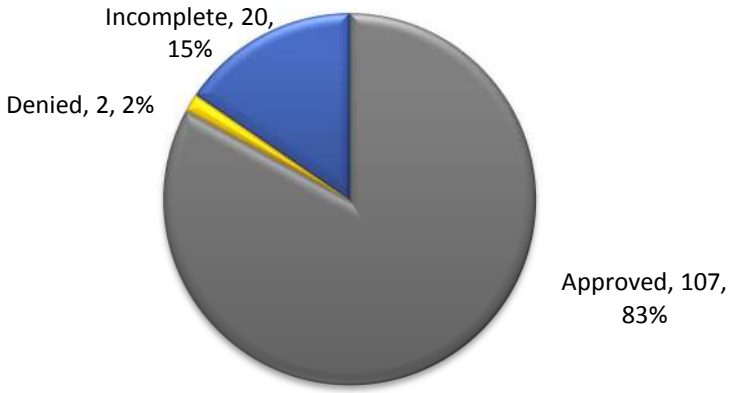
During fiscal year 2013 a total of 6,575 petitions were submitted for this category. The point-of-sale system is in place to look for claims of lower-tiered products and allow movement to higher tiers when appropriate without manual prior authorization. The following are the status of the submitted petitions:

Status of Petitions: Fiscal Year 2013



There were a total of 129 petitions submitted for a total of 110 unique members that were referred for a psychiatric consultation. Most requests were for children between the ages of 0 and 4 years old. The following shows the status of these petitions.

Status of Psychiatric Consultations: Fiscal Year 2013



Market News and Updates

Anticipated Patent Expirations:

- Geodon® (ziprasidone) – generic formulations are available; however, the state maximum allowable cost is at $3.27 per tablet, which is significantly higher than other available generics in this category, which are approximately 20¢ to 60¢ per tablet.
- Abilify® (aripiprazole) – 2014
- Invega® (paliperidone) – 2014
- Fanapt® (iloperidone) – 2016
- Seroquel XR® (quetiapine ER) – 2017
- Symbyax® (olanzapine/fluoxetine) – 2017
- Latuda® (lurasidone) – 2018
- Fazaclo® (clozapine) – 2018
- Saphris® (asenapine) – 2026

Market News:

- Sunovion Pharmaceuticals Inc. announced June 28, 2013 the FDA approval of new indications for **Latuda® (lurasidone)** as monotherapy and adjunctive therapy in adult patients with bipolar depression.[1] The maximum recommended dose for the treatment of patients with bipolar depression and schizophrenia may be as high as 120-160 mg/day. However, in the mono-therapy study, patients taking Latuda® 80 mg/day to 120 mg/day did not experience additional efficacy on average, compared to patients taking 20 mg/day - 60 mg/day.

- On June 18, 2013 the FDA issued a drug safety communication regarding the investigation of two unexplained deaths in patients who received an intramuscular injection of the antipsychotic drug **Zyprexa Relprevv® (olanzapine pamoate)**[2]. The patients died 3-4 days after receiving an appropriate dose of the drug, well after the 3-hour post-injection monitoring period required under the Zyprexa Relprevv® Risk Evaluation and Mitigation Strategy (REMS). Under the REMS, patients are required to receive the Zyprexa Relprevv® injection at a REMS-certified health care facility, to be continuously monitored at the facility for at least 3 hours following an injection, and to be accompanied home from the facility. Both patients were found to have very high olanzapine blood levels after death. The Zyprexa Relprevv® label contains warnings about the risk of post-injection delirium sedation syndrome (PDSS), a serious condition in which the drug enters the blood too fast following an intramuscular injection, causing greatly elevated blood levels with marked sedation (possibly including coma) and/or delirium.

- Otsuka Pharmaceutical Co., Ltd. and Lundbeck Pharmaceuticals announced on February 28, 2013 the FDA approval of **Abilify Maintena® (aripiprazole extended-release injectable suspension)**[3]**,** an intramuscular depot formulation indicated for the treatment of schizophrenia[4]. Abilify Maintena® is indicated to be given once monthly and is available in 300mg and 400mg strength vials of lyophilized powder for reconstitution.

- Alexza Pharmaceuticals, Inc. announced December 21, 2012 the FDA approval of **Adasuve™ (loxapine) Inhalation Powder** 10mg for the acute treatment of agitation associated with schizophrenia or bipolar I disorder in adults.[5] Adasuve™ combines Alexza's proprietary *Staccato®* delivery system with the antipsychotic drug loxapine. The *Staccato®* system is a hand-held inhaler that delivers a drug aerosol to the deep lung which results in rapid systemic delivery and absorption of the drug. Adasuve™ is restricted to inpatient administration at REMS-certified facilities[6], with equipment and staffing trained to carefully monitor for and respond to bronchopulmonary spasms that may result in respiratory distress and/or respiratory arrest. Adasuve™ dosing is limited to one dose of 10mg every 24 hours.

- February 6, 2013 the FDA approved **Versacloz™ (clozapine oral suspension)** to reduce suicidal behavior in patients with schizophrenia or schizoaffective disorder, and use in treatment-resistant schizophrenia.[7] Clozapine is currently available as an oral tablet (Clozaril®) and an orally disintegrating oral tablet (Fazaclo®). Due to the serious risk of agranulocytosis, these two formulations are currently available only through a limited distribution system that ensures monitoring of white blood cell counts (WBC) and absolute neutrophil counts (ANC) before, during, and after use of this medication. Versacloz™ will only be available through a REMS program that ensures close monitoring required for use of this medication.[8] Other black box warnings include increased risk of seizures, myocarditis, orthostatic hypotension with or without syncope that may result in collapse, respiratory or cardiac arrest. Versacloz™ will be available as 50mg/mL amber bottles containing 100mLs each.

Utilization of Long Acting Injectable Antipsychotics

Currently Available Formulations of Long Acting Injectable Atypical Antipsychotics

Medication	FDA Approved Indication(s)
Risperdal Consta® (risperidone LAI)	Tx of schizophrenia & maintenance of Bipolar I Disorder
Zyprexa Relprevv® (olanzapine LAI)	Tx of schizophrenia
Invega Sustenna® (paliperidone LAI)	Tx of schizophrenia
Abilify Maintena® (aripiprazole LAI)	Tx of schizophrenia

Medication	Initial Dose	Recommended Max Dose	Time Between Injections	Titration†
Risperidone*	25mg q 2 wks IM	50mg q 2 wks	14 days	3 weeks oral
Olanzapine*	150mg q 2wks IM	405mg q 4 wks or 300mg q 2 wks	14 to 28 days	Not listed
Paliperidone	234mg day 1, 156mg one wk later, then 117mg q month IM	234mg q 28 days	28 days	Initiation doses
Aripiprazole*	300mg-400mg q month IM	300mg-400mg q month	month	14 days oral

*Immediate release injectable formulations available
†Tolerability should be established on short acting formulation before initiation with long acting formulations.

Each injectable formulation consists of the active medication that's also found in the oral formulations, therefore similar contraindications, warnings, and precautions apply. There may be additional monitoring required with use of the injectable formulations (e.g. PDSS with olanzapine.) There are no known differences in efficacy between the long acting injectable antipsychotics, regardless of its classification as first or second generation.

Long acting formulations of antipsychotics have demonstrated efficacy in schizophrenia and bipolar disorders when compared to placebo. However, meta-analyses of randomized controlled clinical trials have generally not found long acting injectable antipsychotics to improve duration of medication persistence, reduce relapse, or re-hospitalization rates in patients with schizophrenia compared to oral antipsychotics.[9] The bulk of information regarding long acting injectable antipsychotics is from clinical trials of first generation antipsychotics. One clinical trial published in 2011 compared long acting risperidone injection with an oral antipsychotic of the doctor's choice to determine if use of long acting injectables can improve adherence to treatment and healthcare outcomes in high risk schizophrenic patients. The two year trial showed that long-acting injectable risperidone was not superior to a psychiatrist's choice of oral treatment in patients with schizophrenia and schizoaffective disorder who were hospitalized or at high risk for hospitalization, and it was associated with more local injection-site and extrapyramidal adverse effects.[10]

Long acting injectable antipsychotics are typically recommended for patients with schizophrenia who relapse due to medication noncompliance, and it may help some patients break a cycle of multiple hospitalizations due to a combination of factors such as unstable illness, chaotic social structure, and/or substance abuse.

Parenteral formulations of atypical antipsychotic medications are currently not part of the Product Based Prior Authorization Program. Pharmacy and medical claims for SoonerCare members were reviewed to evaluate the utilization trends for parenteral formulations of atypical antipsychotics during fiscal year 2013. Currently, the average cost per day of LAIs is $36 and average cost per claim is $1,069.

Pharmacy Utilization Trends of Injectable Antipsychotics

Fiscal Year	Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2011	766	4,769	$3,061,408.54	$641.94	$21.96	10,621	139,417
2012	971	6,363	$5,610,819.68	$881.79	$29.65	11,975	189,237
2013	1,109	7,411	$7,927,314.50	$1,069.67	$36.23	12,708	218,782

Pharmacy Utilization Summary: Fiscal Year 2013

CHEMICAL NAME	BRAND NAME	CLAIMS	MEMBERS	COST	CLAIMS/ MEMBER	COST/ DAY
Paliperidone ER	**INVEGA SUSTENNA® INJ**	4,464	697	$6,461,981.56	6.4	$50.01
Risperidone ER	**RISPERDAL CONSTA® INJ**	1,613	198	$1,263,467.30	8.15	$32.07
Haloperidol dec	**HALDOL INJ**	1,080	217	$138,730.68	4.98	$3.38
Fluphenazine dec	**FLUPHENAZINE INJ**	192	53	$23,574.62	3.62	$2.83
Aripiprazole ER	**ABILIFY MAINTENA™ INJ**	26	15	$37,541.60	1.73	$49.53
Ziprasidone IR	**GEODON® INJ**	24	10	$1,401.27	2.4	$28.60
Aripiprazole IR	**ABILIFY® INJ**	7	1	$207.91	7	$20.79
Olanzapine IR	**ZYPREXA® INJ IR**	5	4	$409.56	1.25	$58.51
	TOTAL	**7,411**	**1,109***	**$7,927,314.50**	**6.68**	**$36.23**

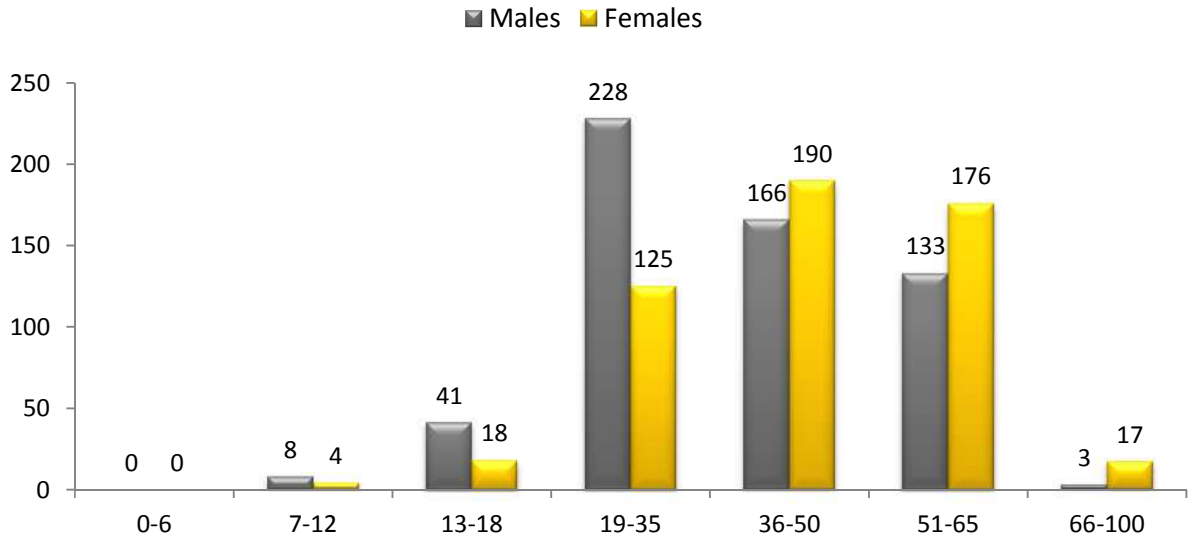
*Total number of unduplicated members

Medical Utilization Summary: Fiscal Year 2013

Claims	HCPCS Code Description	Brand Name Description
312	J1631 - HALOPERIDOL DECANOATE INJ	**HALOPERIDOL LACTATE**
183	J3486 - ZIPRASIDONE MESYLATE	**GEODON®**
162	J2680 - FLUPHENAZINE DECANOATE 25 MG	**FLUPHENAZINE DECANOATE**
14	J2358 - OLANZAPINE LONG-ACTING INJ	**ZYPREXA RELPREVV®**
5	J2794 - RISPERIDONE, LONG ACTING	**RISPERDAL CONSTA®**
2	J0400 - ARIPIPRAZOLE IR INJECTION	**ABILIFY®**
1	J2426 - PALIPERIDONE PALMITATE INJ	**INVEGA SUSTENNA®**

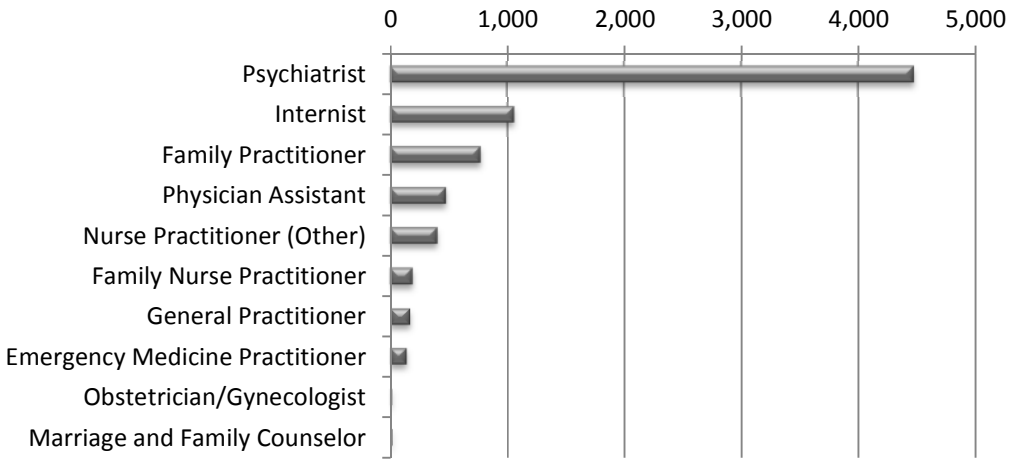
Cost data not available due to variable and bundled payment methods.

Demographics of Injectable Antipsychotics*: Fiscal Year 2013



*Based on Pharmacy Utilization Data

Top Prescribers of Injectable Antipsychotics*: Fiscal Year 2013



*Based on Pharmacy Utilization Data

Anticipated Patent Expirations of Injectable Atypical Antipsychotics:

- Risperdal Consta® (long acting risperidone) – as early as 2014 up to 2020
- Invega Sustenna® (long acting paliperidone) – as early as 2013 up to 2015
- Zyprexa Revprevv® (long acting olanzapine) – 2018
- Geodon® (immediate release ziprasidone) – 2017
- Abilify® (immediate release aripiprazole) – as early as 2014 up to 2025

Recommendations

The College of Pharmacy recommends the addition of the outpatient administered long acting injectable atypical antipsychotics to the Atypical Antipsychotics Product Based Prior Authorization program. The following tier structure and criteria will apply:

Long Acting Injectable Atypical Antipsychotics	
Tier 1	**Tier 2**
Lowest Net Cost Medication	aripiprazole **(Abilify Maintena®)** paliperidone **(Invega Sustenna®)** risperidone (**Risperdal Consta®)**

Outpatient administered long acting injectable atypical antipsychotics will require a prior authorization for all members under the age of 18.

Pediatric Prior Authorization Criteria:

1. FDA-approved diagnosis; and
2. Patient specific clinically significant reason why a long acting injectable antipsychotic is necessary; and
3. Verification from the prescriber that tolerance has been established with short acting formulation.
4. Members currently stabilized on long acting injectable antipsychotics in the previous 30 days will be grandfathered.

Adult Prior Authorization Criteria:

1. FDA-approved diagnosis; and
2. A trial of one Tier 1 product, at least 28 days in duration, titrated to recommended dose, that did not yield adequate response or resulted in intolerable adverse effects.
3. Verification from the prescriber that tolerance has been established with short acting formulation.
4. Members currently stabilized on long acting injectable antipsychotics in the previous 30 days will be grandfathered.

Utilization Details: Fiscal Year 2013

CHEMICAL NAME	BRAND NAME	CLAIMS	MEMBERS	COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ DAY	% COST
Risperidone	RISPERIDONE TAB 1MG	23,984	6,174	$312,113.04	1.46	3.88	$0.43	0.69%
Risperidone	RISPERIDONE TAB 0.5MG	17,805	4,817	$225,370.63	1.5	3.7	$0.42	0.50%
Risperidone	RISPERIDONE TAB 2MG	13,130	3,433	$177,548.10	1.38	3.82	$0.43	0.39%
Risperidone	RISPERIDONE TAB 0.25MG	7,287	2,038	$86,894.07	1.59	3.58	$0.40	0.19%
Risperidone	RISPERIDONE TAB 3MG	6,557	1,415	$96,468.45	1.4	4.63	$0.47	0.21%
Risperidone	RISPERIDONE TAB 4MG	3,491	718	$57,951.85	1.38	4.86	$0.52	0.13%
Risperidone	RISPERIDONE SOL 1MG/ML	1,048	196	$53,769.78	2.04	5.35	$1.60	0.12%
Risperidone	RISPERDAL INJ 50MG	909	115	$890,703.61	0.07	7.9	$38.87	1.96%
Risperidone	RISPERDAL INJ 25MG	376	69	$173,742.66	0.07	5.45	$19.41	0.38%
Risperidone	RISPERIDONE TAB 1MG ODT	344	98	$34,093.60	1.57	3.51	$3.34	0.07%
Risperidone	RISPERIDONE TAB 0.5MG OD	318	93	$20,920.67	1.45	3.42	$2.22	0.05%
Risperidone	RISPERDAL INJ 37.5MG	303	42	$193,018.24	0.07	7.21	$27.88	0.42%
Risperidone	RISPERIDONE TAB 2MG ODT	232	76	$23,939.47	1.36	3.05	$3.40	0.05%
Risperidone	RISPERIDONE TAB 0.25 ODT	67	20	$11,004.34	1.61	3.35	$5.56	0.02%
Risperidone	RISPERIDONE TAB 3MG ODT	67	24	$24,601.14	1.57	2.79	$10.97	0.05%
Risperidone	RISPERIDONE TAB 4MG ODT	65	13	$28,064.51	1.43	5	$15.17	0.06%
Risperidone	RISPERDAL TAB 3MG	41	6	$33,068.14	2.03	6.83	$25.57	0.07%
Risperidone	RISPERDAL TAB 1MG	26	4	$5,065.29	1.58	6.5	$6.49	0.01%
Risperidone	RISPERDAL INJ 12.5MG	25	5	$6,002.79	0.07	5	$9.91	0.01%
Risperidone	RISPERDAL TAB 0.5MG	20	3	$6,972.70	1.9	6.67	$11.62	0.02%
Risperidone	RISPERDAL TAB 2MG	18	2	$15,504.51	2.67	9	$28.71	0.03%
Risperidone	RISPERDAL SOL 1MG/ML	16	2	$9,210.52	4	8	$19.19	0.02%
Risperidone	RISPERDAL TAB 0.25MG	11	4	$4,053.13	2.55	2.75	$12.28	0.01%
Risperidone	RISPERDAL TAB 4MG	9	1	$6,983.94	1.5	9	$25.87	0.02%
Risperidone	RISPERDAL M TAB 0.5MG	5	1	$1,894.25	2	5	$12.63	0.00%
Risperidone	RISPERDAL M TAB 3MG	1	1	$904.01	2	1	$32.29	0.00%
	Subtotal	**76,155**		**$2,499,863.44**	**1.44**	**5.05**	**$1.07**	**5.48%**
Quetiapine	QUETIAPINE TAB 100MG	6,291	1,859	$115,477.61	1.43	3.38	$0.59	0.25%
Quetiapine	QUETIAPINE TAB 300MG	5,142	1,148	$173,808.53	1.54	4.48	$1.09	0.38%
Quetiapine	QUETIAPINE TAB 200MG	5,129	1,316	$114,658.51	1.41	3.9	$0.71	0.25%
Quetiapine	QUETIAPINE TAB 400MG	4,437	904	$162,549.07	1.5	4.91	$1.17	0.36%
Quetiapine	QUETIAPINE TAB 50MG	3,993	1,280	$72,282.67	1.5	3.12	$0.59	0.16%
Quetiapine	QUETIAPINE TAB 25MG	2,216	716	$34,164.05	1.63	3.09	$0.51	0.08%
Quetiapine	SEROQUEL XR TAB 300MG	2,118	460	$1,417,067.80	1.32	4.6	$21.38	3.12%
Quetiapine	SEROQUEL XR TAB 400MG	2,061	374	$1,762,418.51	1.43	5.51	$27.27	3.88%
Quetiapine	SEROQUEL XR TAB 200MG	1,071	250	$422,040.87	1.01	4.28	$12.56	0.93%
Quetiapine	SEROQUEL XR TAB 150MG	980	272	$355,815.86	1.01	3.6	$11.18	0.78%
Quetiapine	SEROQUEL XR TAB 50MG	511	143	$128,018.35	1.34	3.57	$8.39	0.28%
Quetiapine	SEROQUEL TAB 100MG	87	45	$1,563.63	1.28	1.93	$0.61	0.00%
Quetiapine	SEROQUEL TAB 400MG	58	23	$24,834.23	1.13	2.52	$14.53	0.05%
Quetiapine	SEROQUEL TAB 300MG	52	17	$25,754.92	1.56	3.06	$16.89	0.06%
Quetiapine	SEROQUEL TAB 25MG	27	9	$405.70	1.62	3	$0.54	0.00%
Quetiapine	SEROQUEL TAB 200MG	8	4	$216.18	1.75	2	$0.90	0.00%
Quetiapine	SEROQUEL TAB 50MG	1	1	$774.50	4	1	$25.82	0.00%
	Subtotal	**34,182**		**$4,811,850.99**	**1.44**	**3.41**	**$4.53**	**10.58%**

Continued:

CHEMICAL NAME	BRAND NAME	CLAIMS	MEMBERS	COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ DAY	% COST
Aripiprazole	ABILIFY TAB 10MG	7,804	2,059	$5,078,672.83	0.99	3.79	$20.95	11.17%
Aripiprazole	ABILIFY TAB 5MG	7,768	2,123	$4,907,675.94	0.98	3.66	$20.60	10.79%
Aripiprazole	ABILIFY TAB 15MG	5,262	1,349	$3,326,872.96	0.95	3.9	$19.98	7.32%
Aripiprazole	ABILIFY TAB 20MG	3,997	889	$3,777,922.87	1	4.5	$29.90	8.31%
Aripiprazole	ABILIFY TAB 30MG	2,909	546	$2,819,740.70	0.99	5.33	$29.55	6.20%
Aripiprazole	ABILIFY TAB 2MG	2,223	642	$1,426,100.81	1.01	3.46	$21.06	3.14%
Aripiprazole	ABILIFY SOL 1MG/ML	128	25	$55,690.54	3.13	5.12	$14.12	0.12%
Aripiprazole	ABILIFY DISC TAB 10MG	32	7	$24,567.58	0.95	4.57	$24.72	0.05%
Aripiprazole	ABILIFY MAIN INJ 400MG	20	11	$30,641.40	0.03	1.82	$52.65	0.07%
Aripiprazole	ABILIFY DISC TAB 15MG	8	2	$6,504.19	1	4	$25.02	0.01%
Aripiprazole	ABILIFY INJ 9.75MG	7	1	$207.91	1.17	7	$20.79	0.00%
Aripiprazole	ABILIFY MAIN INJ 300MG	6	4	$6,900.20	0.03	1.5	$39.21	0.02%
	Subtotal	**30,164**		**$21,461,497.93**	**0.99**	**4.05**	**$22.77**	**47.20%**
Olanzapine	OLANZAPINE TAB 20MG	3,970	676	$118,789.68	1.04	5.87	$0.90	0.26%
Olanzapine	OLANZAPINE TAB 10MG	2,973	785	$52,556.63	1.01	3.79	$0.56	0.12%
Olanzapine	OLANZAPINE TAB 5MG	1,465	475	$22,710.82	1.02	3.08	$0.47	0.05%
Olanzapine	OLANZAPINE TAB 15MG	1,286	309	$29,728.26	1.07	4.16	$0.74	0.07%
Olanzapine	OLANZAPINE TAB 2.5MG	423	126	$5,769.16	1.05	3.36	$0.45	0.01%
Olanzapine	OLANZAPINE TAB 20MG ODT	346	93	$115,496.33	1	3.72	$8.97	0.25%
Olanzapine	OLANZAPINE TAB 10MG ODT	311	100	$54,005.43	1.07	3.11	$5.01	0.12%
Olanzapine	OLANZAPINE TAB 20MG	287	72	$8,141.71	1.08	3.99	$0.91	0.02%
Olanzapine	OLANZAPINE TAB 7.5MG	234	56	$3,728.64	1	4.18	$0.53	0.01%
Olanzapine	OLANZAPINE TAB 15MG ODT	228	70	$68,822.71	1.16	3.26	$7.68	0.15%
Olanzapine	OLANZAPINE TAB 5MG ODT	204	61	$19,283.19	1.09	3.34	$3.27	0.04%
Olanzapine	OLANZAPINE 5MG TAB	107	25	$1,533.78	1.03	4.28	$0.50	0.00%
Olanzapine	ZYPREXA TAB 20MG	42	6	$46,217.91	1.05	7	$36.68	0.10%
Olanzapine	ZYPREXA TAB 10MG	17	5	$6,519.12	1	3.4	$12.78	0.01%
Olanzapine	ZYPREXA ZYDI TAB 15MG	14	2	$48,094.98	3.79	7	$114.51	0.11%
Olanzapine	ZYPREXA TAB 2.5MG	10	2	$3,633.09	1.2	5	$12.11	0.01%
Olanzapine	ZYPREXA INJ 10MG	3	2	$300.78	1.4	1.5	$60.16	0.00%
Olanzapine	OLANZAPINE INJ 10MG	2	2	$108.78	1.5	1	$54.39	0.00%
Olanzapine	ZYPREXA TAB 5MG	1	1	$1,167.02	3	1	$38.90	0.00%
Olanzapine	ZYPREXA ZYDI TAB 10MG	1	1	$209.10	1	1	$20.91	0.00%
	Subtotal	**11,924**		**$606,817.12**	**1.04**	**3.65**	**$1.57**	**1.33%**
Clozapine	CLOZAPINE TAB 100MG	4,179	310	$334,966.67	3.86	13.48	$4.58	0.74%
Clozapine	FAZACLO TAB 100/ODT	1,256	135	$798,277.18	3.58	9.3	$28.22	1.76%
Clozapine	FAZACLO TAB 150MG	757	70	$318,381.52	2.25	10.81	$21.82	0.70%
Clozapine	CLOZAPINE TAB 50MG	571	59	$22,076.11	2.51	9.68	$2.74	0.05%
Clozapine	CLOZAPINE TAB 25MG	520	60	$12,577.16	2.82	8.67	$1.58	0.03%
Clozapine	CLOZAPINE TAB 200MG	401	41	$34,730.76	2.55	9.78	$5.99	0.08%
Clozapine	FAZACLO TAB 200MG	356	43	$248,782.96	2.08	8.28	$27.19	0.55%
Clozapine	CLOZAPINE TAB 100/ODT	339	44	$157,449.39	3.04	7.7	$21.13	0.35%
Clozapine	FAZACLO TAB 25MG ODT	293	39	$61,682.57	3.46	7.51	$10.56	0.14%
Clozapine	CLOZAPINE TAB 25MG ODT	96	21	$21,451.75	3.54	4.57	$9.13	0.05%
Clozapine	CLOZARIL TAB 100MG	38	5	$47,913.88	5.13	7.6	$45.50	0.11%
	Subtotal	**8,806**		**$2,058,289.95**	**3.35**	**8.85**	**$12.58**	**4.56%**

Continued:

CHEMICAL NAME	BRAND NAME	CLAIMS	MEMBERS	COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ DAY	% COST
Paliperidone	INVEGA SUST INJ 234/1.5	2,210	448	$3,954,944.04	0.05	4.93	$61.57	8.70%
Paliperidone	INVEGA SUST INJ 156MG/ML	1,757	384	$2,083,542.38	0.03	4.58	$41.09	4.58%
Paliperidone	INVEGA TAB 6MG	1,604	295	$1,215,664.32	1.29	5.44	$24.54	2.67%
Paliperidone	INVEGA TAB 9MG	956	166	$907,562.03	1.01	5.76	$28.64	2.00%
Paliperidone	INVEGA TAB 3MG	578	132	$345,528.90	1	4.38	$19.09	0.76%
Paliperidone	INVEGA SUST INJ 117/0.75	466	115	$407,733.20	0.03	4.05	$30.43	0.90%
Paliperidone	INVEGA SUST INJ 78/0.5ML	24	11	$13,687.22	0.02	2.18	$20.19	0.03%
Paliperidone	INVEGA TAB 1.5MG	19	6	$8,920.56	1	3.17	$19.65	0.02%
Paliperidone	INVEGA SUST INJ 39/0.25	7	4	$2,074.72	0.01	1.75	$10.32	0.00%
	Subtotal	**7,621**		**$8,939,657.37**	**0.52**	**4.03**	**$39.04**	**19.66%**
Ziprasidone	ZIPRASIDONE CAP 80MG	3,132	517	$698,781.35	1.81	6.06	$7.20	1.54%
Ziprasidone	ZIPRASIDONE CAP 60MG	1,410	292	$294,730.90	1.71	4.83	$6.80	0.65%
Ziprasidone	ZIPRASIDONE CAP 40MG	1,381	370	$199,991.22	1.51	3.73	$4.68	0.44%
Ziprasidone	ZIPRASIDONE CAP 20MG	663	183	$99,046.77	1.58	3.62	$4.85	0.22%
Ziprasidone	GEODON CAP 80MG	32	9	$12,344.46	1.53	3.56	$12.86	0.03%
Ziprasidone	GEODON CAP 60MG	26	5	$12,340.01	1.48	5.2	$15.43	0.03%
Ziprasidone	GEODON INJ 20MG	24	10	$1,401.27	1.47	2.4	$28.60	0.00%
Ziprasidone	GEODON CAP 20MG	23	5	$8,238.85	1.91	4.6	$11.94	0.02%
Ziprasidone	GEODON CAP 40MG	18	5	$10,772.89	2.52	3.6	$20.96	0.02%
	Subtotal	**6,709**		**$1,337,647.72**	**1.71**	**4.18**	**$6.48**	**2.95%**
Iloperidone	FANAPT TAB 6MG	786	217	$448,330.74	1.64	3.62	$19.04	0.99%
Iloperidone	FANAPT TAB 8MG	430	103	$259,981.43	1.77	4.17	$20.63	0.57%
Iloperidone	FANAPT TAB 4MG	349	95	$222,263.00	1.86	3.67	$21.67	0.49%
Iloperidone	FANAPT TAB 12MG	263	44	$175,345.79	1.9	5.98	$22.39	0.39%
Iloperidone	FANAPT TAB 2MG	236	67	$155,769.05	1.95	3.52	$22.81	0.34%
Iloperidone	FANAPT TAB 10MG	152	36	$100,339.24	1.98	4.22	$23.17	0.22%
Iloperidone	FANAPT TAB 1MG	15	11	$8,349.10	1.71	1.36	$19.51	0.02%
Iloperidone	FANAPT PAK	7	7	$660.28	0.58	1	$6.81	0.00%
	Subtotal	**2,238**		**$1,371,038.63**	**1.78**	**3.44**	**$20.80**	**3.02%**
Lurasidone	LATUDA TAB 80MG	1,020	273	$649,992.87	1.14	3.74	$20.38	1.43%
Lurasidone	LATUDA TAB 40MG	882	334	$553,011.25	1.14	2.64	$20.45	1.22%
Lurasidone	LATUDA TAB 120MG	108	47	$106,871.50	1.01	2.3	$28.83	0.24%
Lurasidone	LATUDA TAB 20MG	79	35	$51,618.98	1.28	2.26	$22.18	0.11%
	Subtotal	**2,089**		**$1,361,494.60**	**1.14**	**2.74**	**$20.96**	**3.00%**
Asenapine	SAPHRIS SUB 10MG	1,228	366	$689,818.11	1.65	3.36	$18.45	1.52%
Asenapine	SAPHRIS SUB 5MG	639	262	$338,599.86	1.59	2.44	$17.55	0.74%
	Subtotal	**1,867**		**$1,028,417.97**	**1.63**	**2.78**	**$18.14**	**2.26%**
	Total	**181,755**	**26,134**	**$45,476,575.72**	**1.37**	**6.95**	**$8.26**	**100%**

[1] Sunovion Pharmaceuticals Inc. Announces FDA Approval of Latuda (lurasidone HCl) as Monotherapy and Adjunctive Therapy in Adult Patients with Bipolar Depression. Drugs.com. Available at: http://www.drugs.com/newdrugs/sunovion-pharmaceuticals-inc-announces-fda-approval-latuda-lurasidone-hcl-monotherapy-adjunctive-3836.html#hhHjPvyj1SSYiWFL.99. Last accessed 7/25/2013

[2] http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm357601.htm

[3] Abilify Maintena Product Information. Otsuka Pharmaceutical Co. Available online at: http://www.otsuka-us.com/Products/Documents/Abilify.M.PI.pdf. Last accessed 7/29/2013.

[4] Abilify Maintena Approved for Schizophrenia. MPR. Available at: http://www.empr.com/abilify-maintena-approved-for-schizophrenia/article/282490/. Last accessed on 7/25/2013.

[5] FDA Approves Adasuve (loxapine) Inhalation Powder for the Acute Treatment of Agitation Associated with Schizophrenia or Bipolar I Disorder in Adults. Drugs.com. Available at: http://www.drugs.com/newdrugs/fda-approves-adasuve-loxapine-inhalation-powder-acute-agitation-associated-schizophrenia-bipolar-3606.html#TpeWrWwi5gz4HWCj.99. Last accessed on 7/25/2013.

[6] Initial REMS Approval for Adasuve. Available online at: http://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM333242.pdf Last accessed 7/25/2013.

[7] Versacloz™ Product Label. FDA. Available at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/203479s000lbl.pdf. Last accessed 7/25/2013.

[8] Versacloz REMS Program. FDA. Available at: http://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM338961.pdf Last accessed 7/28/2013.

[9] Lauriello, John. Campbell, Austin. Pharmacotherapy for schizophrenia: Long-acting injectable antipsychotic drugs. UptoDate. February 2013. Available at http://www.uptodate.com/contents/pharmacotherapy-for-schizophrenia-long-acting-injectable-antipsychotic-drugs. Last accessed 77/26/2013.

[10] Rosenheck RA, Krystal JH, Lew R, Barnett PG, Fiore L, Valley D, Thwin SS, Vertrees JE, Liang MH, CSP555 Research Group. Long-Acting Risperidone and Oral Antipsychotics in Unstable Schizophrenia. N Engl J Med. 2011;364(9):842.

Appendix G

Drug Utilization Review of Tysabri® (Natalizumab)

Oklahoma Health Care Authority
August 2013

Tysabri® Medication Summary

Tysabri® (natalizumab) was approved by the FDA in November of 2004 to treat multiple sclerosis (MS). It is a humanized monoclonal antibody against alpha-4 (α4) integrins, the first drug developed in the class of selective adhesion molecule inhibitors, for patients who had an inadequate response, or are unable to tolerate conventional MS therapies. Alpha-4 integrin is required for white blood cells to move into organs, and Tysabri®'s mechanism of action is believed to prevent immune cells from migrating from the bloodstream into the brain and other organs where they can cause inflammation and potentially damage nerve fibers and the insulating myelin sheath. The FDA suspended marketing for Tysabri® in February of 2005 due to three cases of progressive multifocal leukoencephalopathy (PML) being reported in association with receiving Tysabri®. In June of 2006, after a recommendation by an advisory committee and a review of two years of safety and efficacy data, the FDA re-approved Tysabri® for patients with all relapsing forms of MS. In January of 2008 Tysabri® was approved by the FDA to treat moderate to severe Crohn's disease (CD) in patients with evidence of inflammation who have had an inadequate response to, or are unable to tolerate, conventional Crohn's disease therapies.

Tysabri® is available as a 300mg per 15ml vial. The recommended dose for both multiple sclerosis and Crohn's disease therapy is infusion of Tysabri® 300 mg in 100 ml 0.9% sodium chloride injection over one hour every four weeks. Tysabri® is a Pregnancy Category C medication. The most common side effects reported when using Tysabri® are:

- headache
- fatigue
- arthralgia
- urinary tract infection
- upper and lower respiratory tract infection
- gastroenteritis
- vaginitis
- depression
- pain in extremity
- abdominal discomfort
- diarrhea
- rash
- nausea

Tysabri® increases the risk for development of progressive multifocal leukoencephalopathy (PML), a potentially deadly brain infection. 201 cases of PML have been reported among approximately 96,582 patients treated with Tysabri® worldwide through January 4, 2012.[1] New data has identified the presence of anti-John Cunningham Virus (JCV) antibodies as a risk factor for developing PML in Tysabri®-treated patients. The Stratify JCV Antibody ELISA test, which can detect these antibodies, was cleared by the FDA on January 20, 2012[2]. Due to the increased risk of PML, patients should weigh the risks and benefits of continuing treatment with Tysabri® if they are found to be anti-JCV antibody positive and have one or more of the following additional risk factors:

- longer treatment duration- especially beyond 2 years
- prior treatment with an immunosuppressant (e.g., mitoxantrone, azathioprine, methotrexate, cyclophosphamide, or mycophenolate mofetil)

Estimated PML Incidence Stratified by Risk Factor[1]

	Anti-JCV Antibody Positive*	**Anti-JCV Antibody Positive***
Tysabri® Exposure†	No Prior Immunosuppressant Use	Prior Immunosuppressant Use
1-24 months	<1/1,000	2/1,000
25-48 months	4/1,000	11/1,000

Notes: Based on postmarketing PML data and Tysabri® use data as of September 1, 2011.
†Data beyond 4 years of treatment are limited.
* Risk in anti-JCV antibody positive patients was estimated based on the assumptions that 18% of Tysabri®-treated MS patients have a history of prior immunosuppressant treatment and that 55% of Tysabri®-treated MS patients are anti-JCV antibody positive.
The anti-JCV antibody status was determined using an anti-JCV antibody test (ELISA) that has been analytically and clinically validated and is configured with detection and inhibition steps to confirm the presence of JCV-specific antibodies with a false negative rate of 3%.

To decrease the possibility of patients developing PML, the manufacturer of Tysabri®, Biogen-IDEC, submitted to the FDA a Risk Management Plan, called the TOUCH Prescribing Program, to ensure safe use of the product. The FDA has determined that Tysabri® can be made available under the TOUCH Prescribing Program with the following main features:

- Tysabri® will only be administered to patients who are enrolled in the program.
- Patients on Tysabri® are to be evaluated at 3 and 6 months after the first infusion and every 6 months after that, and their status will be reported regularly to the product's manufacturer.
- Prior to initiating the therapy, health care professionals are to obtain the patient's magnetic resonance imaging (MRI) scan to help differentiate potential future MS symptoms from PML.
- The drug will only be prescribed, distributed, and infused by prescribers, infusion centers, and pharmacies registered with the program.

Due to the risks associated with Tysabri®, this medication is generally reserved for patients with multiple sclerosis who have had an inadequate response, or are not tolerant of the interferons or glatiramer acetate.[3] Tysabri® is also used to treat and prevent episodes of symptoms in people who have Crohn's disease, a condition in which the immune system attacks the lining of the digestive tract causing pain, diarrhea, weight loss, and fever. Its place in Crohn's therapy is also reserved for patients who did not respond to conventional therapies and inhibitors of TNF-α.[4]

Utilization of Tysabri® (Natalizumab)

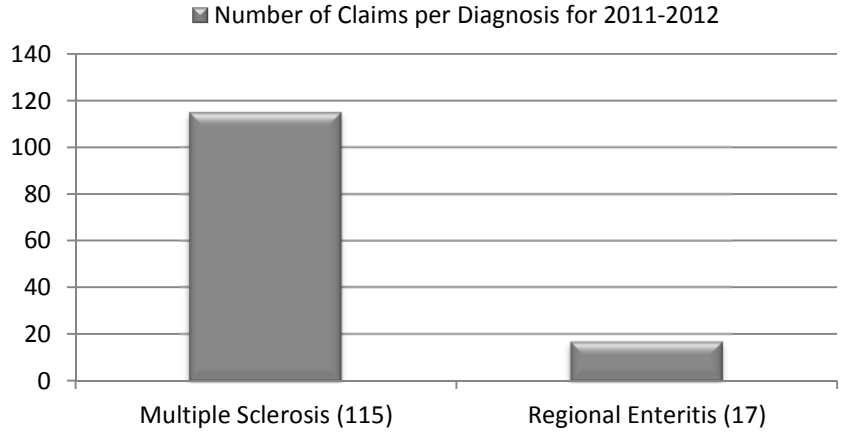
Medical Claims: CY 2011-2012

CALENDAR YEAR	MEMBERS	MEDICAL CLAIMS	COST	COST/ CLAIM
2011	10	66	$180,077.77	$2,728.45
2012	10	66	$203,603.67	$3,084.90
% Change	0.00%	0.00%	13%	13%
Change	0	0	$23,525.90	$356.45

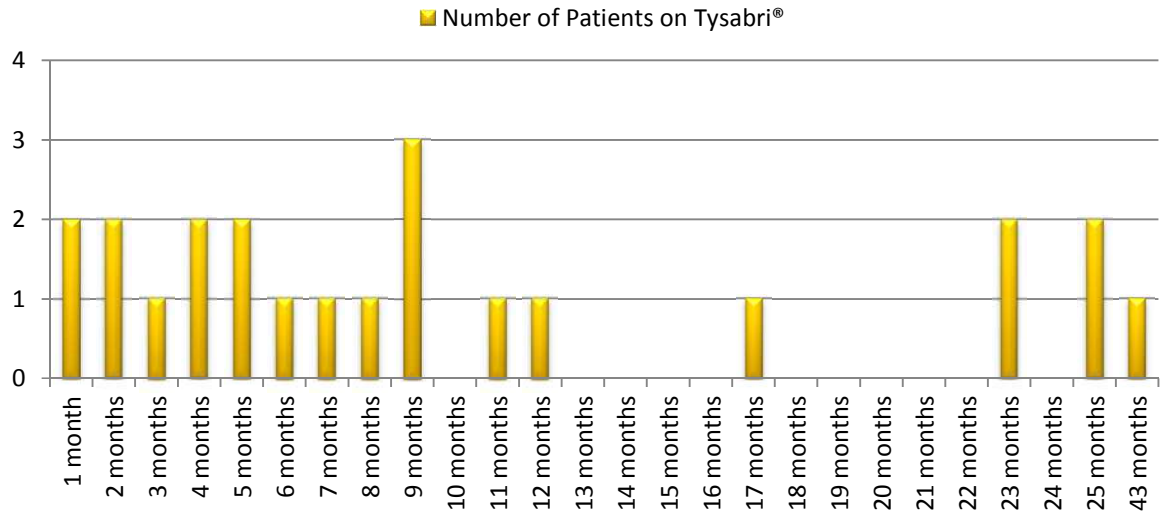
Pharmacy Claims: CY 2011-2012

CALENDAR YEAR	CLAIMS	MEMBERS	COST	CLAIMS/ MEMBER	COST/ CLAIM	COST/ MEMBER
2011	15	3	$46,783.80	5	$3,118.92	$15,594.60
2012	38	6	$133,305.99	6.33	$3,508.05	$22,217.67
% Change	153%	100%	184%	26%	12%	42%
Change	23	3	$86,522.19	1.33	$389.13	$6,623.07

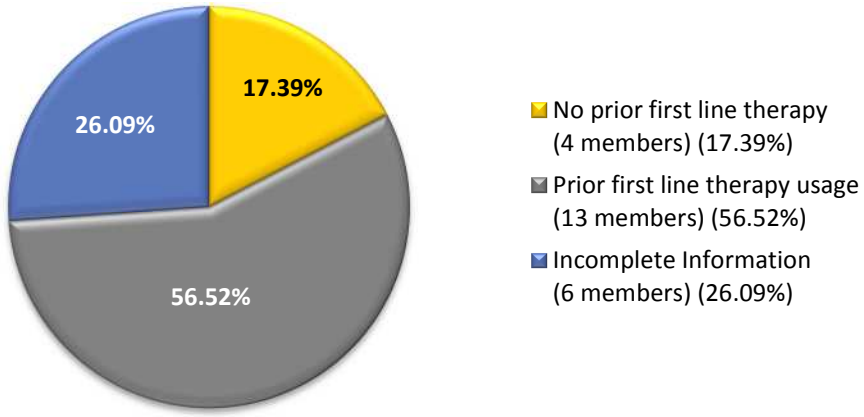
Diagnosis for Tysabri® Medical Claims Calendar Years 2011 & 2012



Duration of Tysabri® Treatment CY 2010-2013



First Line Therapy Usage Prior to Tysabri® for MS and CD
Calendar Years 2010-2013



Conclusions

- The FDA recommends negative anti-JCV patients testing every 6 months during treatment with Tysabri®.[5]
- In order to ensure broad access to Stratify JCV, Biogen Idec and Elan Pharmaceuticals are currently working with Quest Diagnostics to provide the test at no charge to patients with multiple sclerosis where allowed.
- Medical claims show the same number of members and claims were reported for 2011 and 2012; however, the cost of Tysabri increased in 2012 by a total of $23,525.90 and by $356.45 per claim.
- Pharmacy claims increased by 153.33% for 2012 compared to 2011. The number of members doubled from 3 to 6 members. The total cost increased by $86,522.19 and by $389.13 per claim.

Recommendations

The College of Pharmacy recommends medical and pharmacy prior authorization of Tysabri® (natalizumab) with the following criteria:

Tysabri® (Natalizumab) Prior Authorization Criteria:

1. FDA approved diagnosis of multiple sclerosis or Crohn's disease.
2. Treatment with at least two other MS or CD first line therapies that have failed to yield an adequate clinical response, or patient specific, clinically significant reason why the member cannot use all available first and second line alternatives.
3. Prescriber, infusion center, and member must enroll in the TOUCH Prescribing Program.

PRODUCT DETAILS OF TYSABRI® (NATALIZUMAB) INJECTION[6]

FDA-APPROVED in November 2004 for MS, January 2008 for Crohn's Disease

INDICATIONS:
Treatment of relapsing forms of multiple sclerosis to delay the accumulation of physical disability and reduce the frequency of clinical exacerbations. Tysabri® is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternate multiple sclerosis therapy.

Indicated for inducing and maintaining clinical response and remission in adult patients with moderate to severe Crohn's disease with evidence of inflammation who have had an inadequate response to, or are unable to tolerate, conventional CD therapies and inhibitors of TNF-α.

DOSAGE FORMS: Tysabri® is available as 300mg natalizumab in a sterile, single-use 15 ml vial free of preservatives.

- Tysabri® is a colorless, clear to slightly opalescent concentrate that must be diluted prior to intravenous infusion.
- Recommended dosage for treatment of multiple sclerosis and Crohn's disease is 300 mg intravenous infusion over one hour every four weeks.
- Only prescribers registered in the MS TOUCH® Prescribing Program may prescribe Tysabri® for multiple sclerosis.
- Only prescribers registered in the CD TOUCH® Prescribing Program may prescribe Tysabri® for Crohn's disease.
- Following dilution, infuse Tysabri® immediately or refrigerate solution at 2 to 8°C, and use within 8 hours. If stored at 2 to 8°C, allow solution to warm to room temperature prior to infusion.

ADMINISTRATION:

- Infuse Tysabri® 300 mg in 100 ml 0.9% Sodium Chloride Injection over one hour (infusion rate of 5mg per minute). No other IV diluents may be used.
- Tysabri® should not be used with concomitant immunosuppressants or concomitant inhibitors of TNF- α. Aminosalicylates may be continued during treatment.
- After the infusion is complete, flush with 0.9% Sodium Chloride Injection.
- Observe patients during the infusion and for one hour after the infusion is complete. Promptly discontinue the infusion upon the first observation of any signs of symptoms consistent with a hypersensitivity- type reaction.
- Consideration should be given to testing patients for anti-JCV antibody status prior to treatment or during treatment if antibody status is unknown.
- Patient should be retested for the anti-JCV antibody periodically.
- Evaluate the patient three months after the first infusion, six months after the first infusion, and every six months thereafter.
- Determine every six months whether patients should continue on treatment.
- In MS patients, an MRI scan should be obtained prior to initiating therapy with Tysabri®. This MRI may be helpful in differentiating subsequent MS symptoms from PML.
- In Crohn's disease patients, a baseline brain MRI may also be helpful to distinguish pre-existent lesions from newly developed lesions.

- Healthcare professionals should monitor patients on Tysabri® for any new sign or symptom suggestive of PML. Typical symptoms associated with PML are diverse, progress over days to weeks, and include progressive weakness on one side of the body or clumsiness of the limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes. Withhold Tysabri® dosing immediately at the first sign or symptom suggestive of PML.
- Corticosteroids should be tapered in those patients with Crohn's disease who are on chronic corticosteroids when they start Tysabri®.

CONTRAINDICATIONS:

- Patients who have or have had progressive multifocal leukoencephalopathy (PML)
- Patients who have a hypersensitivity reaction to Tysabri®

SPECIAL POPULATIONS:

- **Pregnancy:** Pregnancy Category C. Tysabri® has been shown to reduce pup survival in guinea pigs when given in doses 7 times the human dose, and has been shown to have hematologic effects on the fetus in monkeys when given in doses 2.3 times the human dose. There are no adequate or well-controlled studies in pregnant women. Tysabri® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

- **Nursing Mothers:** Tysabri® has been detected in human milk. The effects of this exposure on infants are unknown.

- **Pediatric Use**: Safety and effectiveness of Tysabri® in pediatric patients with multiple sclerosis or Crohn's disease below the age of 18 years have not been established. Tysabri® is not indicated for use in pediatric patients.

- **Geriatrics:** Clinical studies of Tysabri® did not include sufficient numbers of patients over 65 years and older to determine whether they respond differently than younger patients. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

WARNINGS AND PRECAUTIONS:

- **Progressive Multifocal Leukoencephalopathy (PML):** PML, an opportunistic infection caused by the JC virus (JCV) that typically only occurs in patients who are immunocompromised, developed in three patients who received Tysabri® in clinical trials. Two cases of PML were observed among 1869 patients with multiple sclerosis treated for a median of 120 weeks. The third case occurred among 1043 patients with Crohn's disease after the patient received eight doses. Both MS patients were receiving concomitant immunomodulatory therapy and the Crohn's disease patient had been treated in the past with immunosuppressive therapy. Additional cases of PML have been reported in multiple sclerosis and Crohn's disease patients who were receiving no concomitant immunomodulatory therapy. Three factors that are known to increase the risk of PML in Tysabri®- treated patients have been identified:
    - Longer treatment duration, especially beyond 2 years. There is limited experience in patients who have received more than 4 years of Tysabri® treatment.

- Prior treatment with an immunosuppressant (e.g., mitoxantrone, azathioprine, methotrexate, cyclophosphamide, mycophenolate mofetil).
- The presence of anti-JCV antibodies. Patients who are anti-JCV antibody positive have a higher risk for developing PML.

The risks and benefits of continuing treatment with Tysabri® should be carefully considered in patients who are found to be anti-JCV antibody positive and have one of more additional risk factors. Patients with all three known risk factors have an estimated risk of PML of 11/1,000. Patients who are anti-JCV antibody negative are still at risk for the development of PML due to the potential for a new JCV infection or a false negative test result. Therefore, patients with a negative anti-JCV antibody test result should be retested periodically. For purposes of risk assessment, a patient with a positive anti-JCV antibody test at any time is considered anti-JCV antibody positive regardless of the results of any prior or subsequent anti-JCV antibody testing. When assessed, anti-JCV antibody status should be determined using an analytically and clinically validated immunoassay.

- **Hypersensitivity/ Antibody Formation:** Hypersensitivity reactions have occurred in patients receiving Tysabri®, including serious systemic reactions (e.g., anaphylaxis) which occurred at an incidence of <1%. These reactions usually occur within two hours of the start of the infusion. Symptoms associated with these reactions can include urticaria, dizziness, fever, rash, rigors, pruritus, nausea, flushing, hypotension, dyspnea, and chest pain. Generally, these reactions are associated with antibodies of Tysabri®.

  If a hypersensitivity reaction occurs, discontinue administration of Tysabri® and initiate appropriate therapy. Patients who experience a hypersensitivity reaction should not be re-treated with Tysabri®. Hypersensitivity reactions were more frequent in patients with antibodies to Tysabri® compared to patients who did not develop antibodies to Tysabri® in both MS and CD studies. Therefore, the possibility of antibodies to Tysabri® should be considered in patients who have hypersensitivity reactions.

  Antibody testing: If the presence of persistent antibodies is suspected, antibody testing should be performed. Antibodies may be detected and confirmed with sequential serum antibody tests. Antibodies detected early in the treatment course (e.g., within the first six months) may be transient and disappear with continued dosing. Repeat testing at three months after initial positive result is recommended in patients in whom antibodies are detected to confirm that antibodies are persistent. Prescribers should consider the overall benefits and risks of Tysabri® in a patient with persistent antibodies.

  Experience with monoclonal antibodies, including Tysabri®, suggests that patients who receive therapeutic monoclonal antibodies after an extended period without treatment may be at higher risk of hypersensitivity reactions than patients who received regularly scheduled treatment. Given that patients with persistent antibodies to Tysabri® experience reduced efficacy, and that hypersensitivity reactions are more common in such patients, consideration should be given to testing for the presence of antibodies in patients who wish to recommence therapy following a dose interruption. Following a period of dose interruption, patients testing negative for antibodies prior to re-dosing have a risk of antibody development with re-treatment that is similar to Tysabri® naïve patients.

- **Immunosuppression/ Infections:** The immune system effects of Tysabri® may increase the risk for infections. In a clinical study for MS, certain types of infections, including pneumonias and urinary tract infections, gastroenteritis, vaginal infections, tooth infections, tonsillitis, and herpes infections occurred more often in Tysabri®- treated patients than in placebo-treated patients. One opportunistic infection, cryptosporidial gastroenteritis with a prolonged course, was observed in a patient who received Tysabri®.

  MS and CD clinical studies both show an increase in infections was seen in patients concurrently receiving courses of corticosteroids; however, the increase in infections in Tysabri®-treated patients who received steroids was similar to the increase in placebo-treated patients who received steroids.

  In Crohn's disease clinical studies, opportunistic infections (pneumocystis carinii pneumonia, pulmonary mycobacterium avium intracellulare, bronchopulmonary aspergillosis, and burkholderia cepacia) have been observed in <1% of Tysabri®-treated patients; some of these patients were receiving immunosuppressants.

  Concurrent use of antineoplastic, immunosuppressant, or immunomodulating agents may further increase the risk of infections, including PML and other opportunistic infections, over the risk observed with use of Tysabri® alone. The safety and efficacy of Tysabri® in combination with antineoplastic, immunosuppressant, or immunomodulating agents have not been established. Patients receiving chronic immunosuppressant or immunomodulating therapy or who have systemic medical conditions resulting in significantly compromised immune system function should not ordinarily be treated with Tysabri®. The risk of PML is also increased in patients who have been treated with an immunosuppressant prior to receiving Tysabri®.

  For patients with Crohn's disease who start Tysabri® while on chronic corticosteroids, commence steroid withdrawal as soon as a therapeutic benefit has occurred. If the patient cannot discontinue systemic corticosteroids within six months, discontinue Tysabri®.

- **Hepatotoxicity:** Clinically significant liver injury has been reported in patients treated with Tysabri® in the post marketing setting. Signs of liver injury, including markedly elevated serum hepatic enzymes and elevated total bilirubin, occurred as early as six days after the first dose; signs of liver injury have also been reported for the first time after multiple doses. In some patients, liver injury recurred upon rechallenge, providing evidence that Tysabri® caused the injury. The combination of transaminase elevations and elevated bilirubin without evidence of obstruction is generally recognized as an important predictor of severe liver injury that may lead to death or the need for a liver transplant in some patients. Tysabri® should be discontinued in patients with jaundice or other evidence of significant liver injury.

- **Lab Test Abnormalities:** In clinical trials, Tysabri® was observed to induce increases in circulating lymphocytes, monocytes, eosinophils, basophils, and nucleated red blood cells. Observed changes persisted during Tysabri® exposure, but were reversible, returning to baseline levels usually within 16 weeks after the last dose. Elevations of neutrophils were not observed. Tysabri® induces mild decreases in hemoglobin levels that are frequently transient.

- **Immunizations:** No data are available on the effects of vaccination in patients receiving Tysabri®. No data are available on the secondary transmission of infection by live vaccines in patients receiving Tysabri®.

- **Distribution Program for Tysabri®:** Tysabri®is available only under a special restricted distribution program called the TOUCH Prescribing Program. Under the TOUCH Prescribing Program, only prescribers, infusion centers, and pharmacies associated with infusion centers registered with the program are able to prescribe, distribute, or infuse the product. For prescribers and patients, the TOUCH Prescribing Program has two components: MS TOUCH (for patients with multiple sclerosis) and CD TOUCH (for patients with Crohn's disease). Tysabri® must be administered only to patients who are enrolled in and meet all the conditions of the MS or CD TOUCH Prescribing Program.

- To enroll in the TOUCH Prescribing Program, prescribers and patients are required to understand the risks of treatment with Tysabri®, including PML and other opportunistic infections. Prescribers are required to understand the information in the Prescribing Information and to be able to:
    - Educate patients on the benefits and risks of treatment with Tysabri®, ensure that the patient receives the Medication Guide, instruct them to read it, and encourage them to ask questions when considering Tysabri®. Patients may be educated by the enrolled prescriber or a healthcare provider under that prescriber's direction.
    - Review the TOUCH Prescriber/ Patient Enrollment form for Tysabri® with the patient and answer all questions.
    - As part of the initial prescription process for Tysabri®, obtain the patient's signature and initials on the TOUCH program enrollment form, sign it, place the original signed form in the patient's medical record, send a copy to Biogen Idec, and give a copy to the patient.
    - Report serious opportunistic and atypical infections with Tysabri® to Biogen Idec or Elan and the FDA MedWatch Program.
    - Evaluate the patient three months after the first infusion, six months after the first infusion, and every six months thereafter.
    - Determine every six months whether patients should continue on treatment and if so reauthorize treatment every six months.
    - Submit to Biogen Idec the Tysabri® Patient Status Report and Reauthorization Questionnaire six months after initiating treatment and every six months thereafter.
    - Complete an "Initial Discontinuation Questionnaire" when Tysabri® is discontinued and a "6-Month Discontinuation Questionnaire" following discontinuation of Tysabri®.

ADVERSE REACTIONS:

- **Serious adverse reactions:** Progressive multifocal leukoencephalopathy, hypersensitivity, antibody formation, immunosuppression and infections.

- **Other adverse reactions in clinical trials:** The most common adverse reactions (incidence ≥ 10%) were headache and fatigue in both the multiple sclerosis and Crohn's disease studies. Other common adverse reactions (incidence ≥ 10%) in the MS population were arthralgia, urinary tract infection, lower respiratory tract infection, gastroenteritis, vaginitis, depression, pain in extremity, abdominal discomfort, diarrhea, and rash. Other common adverse reactions (incidence ≥ 10%) in the CD population were upper respiratory tract infections and nausea.

- The most frequently reported adverse reactions resulting in clinical intervention (i.e., discontinuation of TYSABRI®), in the MS studies were urticaria (1%) and other hypersensitivity reactions (1%), and in the CD studies were the exacerbation of Crohn's disease (4.2%) and acute hypersensitivity reactions (1.5%).

DRUG INTERACTIONS:
Because of the potential for increased risk of PML and other infections, Crohn's disease patients receiving Tysabri® should not be treated with concomitant immunosuppressants (e.g., 6-mercaptopurine, azathioprine, cyclosporine, or methotrexate) or inhibitors of TNF-α, and corticosteroids should be tapered in those patients with Crohn's disease who are on chronic corticosteroids when they start TYSABRI®® therapy. Ordinarily, MS patients receiving chronic immunosuppressant or immunomodulatory therapy should not be treated with Tysabri®.

PATIENT COUNSELING INFORMATION:

- Counsel patients regarding the risks and benefits of Tysabri® before an initial prescription is written. The patient may be educated by either the enrolled prescriber or a healthcare provider under that prescriber's direction. INSTRUCT PATIENTS USING TYSABRI® TO:
    - Read the Medication Guide before starting Tysabri® and before each Tysabri® infusion.
    - Promptly report any new or continuously worsening symptoms that persist over several days to their prescriber.
    - Inform all of their physicians that they are receiving Tysabri®.
    - Plan to see their prescriber three months after the first infusion, six months after the first infusion, and at least as frequently as six months thereafter.

- Inform patients that progressive multifocal leukoencephalopathy (PML) has occurred in patients who received Tysabri®. Instruct the patient of the importance of contacting their doctor if they develop any symptoms suggestive of PML. Instruct the patient that typical symptoms associated with PML are diverse, progress over days to weeks, and include progressive weakness on one side of the body or clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes. Instruct the patient that the progression of deficits usually leads to death or severe disability over weeks or months.

- Instruct patients to continue to look for new signs and symptoms suggestive of PML for approximately 6 months following discontinuation of Tysabri®.

- Instruct patients to report immediately if they experience symptoms consistent with a hypersensitivity reaction (e.g., urticarial with or without associated symptoms) during or following an infusion of Tysabri®.

- Inform patients that Tysabri® may lower the ability of their immune system to fight infections. Instruct the patient of the importance of contacting their doctor if they develop any symptoms of infection.

- Inform patients that Tysabri® may cause liver injury. Instruct the patient to contact their doctor if they develop symptoms of hepatotoxicity.

[1]U.S. National Library of Medicine. National Institutes of Health. Health Topics-Progressive multifocal leukoencephalopathy. Available at: http://www.nlm.nih.gov/medlineplus/ency/article/000674.htm. Accessed 06/25/2013

[2]Tysabri® Full Prescribing Information. Biogen Idec Inc. & Elan Pharmaceuticals, Inc. Available online at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/125104s813lbl.pdf. Last revised: May 2013; Accessed 06/19/2013

[3]AHFS Consumer Medication Information. Bethesda, MD: American Society of Health-System Pharmacists, Inc.; ©2013. Natalizumab Injection. Available from: http://www.nlm.nih.gov/medlineplus/druginfo/meds/a605006.html. Last revised May 2012; Accessed 06/27/2013

[4] Tysabri Gains Crohn's Disease Indication. FDAnews Drug Daily Bulletin. Available at: http://www.fdanews.com/newsletter/article?articleId=103110&issueId=11213. Last revised: Jan 2008; Accessed: 06/27/2013

[5] Tysabri® (natalizumab). National Multiple Sclerosis Society. Available at: http://www.nationalmssociety.org/about-multiple-sclerosis/what-we-know-about-ms/treatments/medications/natalizumab/index.aspx. Accessed 06/27/2013

[6]Choosing a Disease Modifying Therapy (DMT) to Use for Multiple Sclerosis. U.S. Department of Veterans Affairs. Available online at: http://www.va.gov/MS/articles/Choosing_A_Disease_Modifying_Therapy_DMT_to_Use_for_Multiple_Sclerosis.asp. Last revised: April 2012; Accessed 06/27/2013

Appendix H

30 Day Notice to Prior Authorize Diclegis® (Doxylamine/Pyridoxine)

Oklahoma Health Care Authority
August 2013

Manufacturer	Duchesnay USA, Inc.
Classification	Antiemetic
Status	Prescription Only

Introduction

Doxylamine/pyridoxine was previously available under the brand name Bendectin®. Although multiple studies showed no increased risk of birth defects, the manufacturer voluntarily withdrew Bendectin® from the market in 1983 because of litigation.[1,2,3] The FDA published a statement in the Federal Register in 1999 that summarized their opinion regarding the safety of doxylamine/pyridoxine during pregnancy and determined that Bendectin® was not withdrawn from the market for reasons of safety or effectiveness.[4] This determination permitted the FDA to approve abbreviated new drug applications (ANDAs) for the combination of doxylamine and pyridoxine for use in pregnancy. Diclegis® (doxylamine/pyridoxine) was approved by the FDA in April 2013.[5]

Diclegis® (Doxylamine/Pyridoxine) Medication Summary[6,7,8]

Diclegis® is indicated for the management of nausea and vomiting of pregnancy in women who do not respond to conservative management. However, Diclegis® has not been studied in women with hyperemesis gravidarum. Diclegis® is a combination of doxylamine succinate and pyridoxine hydrochloride. Doxylamine is an ethanolamine derivative antihistamine that is used in various over-the-counter sleep aids and prescription allergy products, such as Unisom® and Aldex AN®. Pyridoxine is vitamin B-6. The exact mechanism of action of doxylamine/pyridoxine in pregnancy-related nausea and vomiting is unknown.

Diclegis® is available as oral tablets containing 10mg of doxylamine and 10mg of pyridoxine. Therapy is initiated with two tablets by mouth on an empty stomach at bedtime, and can be increased up to a maximum of 4 tablets per day (one tablet in the morning, one tablet mid-afternoon, and 2 tablets at bedtime). Diclegis® should be taken as a daily prescription and not on an as needed basis. The prescriber should reassess the patient for continued need of Diclegis® as her pregnancy progresses.

Diclegis® is contraindicated in patients taking monoamine oxidase inhibitors (MAOIs), and in patients that have known hypersensitivity to doxylamine, pyridoxine, other ethanolamine derivative antihistamines, or the inactive ingredients of the formulation. Diclegis® may cause somnolence due to the anticholinergic properties of doxylamine, an antihistamine. Patients should avoid engaging in activities requiring complete mental alertness, such as driving or operating heavy machinery while using Diclegis®, until cleared to do so by a healthcare

provider. Concurrent use with alcohol or other CNS depressants is not recommended. This combination may result in severe drowsiness leading to falls or accidents. Use with caution in patients with asthma, increased intraocular pressure, narrow-angle glaucoma, stenosing peptic ulcer, pyloroduodenal obstruction, and urinary bladder-neck obstruction. Diclegis® is excreted into breast milk and infant risk cannot be ruled out, so treatment with Diclegis® is not recommended in women who are breastfeeding.

A double-blind, randomized, multi-center, placebo-controlled study was conducted to support the safety and efficacy of Diclegis® in the treatment of nausea and vomiting of pregnancy. Adult women 18 years of age or older and 7 to 14 weeks gestation (median 9 weeks of gestation) with nausea and vomiting of pregnancy were randomized to 14 days of Diclegis® or placebo. Over the treatment period, 19% of Diclegis®-treated patients remained on 2 tablets daily, 21% received 3 tablets daily, and 60% received 4 tablets daily. The primary endpoint was the change from baseline at day 15 in the Pregnancy Unique-Quantification of Emesis (PUQE) score. The PUQE score incorporates the number of daily vomiting episodes, number of daily heaves, and length of daily nausea in hours, for an overall score of symptoms rated from 3 (no symptoms) to 15 (most severe). At baseline, the mean PUQE score was 9.0 in the Diclegis® arm and 8.8 in the placebo arm. There was a 0.7 (95% confidence interval 0.2 to 1.2 with p-value 0.006) mean decrease (improvement in nausea and vomiting symptoms) from baseline in PUQE score at day 15 with Diclegis® compared to placebo. Diclegis® was not studied in women with hyperemesis gravidarum or in pediatrics (under 18 years of age). The FDA is requiring a postmarketing study to evaluate the safety and efficacy in pediatrics consisting of an adequately powered safety and efficacy study in pregnant adolescent girls, 12 to 17 years of age, with nausea and vomiting of pregnancy who are appropriate candidates for pharmacological therapy.[9] This required postmarking study is scheduled to end in January 2018.

The cost per tablet is $5.02. Based on the maximum daily dosage of four tablets, the average daily cost is $20.08 and the average monthly cost is $602.40.

Recommendations[10]

The College of Pharmacy recommends prior authorization of Diclegis® with the following criteria:

Diclegis® (Doxylamine/Pyridoxine) Prior Authorization Criteria:

1. Nausea and vomiting associated with pregnancy; and
2. Trials with at least two non-pharmacologic therapies that have failed to relieve nausea and vomiting; and
3. Trials with at least three medications that have failed to relieve nausea and vomiting (must include a trial of ondansetron); and
4. A patient-specific, clinically significant reason why member cannot use OTC doxylamine and OTC Vitamin B-6 (pyridoxine).

PRODUCT DETAILS OF DICLEGIS® (DOXYLAMINE/PYRIDOXINE)

INDICATIONS AND USE: Diclegis® is indicated for the management of nausea and vomiting of pregnancy in women who do not respond to conservative management.

DOSAGE FORMS: 10mg doxylamine/10mg pyridoxine oral tablets.

ADMINISTRATION:

- The recommended starting dose is two tablets by mouth at bedtime on day 1. If this dose adequately controls symptoms the next day, continue taking two tablets at bedtime.
- However, if symptoms persist into the afternoon of day 2, take the usual dose of two tablets at bedtime that night then take three tablets starting on day 3 (one tablet in the morning and 2 tablets at bedtime). If this dose adequately controls symptoms, continue taking three tablets daily.
- However, if symptoms continue to persist, the dosage is increased to the maximum dose of 4 tablets per day starting on day 4 (one tablet in the morning, one tablet mid-afternoon, and 2 tablets at bedtime).
- Diclegis® should be taken on an empty stomach with a glass of water.
- Diclegis® should be taken as a daily prescription and not on an as needed basis. The prescriber should reassess the patient for continued need of Diclegis® as her pregnancy progresses.
- Diclegis® should be taken whole; do not crush, chew, or split tablets.

CONTRAINDICATIONS:

- Concomitant use of a monoamine oxidase inhibitor (MAOI) may intensify and prolong the adverse central nervous system effects of Diclegis®.
- Known hypersensitivity to doxylamine succinate, other ethanolamine derivative antihistamines, pyridoxine hydrochloride, or any inactive ingredient in the formulation.

SPECIAL POPULATIONS:

- **Pregnancy:** Diclegis® is intended for use in pregnant women, and is a Pregnancy Category A. The combination of doxylamine and pyridoxine has been the subject of many epidemiological studies (cohort, case control, and meta-analyses) designed to detect possible teratogenicity. A meta-analysis of 16 cohort and 11 case-control studies published between 1963 and 1991 reported no increased risk for malformations from first trimester exposure to doxylamine and pyridoxine, with or without dicyclomine (A product available in the UK, Debendox®, contains all three medications: doxylamine, pyridoxine, and dicyclomine). A second meta-analysis of 12 cohort and 5 case-control studies published between 1693 and 1985 reported no statistically significant relationships between fetal abnormalities and the first trimester use of the combination doxylamine and pyridoxine, with or without dicyclomine.
- **Nursing Mothers:** Diclegis® is excreted into breast milk and infant risk cannot be ruled out, so treatment with Diclegis® is not recommended in women who are breastfeeding.
- **Pediatrics:** Safety and effectiveness of Diclegis® in pediatric patients under 18 years of age have not been established.
- **Geriatrics:** No studies have been conducted in geriatric patients.
- **Renal Impairment:** No studies have been conducted in patients with renal impairment.
- **Hepatic Impairment:** No studies have been conducted in patients with hepatic impairment.

WARNINGS AND PRECAUTIONS:

- Diclegis® may cause somnolence due to the anticholinergic properties of doxylamine, an antihistamine. Patients should avoid engaging in activities requiring complete mental alertness, such as driving or operating heavy machinery, while using Diclegis® until cleared to do so by a healthcare provider.
- Concurrent use with alcohol or other CNS depressants is not recommended. This combination may result in severe drowsiness leading to falls or accidents.
- Diclegis® has anticholinergic properties and, therefore, should be used with caution in patients with asthma, increased intraocular pressure, narrow-angle glaucoma, stenosing peptic ulcer, pyloroduodenal obstruction, and urinary bladder-neck obstruction.

ADVERSE REACTIONS:

- Somnolence (14.3%)
- Adverse reactions reported in postmarking experience:
    - **Cardiac disorders:** dyspnea, palpitation, tachycardia
    - **Ear and labyrinth disorders:** vertigo
    - **Eye disorders:** blurred vision, visual disturbances
    - **Gastrointestinal disorders:** abdominal distention, abdominal pain, constipation, diarrhea
    - **General disorders and administration site conditions:** chest discomfort, fatigue, irritability, malaise
    - **Immune system disorders:** hypersensitivity
    - **Nervous system disorders:** dizziness, headache, migraines, paresthesia, psychomotor hyperactivity
    - **Psychiatric disorders:** anxiety, disorientation, insomnia, nightmares
    - **Renal and urinary disorders:** dysuria, urinary retention
    - **Skin and subcutaneous tissue disorders:** hyperhidrosis, pruritus, rash, maculopapular rash

DRUG INTERACTIONS:

- Use of Diclegis® is contraindicated in women who are taking monoamine oxidase inhibitors (MAOIs), which prolong and intensify the anticholinergic effects of antihistamines.
- Concurrent use of alcohol and other CNS depressants (such as hypnotic sedatives and tranquilizers) with Diclegis® is not recommended. This combination may result in severe drowsiness leading to falls or accidents.

PATIENT COUNSELING INFORMATION:

- Diclegis® is used in the management of nausea and vomiting of pregnancy.
- Take Diclegis® tablets whole on an empty stomach with a glass of water at the dosage prescribed by your physician. Do not crush, chew, or split tablets.
- Take Diclegis® as a daily prescription and not on an as needed basis. Your prescriber should reassess you for the continued need of Diclegis® as your pregnancy progresses.
- Diclegis® may cause drowsiness, so avoid engaging in activities requiring complete mental alertness, such as driving or operating heavy machinery, while using Diclegis® until cleared to do so by a healthcare provider.
- Do not take Diclegis® with alcohol or sedating medications, including other antihistamines (present in some cough and cold medications), opiates, and sleep aids because drowsiness could worsen, leading to falls or other accidents.

- Do not take Diclegis® if you take a monoamine oxidase inhibitor (MAOI) or medications that have MAOI properties, not limited to but including isocarboxazid, phenelzine, tranylcypromine, rasagiline, selegiline, isoniazid, linezolid, procarbazine, St. John's Wort, and reservatrol. Ask your healthcare provider for more information regarding this drug interaction.

---

[1] *American Family Physician:* Nausea and Vomiting of Pregnancy, 2003 Jul 1; 68(1): 121-128. Available online at: http://www.aafp.org/afp/2003/0701/p121.html. Last revised: July 2003; Last accessed 7/30/13.

[2] Bendectin® Drug Details. Drugs @ FDA (FDA Approved Drug Products). Available online at: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.DrugDetails. Last revised: 7/15/13; Last accessed 7/16/13.

[3] Bendectin® History, sponsored by Duchesnay USA, Inc. Available online at: http://www.bendectin.com/en/. Last revised: 4/2013; Last accessed 7/31/13.

[4] *Federal Register:* Determination that Bendectin® was not withdrawn from sale for reasons of safety or effectiveness, 1999 Aug 9; 64(152): 43190. Available online at: http://www.gpo.gov/fdsys/pkg/FR-1999-08-09/pdf/99-20362.pdf. Last revised: August 1999; Last accessed 7/16/13.

[5] Diclegis® Drug Details. Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book). Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/docs/obdetail.cfm?Appl_No=021876&TABLE1=OB_Rx. Last revised: June 2013; Last accessed 7/16/13.

[6] Diclegis® Drug Information. Micromedex 2.0. Available online at: http://www.micromedexsolutions.com/micromedex2/librarian/PFDefaultActionId/evidencexpert.DoIntegratedSe. Last revised: 7/11/13; Last accessed 7/16/13.

[7] Diclegis® Package Insert. Med Library.org. Available online at: http://medlibrary.org/lib/rx/meds/diclegis/. Last revised: April 2013; Last accessed 7/16/13.

[8] Diclegis® Full Prescribing Information. Duchesnay USA Inc. Available online at: http://www.diclegis.com/pdf/Diclegis_Full_Prescribing_Information.pdf. Last revised: April 2013; Last accessed 7/16/13.

[9] FDA New Drug Application (NDA) Approval, 4/8/13. Available online at: http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2013/021876Orig1s000ltr.pdf. Last accessed 7/17/13.

[10] *ACOG Practice Bulletin*: Nausea and Vomiting in Pregnancy; April 2004; Number 52. Available online at: http://www.molinahealthcare.com/medicaid/providers/mo/pdf/acog%20nausea%20%20vomiting%20pregnancy.pdf?E=true. Last accessed 7/30/13.

Appendix I

Fiscal Year 2013 Annual Review of Synagis® (Palivizumab)

Oklahoma Health Care Authority
August 2013

Current Prior Authorization Criteria

Prior authorization is required for all members who receive Synagis® in an outpatient setting. Synagis® is approved for members who meet the established criteria based on a modified version of the American Academy of Pediatrics (AAP) guidelines.

Current Criteria for Prior Authorization of Synagis®

A. Member Selection. Members must be included in one of the following age groups at the beginning of the RSV season:*

1) Infants and children less than 24 months old with Chronic Lung Disease (CLD) (formerly bronchopulmonary dysplasia) who have required medical treatment (O_2, bronchodilator, corticosteroid, or diuretic therapy) for CLD in the 6 months prior to RSV season.
2) Infants up to 24 months old with moderate to severe pulmonary hypertension, cyanotic heart disease, or those on medications to control congestive heart failure.
3) Infants less than 12 months of age, born at 28 weeks gestation or earlier.
4) Infants less than 6 months of age, born at 29-31 weeks gestation.
5) Infants less than 12 months of age with congenital abnormalities of the airway.
6) Infants less than 12 months of age with severe neuromuscular disease.
7) Infants, up to 3 months old at the start of RSV season, born at 32-34 weeks gestation, who have one of the following risk factors: (up to three doses only)
    a. Child care attendance
    b. Siblings younger than 5 years of age

* Treatment is authorized for the entire RSV season (as indicated) except for members meeting criteria #7, in which case, a maximum of 3 doses will be authorized. Prescribers may request special consideration for additional doses (up to the end of the RSV season as indicated) on an individual patient basis for members meeting criteria #7.

B. Length of treatment. Synagis® is approved for use only during RSV season. Approval dates were from November 1 through March 31.

C. Units authorized. The maximum duration of therapy is five (5) doses, with a dose to be administered no more often than every 30 days. Infants born at 32-34 weeks gestation will receive a maximum of three doses. Members given doses more frequently than every 30 days will not be authorized for additional doses. Doses administered prior to the member's discharge from a hospital will be counted as one of the approved total.

D. Dose-pooling. To avoid unnecessary risk to the patient, multiple patients are not to be treated from a single vial. Failure to follow this recommendation will result in referral of the provider to the Quality Assurance Committee of the Oklahoma Health Care Authority.

Utilization of Synagis® (Palivizumab)

For the period of November 1, 2012 through March 31, 2013, a total of 578 SoonerCare members received Synagis® from a pharmacy provider. There were no claims submitted by physicians.

Pharmacy Claims

Season	Members	Claims	Cost	Cost/Claim	Units	Days
2011- 12	710	2,747	$5,604,686.87	$2,040.29	2,488	82,398
2012- 13	578	2,258	$4,861,946.40	$2,153.21	2,027	67,700
% Change	-18.60%	-17.80%	-13.30%	5.50%	-18.50%	-17.80%
Change	-132	-489	-$742,740.47	$112.92	-461	-14,698

Pharmacy Claim Details for Season 2012-2013

Product	Total Claims	Total Units	Total Days	Total Cost	Total Members
Synagis® 50 mg/0.5 ml vial	686	343	20,578	$865,487.39	339
Synagis® 100 mg/ml vial	1,572	1,685	47,122	$3,996,459.01	525
Total	**2,258**	**2,028**	**67,700**	**$4,861,946.40**	**578***

*Total unduplicated members

Cost per Vial

Vial Size	Cost per Vial
Synagis® 50 mg/0.5 ml vial	$1,263.98
Synagis® 100 mg/ml vial	$2,386.77

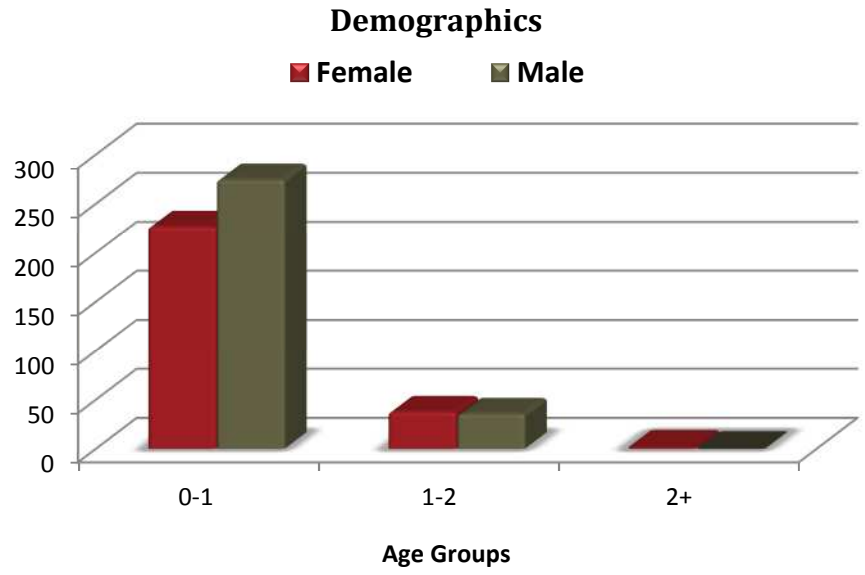
Prior Authorization of Synagis® (Palivizumab)

A total of 1,324 petitions were submitted for consideration of Synagis® (palivizumab) during the 2012-2013 RSV Season. The following shows the status of the petitions submitted.

Approved	700
Denied	230
Incomplete	394
Subsequently Approved	158

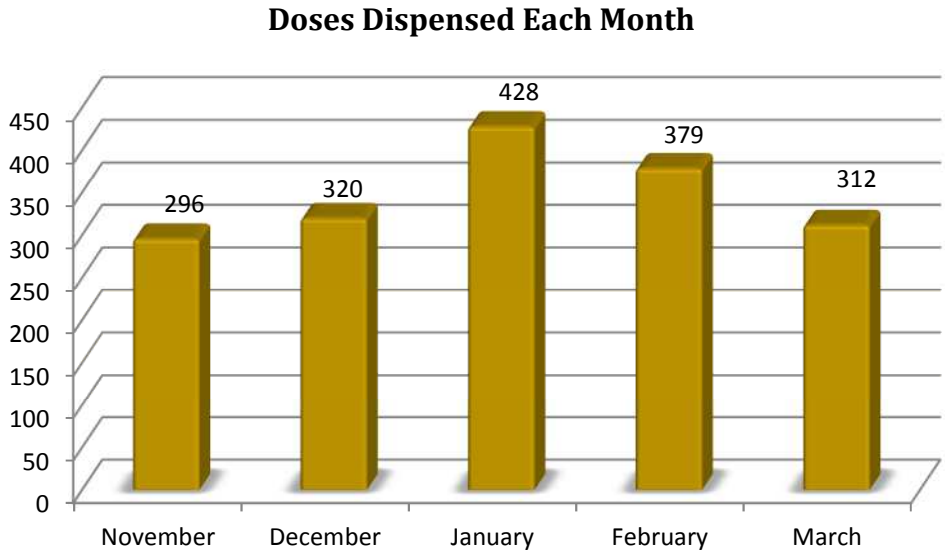
Demographics

Claims were reviewed to determine the age and gender of the members. All members were under 2 years of age at the start of the RSV season.



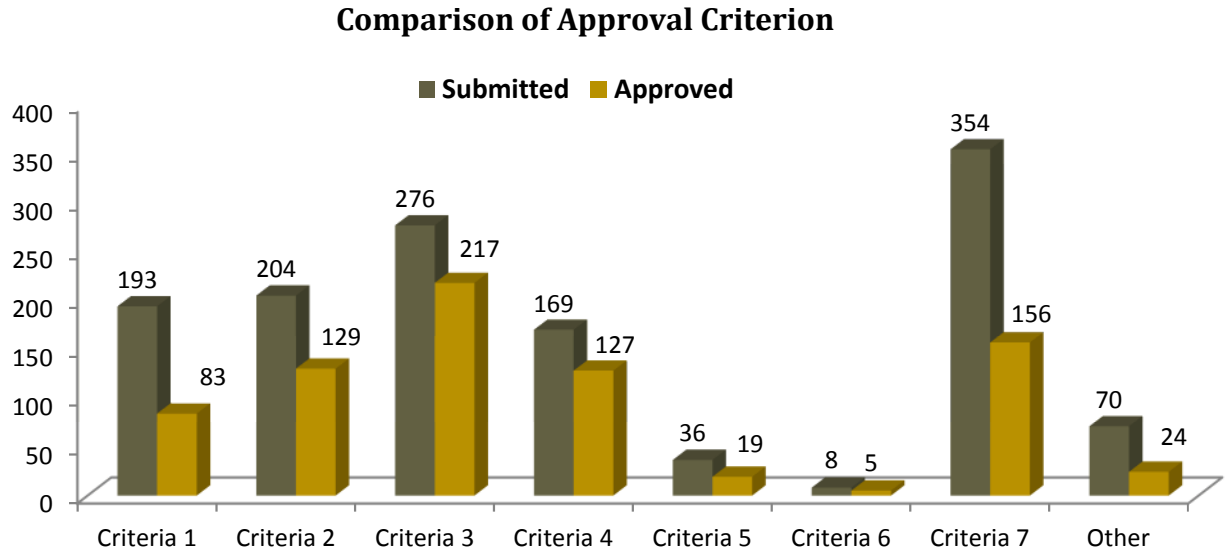
Dosing Data

A total of **1,735 doses** were given through the season. The average cost per dose was **$2,804.00**. Synagis® was limited to 5 doses for the season. Members born at 32-34 weeks gestation received a maximum of 3 doses.

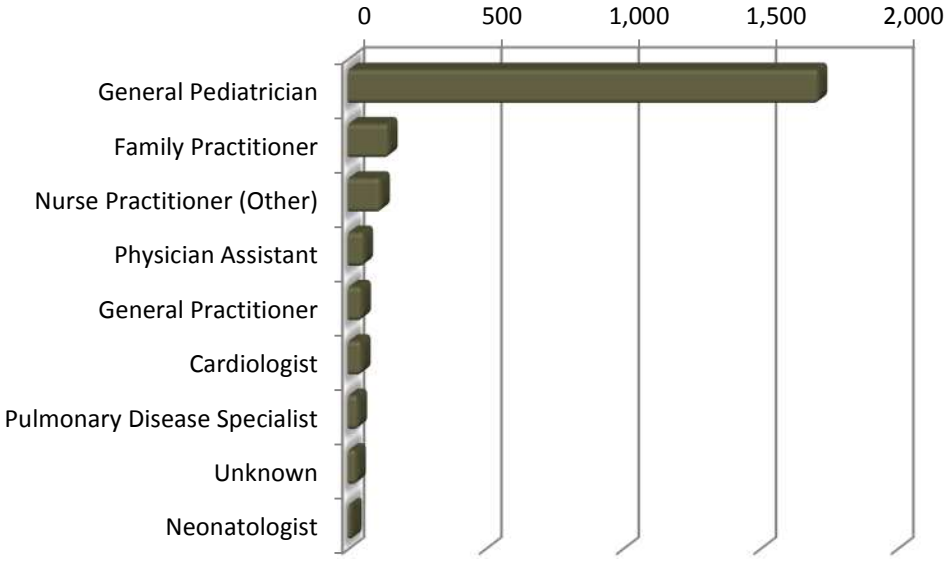


Approval Criteria

The criteria that were submitted and met for the approved petitions were tracked and totaled. Members meeting more than one criterion were counted in each category. A total of 210 doses were reported to have been dispensed prior to discharge from the hospital.



Prescriber Specialty by Number of Claims



Conclusions

Referrals to Care Management Services

To maximize appropriate referrals, continuity of care, and compliance, OHCA Care Management Services are available to assist with infants felt to be at increased risk of noncompliance. Nurse managers contact the parents to discuss and educate them about the importance of getting Synagis® each month, as well as other safety issues. The following message is sent back to the prescriber and the pharmacy with each approved petition:

- *For patients at risk of non-compliance, OHCA Care Management Services are available to assist. Please contact them at 877-252-6002.*

For the 2012-2013 RSV season, **122 children** were referred to the Care Management Services. Of these 83 were contacted.

RSV Season Recap

Oklahoma State Health Department surveillance data indicates a much earlier start to the 2012-2013 RSV season with increased incidence reported in early November. The northwestern quarter of the state reported high incidence of RSV even when the rest of the state reported none, so data may be an accurate reflection of the season. The peak level occurred in mid-December and by early March the number of cases had decreased to below the 10% threshold. The CDC did not do surveillance for Oklahoma during last RSV season.

Recommendations

The College of Pharmacy recommends no changes to this category for the upcoming RSV season.

Appendix J

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

FDA NEWS RELEASE

For Immediate Release: July 12, 2013

FDA approves new treatment for a type of late-stage lung cancer

The U.S. Food and Drug Administration today approved Gilotrif (afatinib) for patients with late stage (metastatic) non-small cell lung cancer (NSCLC) whose tumors express specific types of epidermal growth factor receptor (EGFR) gene mutations, as detected by an FDA-approved test. Lung cancer is the leading cause of cancer-related death among men and women. According to the National Cancer Institute, an estimated 228,190 Americans will be diagnosed with lung cancer, and 159,480 will die from the disease this year. About 85 percent of lung cancers are NSCLC, making it the most common type of lung cancer. EGFR gene mutations are present in about 10 percent of NSCLC, with the majority of these gene mutations expressing EGFR exon 19 deletions or exon 21 L858R substitution.

Gilotrif is a tyrosine kinase inhibitor that blocks proteins that promote the development of cancerous cells. It is intended for patients whose tumors express the EGFR exon 19 deletions or exon 21 L858R substitution gene mutations. Gilotrif is being approved concurrently with the therascreen EGFR RGQ PCR Kit, a companion diagnostic that helps determine if a patient's lung cancer cells express the EGFR mutations.

In May, the FDA approved Tarceva (erlotinib) for first-line treatment of patients with NSCLC. Tarceva's new indication was approved concurrently with the cobas EGFR Mutation Test, a companion diagnostic to identify patients with tumors having the EGFR gene mutations.

The FDA's approval of the therascreen EGFR RGQ PCR Kit is based on data from the clinical study used to support Gilotrif's approval. Tumor samples from NSCLC participants in the clinical trial helped to validate the test's use for detecting EGFR mutations in this patient population.

Gilotrif's safety and effectiveness were established in a clinical study of 345 participants with metastatic NSCLC whose tumors harbored EGFR mutations. Participants were randomly assigned to receive Gilotrif or up to six cycles of the chemotherapy drugs pemetrexed and cisplatin.

Participants receiving Gilotrif had a delay in tumor growth (progression-free survival) that was 4.2 months later than those receiving chemotherapy. There was no statistically significant difference in overall survival.

Common side effects of Gilotrif include diarrhea, skin breakouts that resemble acne, dry skin, itching (pruritus), inflammation of the mouth, skin infection around the nails (paronychia), decreased appetite, decreased weight, inflammation of the bladder (cystitis), nose bleed, runny nose, fever, eye inflammation and low potassium levels in the blood (hypokalemia). Serious side effects include diarrhea that can result in kidney failure and severe dehydration, severe rash, lung inflammation and liver toxicity.

The FDA reviewed Gilotrif under its priority review program, which provides an expedited review for drugs that may provide safe and effective therapy when no satisfactory alternative therapy exists, or offer significant improvement compared to marketed products.

Gilotrif is marketed by Ridgefield, Conn.-based Boehringer Ingelheim Pharmaceuticals, Inc. The therascreen EGFR RGQ PCR Kit is manufactured by QIAGEN Manchester Ltd., based in the United Kingdom. The cobas EGFR Mutation Test is manufactured by the Roche Molecular Systems in Pleasanton, Calif., and Tarceva is co-marketed by California-based Genentech, a member of the Roche Group, and OSI Pharmaceuticals of Farmingdale, N.Y.

Safety Announcements

FDA Drug Safety Communication: FDA approves label changes for antimalarial drug mefloquine hydrochloride due to risk of serious psychiatric and nerve side effects

Safety Announcement

[7-29-2013] The U.S. Food and Drug Administration (FDA) is advising the public about strengthened and updated warnings regarding neurologic and psychiatric side effects associated with the antimalarial drug mefloquine hydrochloride. A boxed warning, the most serious kind of warning about these potential problems, has been added to the drug label. FDA has revised the patient Medication Guide dispensed with each prescription and wallet card to include this information and the possibility that the neurologic side effects may persist or become permanent. The neurologic side effects can include dizziness, loss of balance, or ringing in the ears. The psychiatric side effects can include feeling anxious, mistrustful, depressed, or having hallucinations (For a more complete list of potential side effects, see Additional Information for Patients).

Neurologic side effects can occur at any time during drug use, and can last for months to years after the drug is stopped or can be permanent. Patients, caregivers, and health care professionals should watch for these side effects. When using the drug to prevent malaria, if a patient develops neurologic or psychiatric symptoms, mefloquine should be stopped, and an alternate medicine should be used. If a patient develops neurologic or psychiatric symptoms while on mefloquine, the patient should contact the prescribing health care professional. The patient should not stop taking mefloquine before discussing symptoms with the health care professional.

Malaria is a serious disease caused by a parasite that commonly infects mosquitoes, which then bite humans. It is a major cause of death worldwide but is less common in the United States. The disease is a problem primarily in developing countries with warm climates. Persons who travel to these countries may be at risk of malaria infection and should take drugs to prevent or reduce that risk. People with malaria often experience fever, chills, and flu-like symptoms. Drugs must be taken to treat the disease if you have been infected, but may, themselves, have side effects.

FDA will continue to evaluate the safety of mefloquine and will communicate with the public again if additional information becomes available.

Safety Announcements

FDA Drug Safety Communication: FDA approves label changes to include intestinal problems (sprue-like enteropathy) linked to blood pressure medicine olmesartan medoxomil

Safety Announcement

[7-3-2013] The U.S. Food and Drug Administration (FDA) is warning that the blood pressure drug olmesartan medoxomil (marketed as Benicar, Benicar HCT, Azor, Tribenzor, and generics) can cause intestinal problems known as sprue-like enteropathy. FDA has approved changes to the labels of these drugs to include this concern.

Symptoms of sprue-like enteropathy include severe, chronic diarrhea with substantial weight loss. The enteropathy may develop months to years after starting olmesartan, and sometimes requires hospitalization. If patients taking olmesartan develop these symptoms and no other cause is found, the drug should be discontinued, and therapy with another antihypertensive started. Discontinuation of olmesartan has resulted in clinical improvement of sprue-like enteropathy symptoms in all patients.

Olmesartan medoxomil is an angiotensin II receptor blocker (ARB) approved for the treatment of high blood pressure, alone or with other antihypertensive agents, and is one of eight marketed ARB drugs. Sprue-like enteropathy has not been detected with ARB drugs other than olmesartan.

Safety Announcements

FDA Statement: FDA halts clinical trial of drug Revlimid (lenalidomide) for chronic lymphocytic leukemia due to safety concerns

Safety Announcement

[7-18-2013] The U.S. Food and Drug Administration (FDA) halted a clinical trial of the anti-cancer drug Revlimid (lenalidomide) because of significant safety concerns. The ORIGIN trial (NCT00910910), which was evaluating Revlimid treatment for a new use as an initial therapy for chronic lymphocytic leukemia (CLL) in patients 65 years and older, showed higher rates of death in patients treated with Revlimid compared to those treated with chlorambucil. In addition, FDA has determined that the clinical trial is unlikely to achieve its main objective to reduce the amount of time for the leukemia to progress or the patient to die. FDA is continuing to review the trial results and will communicate any additional important information from its investigation. Patients with CLL receiving Revlimid should discuss their treatment options with their health care professionals.

Health care professionals should be aware that Revlimid is not approved to treat CLL. Tumor flare reactions have occurred during investigational use of Revlimid for CLL. Patients should talk to their health care professionals if they have any questions or concerns about Revlimid.

Revlimid is still considered safe and effective for the following approved uses:

- Treatment of patients with multiple myeloma who have received at least one prior medicine, when taken along with the medicine dexamethasone.
- Treatment of patients who have a type of myelodysplastic syndrome (MDS) known as deletion 5q MDS, where part of chromosome 5 is missing. Patients with this type of

MDS may have low red blood cell counts that require treatment with blood transfusions.

- Treatment of patients with mantle cell lymphoma whose disease does not respond to or comes back after treatment with two prior medicines, one of which was bortezomib. Mantle cell lymphoma is a cancer of a type of white blood cell called lymphocytes that are in the lymph nodes.

Based on the preliminary survival data recently provided to FDA from Revlimid's manufacturer, Celgene, on July 11, 2013, patients with CLL treated with Revlimid had a 92% increased risk for death compared to patients with CLL treated with chlorambucil (34 deaths out of 210 patients in Revlimid arm vs. 18 deaths out of 211 patients in chlorambucil arm, respectively).
FDA will communicate any new information on Revlimid and this clinical trial when it becomes available. FDA urges health care professionals and patients to report adverse events involving Revlimid to the FDA MedWatch program.

Safety Announcements

FDA Drug Safety Communication: FDA limits usage of Nizoral (ketoconazole) oral tablets due to potentially fatal liver injury and risk of drug interactions and adrenal gland problems

Safety Announcement
[7-26-2013] The U.S. Food and Drug Administration (FDA) is taking several actions related to Nizoral (ketoconazole) oral tablets, including limiting the drug's use, warning that it can cause severe liver injuries and adrenal gland problems and advising that it can lead to harmful drug interactions with other medications. FDA has approved label changes and added a new Medication Guide to address these safety issues. As a result, Nizoral oral tablets should not be a first-line treatment for any fungal infection. Nizoral should be used for the treatment of certain fungal infections, known as endemic mycoses, only when alternative antifungal therapies are not available or tolerated.
The topical formulations of Nizoral have not been associated with liver damage, adrenal problems, or drug interactions. These formulations include creams, shampoos, foams, and gels applied to the skin, unlike the Nizoral tablets, which are taken by mouth.
Liver Injury (Hepatotoxicity)
Nizoral tablets can cause liver injury, which may potentially result in liver transplantation or death. FDA has revised the Boxed Warning, added a strong recommendation against its use (contraindication) in patients with liver disease, and included new recommendations for assessing and monitoring patients for liver toxicity.
Serious liver damage has occurred in patients receiving high doses of Nizoral for short periods of time as well as those receiving low doses for long periods. Some of these patients had no obvious risk factors for liver disease. The liver injury is sometimes reversible upon stopping the drug, but that is not always possible.
Adrenal Gland Problems (Adrenal Insufficiency)
Nizoral tablets may cause adrenal insufficiency by decreasing the body's production of hormones called corticosteroids. Corticosteroids are produced by the adrenal glands, which are small glands located on top of each kidney. Corticosteroids affect the body's balance of water and salts and minerals (electrolytes). Health care professionals should monitor adrenal function

in patients taking Nizoral tablets who have existing adrenal problems or in patients who are under prolonged periods of stress such as those who have had a recent major surgery or who are under intensive care in the hospital.

Drug Interactions

Nizoral tablets may interact with other drugs a patient is taking and can result in serious and potentially life-threatening outcomes, such as heart rhythm problems. All medications that a patient is currently taking should be assessed for possible interactions with Nizoral tablets.

In summary, the drug label for Nizoral tablets has been updated to include the following information:

- Limitation of the usage of Nizoral tablets by removing indications in which the risk outweighs the benefits. The use of ketoconazole tablets in *Candida* and dermatophyte infections is no longer indicated. Nizoral tablets should be used only when other antifungal drugs are not available or tolerated by the patient.
- Nizoral tablets are indicated only for the treatment of the following fungal infections: blastomycosis, coccidioidomycosis, histoplasmosis, chromomycosis, and paracoccidioidomycosis in patients in whom other treatments have failed or who are intolerant to other therapies.
- Nizoral tablets are not indicated for the treatment of fungal infections of the skin or nails.
- A new contraindication that Nizoral tablets should not be used in patients with acute or chronic liver disease.
- Updated information on the risk of liver injury, or hepatotoxicity, with new assessment and monitoring recommendations.
- Updated information on drug interactions.
- A warning regarding adrenal insufficiency with recommendations for monitoring populations at risk.

FDA has also approved a new patient Medication Guide containing information on the potential risks associated with Nizoral tablets, which must be dispensed with every prescription for the drug.

In addition to the indications for treatment of infections caused by dermatophytes and Candida, the previous US drug label also included indications for the following serious fungal infections: blastomycosis, coccidioidomycosis, histoplasmosis, chromomycosis, and paracoccidioidomycosis. In the revised US drug label, indications for dermatophyte and Candida infections have been removed and the indications for treatment of blastomycosis, coccidioidomycosis, histoplasmosis, chromomycosis, and paracoccidioidomycosis have been retained only for patients in whom other antifungal treatments have failed or are not tolerated.

FDA will continue to evaluate the safety of Nizoral tablets and will communicate with the public again if additional information becomes available.

Current Drug Shortages Index (as of July 24, 2013):

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

Acetylcysteine Inhalation Solution UPDATED 7/19/2013
Acyclovir Sodium Injection (initial posting 11/13/2012)
Alteplase (Cathflo Activase) (initial posting 1/27/2012)
Amikacin Injection UPDATED 7/22/2013
Aminocaproic Acid Injection (initial posting 3/8/2013)
Aminophylline (initial posting 12/10/2012) UPDATED 7/18/2013
Ammonium Chloride Injection (initial posting 3/8/2013)
Amytal Sodium Injection (initial posting date 1/31/2013)
Atracurium Besylate (initial posting 2/27/2012)
Atropine Sulfate Injection UPDATED 7/18/2013
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) UPDATED 7/22/2013
Bumetanide Injection (initial posting 6/21/2012)
Bupivacaine Hydrochloride (Marcaine, Sensorcaine) Injection UPDATED 7/18/2013
Buprenorphine Hydrochloride (Buprenex) Injection
Caffeine and Ergotamine Tartrate (Cafergot) Tablets (initial posting 3/8/2012)
Caffeine Anhydrous (125mg/mL); Sodium Benzoate (125mg/mL) Injection
Calcium Chloride Injection (initial posting 12/13/2012) UPDATED 7/18/2013
Calcium Gluconate Injection (initial posting 1/10/2013) UPDATED 7/19/2013
Chromic Chloride Injection UPDATED 7/18/2013
Cidofovir Injection (initial posting 2/15/2013)
Citric Acid; Gluconolactone; Magnesium Carbonate (Renacidin) Solution for Irrigation (initial posting 6/30/2012)
Copper (Cupric Chloride) Injection (initial posting 4/25/2013)
Cyanocobalamin Injection (initial posting 1/25/2013) UPDATED 7/22/2013
Daunorubicin Hydrochloride Solution for Injection
Denileukin Diftitox (Ontak) (initial posting 9/22/2012)
Desmopressin Acetate (DDAVP) Injection (initial posting 5/7/2013)
Dexamethasone Sodium Phosphate Injection (initial posting 1/15/2013)
Dexrazoxane (Zinecard) Injection
Dextrose Injection (initial posting 5/23/2012) UPDATED 7/18/2013
Dipyridamole Injection (initial posting 7/24/2012)
Dobutamine Hydrochloride Injection (initial posting 4/26/2013)
Doxorubicin (Adriamycin) Lyophilized Powder (initial posting 12/2/2011)
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 7/23/2013
Epinephrine 1mg/mL (Preservative Free) (initial posting 6/21/2012)
Ethiodol (Ethiodized Oil) Ampules
Etomidate (Amidate) Injection (initial posting 2/9/2012) UPDATED 7/18/2013
Fentanyl Citrate (Sublimaze) Injection UPDATED 7/18/2013
Fluphenazine Decanoate Injection 4/25/2013 UPDATED 7/18/2013

Fluphenazine Hydrochloride Injection 4/29/2013 UPDATED 7/19/2013
Fluticasone Propionate and Salmeterol (Advair HFA) Inhalation Aerosol (initial posting date) - 10/17/2012)
Fosphenytoin Sodium (Cerebyx) Injection (initial posting 3/30/2012) UPDATED 7/22/2013
Furosemide Injection (initial posting 6/20/2012) UPDATED 7/18/2013
Gallium Nitrate (Ganite) Injection (initial posting 4/4/2012)
Heparin Sodium Injection (initial posting 7/5/2012) UPDATED 7/18/2013
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) UPDATED 7/18/2013
Intravenous Fat Emulsion
Isoniazid; Rifampin (Rifamate) Capsules 3/15/2013
Ketorolac Tromethamine Injection UPDATED 7/19/2013
Leucovorin Calcium Lyophilized Powder for Injection UPDATED 7/22/2013
Leuprolide Acetate Injection
Levothyroxine Sodium (Levoxyl) Tablets (initial posting date - 3/15/2013)
Lidocaine Hydrochloride (Xylocaine) Injection (initial posting date - 2/22/2012) UPDATED 7/19/2013
Liotrix (Thyrolar) Tablets
Lomustine Capsules (initial posting date - 5/9/2013)
Lorazepam (Ativan) Injection
Magnesium Sulfate Injection UPDATED 7/22/2013
Mannitol (Osmitrol, Resectisol) Injection (initial posting date - 12/21/2011) UPDATED 7/19/2013
Mecasermin [rDNA origin] (Increlex) Injection (initial posting date - 4/26/2013)
Methazolamide (Glauctabs, Neptazane) Tablets
Methoxsalen 1% (Oxsoralen) Topical Lotion
Methyldopate Hydrochloride Injection
Methylin Chewable Tablets (initial posting date - 2 /19/2013)
Methylphenidate Hydrochloride ER Tablets (initial posting date - 2/19/2013)
Methylphenidate Hydrochloride Tablets (initial posting date - 2/19/2013)
Metoclopramide (Reglan) Injection UPDATED 7/22/2013
Midazolam Hydrochloride (Versed) Injection UPDATED 7/22/2013
Morphine Sulfate Injection UPDATED 7/18/2013
Morphine Sulfate (Astramorph PF, Duramorph, Infumorph) Injection (Preservative Free)
Multi-Vitamin Infusion (Adult and Pediatric) UPDATED 7/24/2013
Nalbuphine Hydrochloride (Nubain) Injection (initial posting 5/15/2012)
Neostigmine Methylsulfate Injection (initial posting 1/14/2013)
Nitroglycerin Ointment USP, 2% (Nitro-Bid) (Initial posting 10/23/2012)
Ondansetron (Zofran) 2mg/mL Injection
Oseltamivir Phosphate (Tamiflu) Powder for Oral Suspension (Initial posting 1/10/2013) UPDATED 7/18/2013
Pancuronium Bromide Injection
Papaverine Hydrochloride Injection (initial posting 12/17/2012)

Pentamidine Isethionate (NebuPent) Inhalant (initial posting 8/27/2012)
Pentamidine Isethionate (Pentam 300) Injection (initial posting 8/27/2012)
Phosphate (Glycophos) Injection (initial posting 5/29/2013)
Pilocarpine HCL Opthalmic Gel 4% (Pilopine HS) (initial posting 6/1/2012)
Potassium Acetate Injection, USP 2mEq/mL
Potassium Chloride Injection (initial posting 5/15/2012) UPDATED 7/19/2013
Potassium Phosphate Injection
Procainamide HCL Injection UPDATED 7/18/2013
Prochlorperazine Injection (initial posting 1/30/2012)
Promethazine Injection (initial posting 2/10/2012) UPDATED 7/22/2013
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
Sincalide (Kinevac) Lyophilized Powder for Injection (initial posting 6/21/2013)
Sodium Acetate Injection (initial posting 1/31/2012) UPDATED 7/18/2013
Sodium Benzoate and Sodium Phenylacetate (Ammonul) Injection
Sodium Chloride 0.9% (5.8mL and 20mL) (initial posting 5/4/2012)
Sodium Chloride 23.4% UPDATED 7/19/2013
Sodium Phosphate Injection
Succinylcholine (Anectine, Quelicin) Injection (initial posting 8/17/2012)
Sufentanil Citrate (Sufenta) Injection
Sulfamethoxazole 80mg/ml;Trimethoprim 16mg/ml (SMX/TMP) (Bactrim) Injection
Technetium Tc99m Bicisate for Injection (Neurolite) (initial posting 5/4/2012)
Technetium Tc99m Sestamibi Kit for Injection (Cardiolite) (initial posting 5/4/2012)
Telavancin (Vibativ) Injection
Tetracycline Capsules
Thiotepa (Thioplex) for Injection
Ticarcillin Disodium/Clavulanic Potassium (Timentin) Injection (initial posting 8/16/12) UPDATED 7/18/2013
Tobramycin Solution for Injection UPDATED 7/22/2013
Trace Elements (initial posting 1/24/2013)
Tromethamine (Tham) Injection (initial posting 5/2/2012) UPDATED 7/18/2013
Verapamil Hydrochloride Injection, USP (initial posting 4/17/2013) UPDATED 7/18/2013
Vinblastine Sulfate Injection (initial posting 1/31/2012) UPDATED 7/19/2013
Vitamin A Palmitate (Aquasol A)
Zinc Injection (initial posting 2/15/2012) UPDATED 7/18/2013