# Drug Utilization Review Board

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

Wednesday
September 12, 2012
6:00 p.m.

# The University of Oklahoma

## Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS


MEMORANDUM

TO: Drug Utilization Review Board Members

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

SUBJECT: Packet Contents for Board Meeting – September 12, 2012

DATE: September 6, 2012

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 September meeting. Material is arranged in order of the Agenda.

Call to Order

Public Comment Forum

Action Item – Approval of DUR Board Meeting Minutes – See Appendix A.

Update on DUR / MCAU Program – See Appendix B.

Action Item – Vote to Prior Authorize Select Gonadotropin-Releasing Hormone Analogs for Central Precocious Puberty – See Appendix C.

Action Item – Atypical Antipsychotics Annual Review Follow-Up – See Appendix D.

Action Item – Annual Review of Benign Prostatic Hyperplasia Medications and 30 Day Notice to Prior Authorize Cialis® – See Appendix E.

Action Item – Annual Review of Adcirca® and Revatio® – See Appendix F.

Action Item – Annual Review of Benlysta® – See Appendix G.

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

FDA and DEA Updates – See Appendix I.

Future Business

Adjournment


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# Oklahoma Health Care Authority
# Drug Utilization Review Board
(DUR Board)
**Meeting – September 12, 2012 @ 6:00 p.m.**

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

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## 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. August 8, 2012 DUR Minutes – Vote
- B. August 9, 2012 DUR Recommendation Memorandum
- C. Correspondence

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

**4. Update on DUR / Medication Coverage Authorization Unit – See Appendix B.**
- A. Retrospective Drug Utilization Review Response for March 2012
- B. Medication Coverage Activity for August 2012
- C. Pharmacy Help Desk Activity for August 2012
- D. SoonerCare Atypical Rx Program Update

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

**5. Action Item – Vote to Prior Authorize Select Gonadotropin-Releasing Hormone Analogs for Central Precocious Puberty – See Appendix C.**
- A. COP Recommendations

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

**6. Action Item – Atypical Antipsychotics Annual Review Follow-Up – See Appendix D.**
- A. Background
- B. COP Recommendations

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

**7. Action Item – Annual Review of Benign Prostatic Hyperplasia Medications and 30 Day Notice to Prior Authorize Cialis® – See Appendix E.**

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

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

**8. Action Item – Annual Review of Adcirca® and Revatio® – See Appendix F.**

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

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

**9. Action Item – Annual Review of Benlysta® – See Appendix G.**

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

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

**10. 30 Day notice to Prior Authorize Neupro® – See Appendix H.**

A. Product Summary
B. COP Recommendations
C. Product Details

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

**11. FDA and DEA Updates – See Appendix I.**

**12. Future Business**

A. Annual Reviews
B. New Product Reviews
C. Medical Product Reviews

**13. Adjournment**

# Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES of MEETING of AUGUST 8, 2012

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

| COLLEGE of PHARMACY STAFF: | PRESENT |
|---|---|
| Terry Cothran, D.Ph.; Pharmacy Director | X |
| Karen Egesdal, D.Ph.; SMAC-ProDUR Coordinator/OHCA Liaison | X |
| Shellie Keast, Pharm.D, M.S.; DUR Manager | X |
| Chris Le, Pharm.D.; Clinical Coordinator | X |
| Mark Livesay, Operations Manager | X |
| Carol Moore, Pharm.D.; Clinical Pharmacist | X |
| Brandy Nawaz, Pharm.D.; Clinical Pharmacist | X |
| Neeraj Patel, Pharm.D.; Clinical Pharmacist | X |
| Lester A. Reinke, Ph.D.; Associate Dean for Graduate Studies & Research | X |
| Leslie Robinson, D.Ph.; PA Coordinator | X |
| Jennifer Sipols, Pharm.D.; Clinical Pharmacist | X |
| Jo Nel Weber, Pharm.D.; Clinical Pharmacist | X |
| Graduate Students: Amany Hussein, Manish Mittal | X |
| Visiting Pharmacy Student(s): Christian Banasky, Denton Chancey | X |

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

| OTHERS PRESENT: | | |
|---|---|---|
| Kathy Phillips, Novo Nordisk | Tone Jones, Sunovion | Deron Grothe, Teva Pharm. |
| Kimberly Herriott, BMS | Sam Smothers, MedImmune | Gail Israel, NAMI OK |
| Linda Cantu, BMS | Corben Rosenthal, MHA/Tulsa | Dave Spoat, BMS |
| Ken Stranigan, Ipsen | Jeff Vucelk, Ipsen | Todd Ruffner, Ipsen |
| Warren Tayes, Merck & Co Inc. | Audrey Rattan, Otsuka | Charlene Kaiser, Amgen |
| David Gordon, NAMI | Richard Ponder, J&J | Donald Kempin, Novo Nordisk |
| Brent Bumpes, Endo | Scott LaSoisa, Genentech | Tom O'Donnell, Genentech |
| Chen Ritchie, Otsuka | Michael Hathaway, Otsuka | Clint Degner, Novartis |

| PRESENT FOR PUBLIC COMMENT: | |
|---|---|
| Agenda Item No. 8 | Bill Clark, Bristol Myers Squibb |
| Agenda Item No. 8 | Paul Davis, Mental Health Association/Tulsa |
| Agenda Item No. 9 | Drew Bernstein, MedImmune |

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. 8 Bill Clark, Bristol Myers Squibb

Agenda Item No. 8 Paul Davis, Mental Health Association/Tulsa

Agenda Item No. 9 Drew Bernstein, MedImmune

ACTION: NONE REQUIRED

AGENDA ITEM NO. 3: APPROVAL OF DUR BOARD MINUTES

3A: July 11, 2012 DUR Minutes

Dr. Rhymer moved to approve as amended to add himself to the Board members present on July 11, 2012; seconded by Dr. Feightner.

ACTION: MOTION CARRIED

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

4A: Retrospective Drug Utilization Review: April 2012

4B: Retrospective Drug Utilization Review Response: February 2012

4C: Medication Coverage Activity: July 2012

4D: Pharmacy Help Desk Activity: July 2012

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: VOTE TO PRIOR AUTHORIZE QNASL™ AND DYMISTA™

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

Ms. Varalli-Claypool moved to approve as submitted; seconded by Dr. Feightner.

ACTION: MOTION CARRIED

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

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

Dr. Preslar moved to approve as submitted; seconded by Ms. Varalli-Claypool.

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: VOTE TO PRIOR AUTHORIZE BOTULINUM TOXIN PRODUCTS

Materials included in agenda packet; presented by Drs. Sipols and Keast.

Dr. Rhymer moved to approve as submitted; seconded by Dr. Feightner.

ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: ATYPICAL ANTIPSYCHOTICS ANNUAL REVIEW FOLLOW-UP

For Public Comment: Bill Clark, Bristol Myers Squibb

For Public Comment: Paul Davis, Mental Health Association/Tulsa

Materials included in agenda packet; presented by Drs. Le and Keast.

Dr. Feightner moved to approve with the additional request to review the tier placement of quetiapine long-acting; seconded by Ms. Varalli-Claypool.

ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: ANNUAL REVIEW OF SYNAGIS®
For Public Comment: Drew Bernstein
Materials included in agenda packet; presented by Dr. Moore.
Dr. Preslar moved to approve recommendations with "born before 35 weeks gestation" removed; seconded by Ms. Varalli-Claypool.
ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: 30-DAY NOTICE TO PRIOR AUTHORIZE SELECT GONADOTROPIN-RELEASING HORMONE ANALOGS FOR CENTRAL PRECOCIOUS PUBERTY
Materials included in agenda packet; presented by Drs. Keast and Moore.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 11: FDA & DEA UPDATES
Materials included in agenda packet; presented by Dr. Cothran.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 12: FUTURE BUSINESS
Materials included in agenda packet; submitted by Dr. Cothran.
A: Annual Review of Pradaxa®
B: New Fiscal Year Annual Reviews
C: New Product Reviews
D: Medical Product Reviews
ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: ADJOURNMENT
The meeting was adjourned at 7:10 p.m.

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

# Memorandum

Date: August 9, 2012

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

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

Subject: DUR Board Recommendations from Meeting of August 8, 2012

Note: The minutes for the July meeting were updated to reflect that Dr. Rhymer was present.

Recommendation 1: Vote to Prior Authorize Qnasl™ (beclomethasone dipropionate) and Dymista™ (azelastine/fluticasone)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends placement of Qnasl™ (beclomethasone dipropionate) and Dymista™ (azelastine/fluticasone) into Tier 3 of the Nasal Allergy Product Based Prior Authorization category.

Criteria for nasal allergy products are as follows:

1. The following criteria are required for approval of a Tier 2 product:
    a. Documented adverse effect or contraindication to the preferred products.
    b. Failure with all Tier 1 medications defined as no beneficial response after at least three weeks use at the maximum recommended dose.
2. The following criteria are required for approval of a Tier 3 product:
    a. All Tier 2 criteria must be met.

b. Failure with all available Tier 2 products defined as no beneficial response after at least three weeks use at the maximum recommended dose.

3. Approvals will be for the duration of three months, except for members with chronic diseases such as asthma or COPD, in which case authorizations will be for the duration of one year.
4. No grandfathering of Tier 2 or Tier 3 products will be allowed for this category.
5. For 2 to 4 year olds, the age appropriate lower-tiered generic products must be used prior to the use of higher tiered products.
6. Petitions for Dymista™ (azelastine/fluticasone) also require a patient specific, clinically significant reason why both products cannot be used separately.

| Nasal Allergy Products | | |
|---|---|---|
| Tier 1 | Tier 2 | Tier 3 |
| Fluticasone(Flonase®) | Beclomethasone(Beconase®AQ) | Ciclesonide (Omnaris®) |
| Flunisolide (Nasalide®, Nasarel®) | Olapatadine (Patanase®) | Budesonide (Rhinocort® AQ) |
| Triamcinolone (Nasacort® AQ) | | Fluticasone (Veramyst®) |
| | | Mometasone (Nasonex®) |
| | | Azelastine (Astepro®) |
| | | Azelastine (Astelin®) |
| | | Azelastine/fluticasone (Dymista™ ) |
| | | Beclomethasone (Qnasl™ ) |

Recommendation 2: Vote to Prior Authorize Subsys™ (fentanyl sublingual spray)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends placement of Subsys™ (fentanyl sublingual spray) within the Oncology Only Tier of the Narcotic Analgesics PBPA category subject to the following criteria:

1. FDA approved indication of breakthrough cancer pain.
2. Age of 18 years or older.
3. Quantity limit of #120 sprays per 30 days (4 packs of #30 sprays).
4. Reason why other forms of fentanyl breakthrough pain therapy cannot be used.

Recommendation 3: Vote to Prior Authorize Botulinum Toxin Products

MOTION CARRIED by unanimous approval.

The OHCA physicians who review medical prior authorizations have recommended a list of approved diagnoses codes. The College of Pharmacy recommends:

- Coverage of indications on the recommended list to ensure appropriate use of these medications.
- A diagnosis of chronic migraine will require manual review (tension headaches are not a covered diagnosis).
- Cosmetic indications will not be covered.

| Diagnosis Code | Long Diagnosis Description |
|---|---|
| 333.71 | Athetoid cerebral palsy, double athetosis (syndrome) Vogt's disease, excludes infantile cerebral palsy (343.0-343.9) |
| 333.81 | Blepharospasm |
| 333.82 | Orofacial dyskinesia |
| 333.83 | Spasmodic torticollis |
| 334.1 | Hereditary spastic paraplegia |
| 341.1 | Schilder's disease |
| 342.11 | Spastic hemiplegia affecting dominant side |
| 342.12 | Spastic hemiplegia affecting nondominant side |
| 343.0 | Diplegic infantile cerebral palsy |
| 343.1 | Hemiplegic infantile cerebral palsy |
| 343.2 | Quadriplegic infantile cerebral palsy |
| 343.3 | Monoplegic infantile cerebral palsy |
| 343.4 | Infantile hemiplegia |
| 343.8 | Other specified infantile cerebral palsy |
| 343.9 | Unspecified infantile cerebral palsy |
| 344.01 | Quadriplegia and quadriparesis, C1-C4, complete |
| 344.02 | Quadriplegia and quadriparesis, C1-C4, incomplete |
| 344.03 | Quadriplegia and quadriparesis, C5-C7, complete |
| 344.04 | C5-C7, incomplete |
| 344.1 | Paraplegia |
| 344.2 | Diplegia of upper limbs |
| 344.30 | Monoplegia of lower limb affecting unspecified side |
| 344.31 | Monoplegia of lower limb affecting dominant side |
| 344.32 | Monoplegia of lower limb affecting nondominant side |
| 344.40 | Monoplegia of upper limb affecting unspecified side |
| 344.41 | Monoplegia of upper limb affecting dominant side |
| 344.42 | Monoplegia of upper limb affecting nondominant side |
| 351.8 | Other facial nerve disorders |
| 374.03 | Spastic entropion |
| 374.13 | Spastic ectropion |
| 378.0 | Esotropia |
| 378.00 | Unspecified esotropia |
| 378.01 | Monocular esotropia |
| 378.02 | Monocular esotropia with A pattern |
| 378.03 | Monocular esotropia with V pattern |
| 378.04 | Monocular esotropia with other noncomitancies |
| 378.05 | Alternating esotropia |
| 378.06 | Alternating esotropia with A pattern |
| 378.07 | Alternating esotropia with V pattern |

| | |
|---|---|
| 378.08 | Alternating esotropia with other noncomitancies |
| 378.1 | Exotropia |
| 378.10 | Unspecified exotropia |
| 378.11 | Monocular exotropia |
| 378.12 | Monocular exotropia with A pattern |
| 378.13 | Monocular exotropia with V pattern |
| 378.14 | Monocular exotropia with other noncomitancies |
| 378.15 | Alternating exotropia |
| 378.16 | Alternating exotropia with A pattern |
| 378.17 | Alternating exotropia with V pattern |
| 378.18 | Alternating exotropia with other noncomitancies |
| 378.2 | Intermittent heterotropia |
| 378.20 | Unspecified intermittent heterotropia |
| 378.21 | Intermittent esotropia, monocular |
| 378.22 | Intermittent esotropia, alternating |
| 378.23 | Intermittent exotropia, monocular |
| 378.24 | Intermittent exotropia, alternating |
| 378.3 | Other and unspecified heterotropia |
| 378.30 | Unspecified heterotropia |
| 378.31 | Hypertropia |
| 378.32 | Hypotropia |
| 378.33 | Cyclotropia |
| 378.34 | Monofixation syndrome |
| 378.35 | Accommodative component in esotropia |
| 378.4 | Heterophoria |
| 378.40 | Unspecified heterophoria |
| 378.41 | Esophoria |
| 378.42 | Exophoria |
| 378.43 | Vertical heterophoria |
| 378.44 | Cyclophoria |
| 378.45 | Alternating hyperphoria |
| 378.5 | Paralytic strabismus |
| 378.50 | Unspecified paralytic strabismus |
| 378.51 | Paralytic strabismus, third or oculomotor nerve palsy, partial |
| 378.52 | Paralytic strabismus, third or oculomotor nerve palsy, total |
| 378.53 | Paralytic strabismus, fourth or trochlear nerve palsy |
| 378.54 | Paralytic strabismus, sixth or abducens nerve palsy |
| 378.55 | Paralytic strabismus, external ophthalmoplegia |
| 378.56 | Paralytic strabismus, total ophthalmoplegia |
| 378.6 | Mechanical strabismus |
| 378.60 | Unspecified mechanical strabismus |
| 378.61 | Mechanical strabismus from Brown's (tendon) sheath syndrome |
| 378.62 | Mechanical strabismus from other musculofascial disorders |
| 378..63 | Mechanical strabismus from limited duction associated with other conditions |
| 378.7 | Other specified strabismus |
| 378.71 | Duane's syndrome |
| 378.72 | Progressive external ophthalmoplegia |
| 378.73 | Strabismus in other neuromuscular disorders |

| | |
|---|---|
| 378.8 | Other disorders of binocular eye movements |
| 378.81 | Palsy of conjugate gaze |
| 378.82 | Spasm of conjugate gaze |
| 378.83 | Convergence insufficiency or palsy in binocular eye movement |
| 378.84 | Convergence excess or spasm in binocular eye movement |
| 378.85 | Anomalies of divergence in binocular eye movement |
| 378.86 | Internuclear ophthalmoplegia |
| 378.87 | Other dissociated deviation of eye movements |
| 378.9 | Unspecified disorder of eye movements |
| 478.75 | Laryngeal spasm |
| 530.0 | Achalasia and cardiospasm |
| 565.0 | Anal fissure |
| 754.1 | Congenital musculoskeletal deformity of sternocleidomastoid muscle |
| 784.49 | Other voice and resonance disorders |

## Recommendation 4: Atypical Antipsychotic Annual Review Follow-Up

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends an addition to the atypical antipsychotic's antidepressant criteria:

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.

In addition, the College of Pharmacy also recommends investigation of an academic detailing program to positively influence the prescribing practices of atypical antipsychotics by SoonerCare providers in the state of Oklahoma.

## Recommendation 5: Annual Review of Synagis® (palivizumab)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends updating the existing palivizumab prior authorization criteria in accordance with the AAP guidelines as follows:

5) Infants less than 12 months of age~~, born before 35 weeks gestation~~, with congenital abnormalities of the airway.
6) Infants less than 12 months of age, ~~born before 35 weeks gestation~~, with severe neuromuscular disease.

# NAMI Oklahoma

National Alliance on Mental Illness



Tuesday, August 21, 2012

Chairman John Muchmore, M.D., Ph.D.
Drug Utilization Review Board
Oklahoma Health Care Authority
2401 NW 23rd Street, Suite 1-A
OKC, OK 73107

*RE: NAMI support for current tier system*

Dear Chairman Muchmore and Members of the Board,

NAMI strongly urges this board to continue the inclusion of current exceptions in the PBPA program. It is our position that any move to remove these exceptions will result in increased costs and decrease quality of care for those who need it most. We believe the evidence shows that any restrictions in access to medications for those who need them most will disrupt the continuity of care and are unlikely to result in any increased savings. Indeed, it is our concern that saving money on medications will result in increased expenses in hospitalizations that will result in increases in overall medical costs.

We request that the Board maintain the current tier system with changes to reflect the introduction of new generic medications and new contracts for supplemental rebates with the addition of prior authorization for their use.

***J. David Gordon, M.S.Ed, MBA***
Cell: 405.410.9980
davidgordon44@gmail.com

*"Give light and people will find the way."*

*—Ella Baker*

buildinglives
preventing mental disorders promoting wellness



August 8, 2012

Chairman John Muchmore, M.D., Ph.D.
Drug Utilization Review Board
Oklahoma Health Care Authority
2401 N.W. 23rd Street, Suite 1-A
Oklahoma City, Oklahoma 73107

Dear Chairman Muchmore and Members of the Board,

As you know, expenses from the use of atypical antipsychotic medications accounts for a substantial percentage of the Sooner Care expense on prescription drug coverage. This level of expense, coupled with inconclusive research has driven an effort to manage the costs and utilization of antipsychotic medications. With the critical nature of these medications in the long term health and recovery of SoonerCare members with serious mental illness we have continued to advocate for open access with minimal intrusions into the doctor-patient relationship.

The transition of atypical antipsychotics onto the Product Based Prior Authorization Program(PBPA) has gone smoother than anticipated and we commend the Health Care Authority and their partners on the successful implementation of the prior authorizations. The emphasis on maintaining continuity through grandfathering and an aggressive prior authorization approval effort has been beneficial to SoonerCare members.

In our efforts to understand the impact of the PBPA program on atypical antipsychotics has suggested that this two policies coupled with substantial patient assistance program (PAP) support from pharmaceutical companies has helped to maintain access to medications in Oklahoma. The support from PAP programs to SoonerCare members, is in large part due to the high rates of co-morbidity and chronic disease in the seriously mentally ill population, and medication restrictions on total number of branded medications and prescriptions.

Policies, such as limits on the number of prescriptions per individual, designed to reduce costs incurred by Sooner Care through purchase of prescription drugs could lead to reduced levels of access for those with mental illness to essential anti-psychotic therapies. Beyond this, generally there exists a fear that actions taken by the DURB might target anti-psychotics specifically to lower overall costs of prescription drug coverage since such a large percent of cost is incurred from this class of drugs.

Unlike some other classes of medications, disruption of a member who is currently stabilized on a specific medication can lead to serious consequences, such as hospitalization, violent behavior, and even the loss of life. The long process of stabilization is also a strong reason to minimize the need for forced and multi-step trials. While your recommendations for the restrictions in this class do recommend multiple trials, the exceptions for members stabilized on medications during inpatient hospitalizations and the practice of approval of requests for members stabilized on medications prior to being a SoonerCare member signal your understanding of this fact.

That being said, we must strongly urge the continued inclusion of these exceptions in the PBPA program. The increased costs from medications would not be saved by removing these exceptions due substantial increases in hospitalization, emergency room visits and other avoidable costs of care by maintaining access to medications for individuals who are already stabilized on a specific medication. The thorough and detailed review included in this month's board packet illustrates this fact by the minimal number of approvals granted as a result of stabilization on inpatient hospitalization. Physicians, particularly in an inpatient setting, are faced with weighing the specifics of each patient, including co-morbid illness and disability, symptomology and side-effect profiles of each medication and the needs of each SoonerCare member. While research does show that across broad populations no medication is significantly more effective, it is also clear that no one medication can meet the needs of each member. As much freedom for the physician to prescribe and treat the patient in a manner that best corresponds to that patient's condition must be provided as a critical aspect of anti-psychotic therapy.

Over the next two years, the availability of generic options will result in drastic changes in the atypical antipsychotic category, including reduced cost for SoonerCare in providing these drugs. When weighed with the very real dangers of over-restricting this category coupled with the cost shifting to more expensive areas of the SoonerCare program, such as emergency room care and hospitalization, we strongly urge the Drug Utilization Review Board to stop editing the PBPA program in regards to atypical antipsychotics.

It is our firm opinion that continued edits will realize diminished returns due to the future decreasing costs of these medications. Changes in the policy could contribute to disruption of continuity of care as well as restricted access to medications for those who need them most without increased savings.

As advocates, we realize the importance of managing the purchasing of health care, but we cannot support the sacrifice of essential treatment for cost savings which will likely not be realized. For this purpose we oppose the current changes to the PBPA program to be implemented beginning in January, 2013.

However, we would like to offer support for the proposal to impose restrictions on the use of atypical antipsychotics for adjunctive therapy for individuals suffering from severe and persistent depression. Emphasizing the use of antipsychotics as an adjunct only for those who need it, and not as a first line of treatment is likely a positive policy for managing the purchase of health care. That being said, we still urge the continued acceptance of the philosophy of continuity of care in the implementation of this restriction.

We request that the Board maintain the current tier system with changes to reflect the introduction of new generic medications and new contracts for supplemental rebates with the addition of prior authorization for use as a depression adjunct.

Paul G. Davis
Director of Public Policy and Communications

Michael W. Brose, MSW
Executive Director

# Appendix B

# Retrospective Drug Utilization Review Report

## Claims Reviewed for March 2012

| Module | Drug Interaction | Duplication of Therapy | Drug-Disease Precautions | Dosing & Duration |
|---|---|---|---|---|
| **Limits which were applied** | Established, Major, Males and Females, Age 36-50 | Long Acting Injectable Antipsychotics, Males and Females, Age 0-150 | Contraindicated, Normal Pregnancy, Females, Age 30-35 | High Dose, Duration, Proton Pump Inhibitors, Males, Age 0-10 |

**Response Summary (Prescriber)**
Letters Sent: 19
Response Forms Returned: 12

The response forms returned yielded the following results:

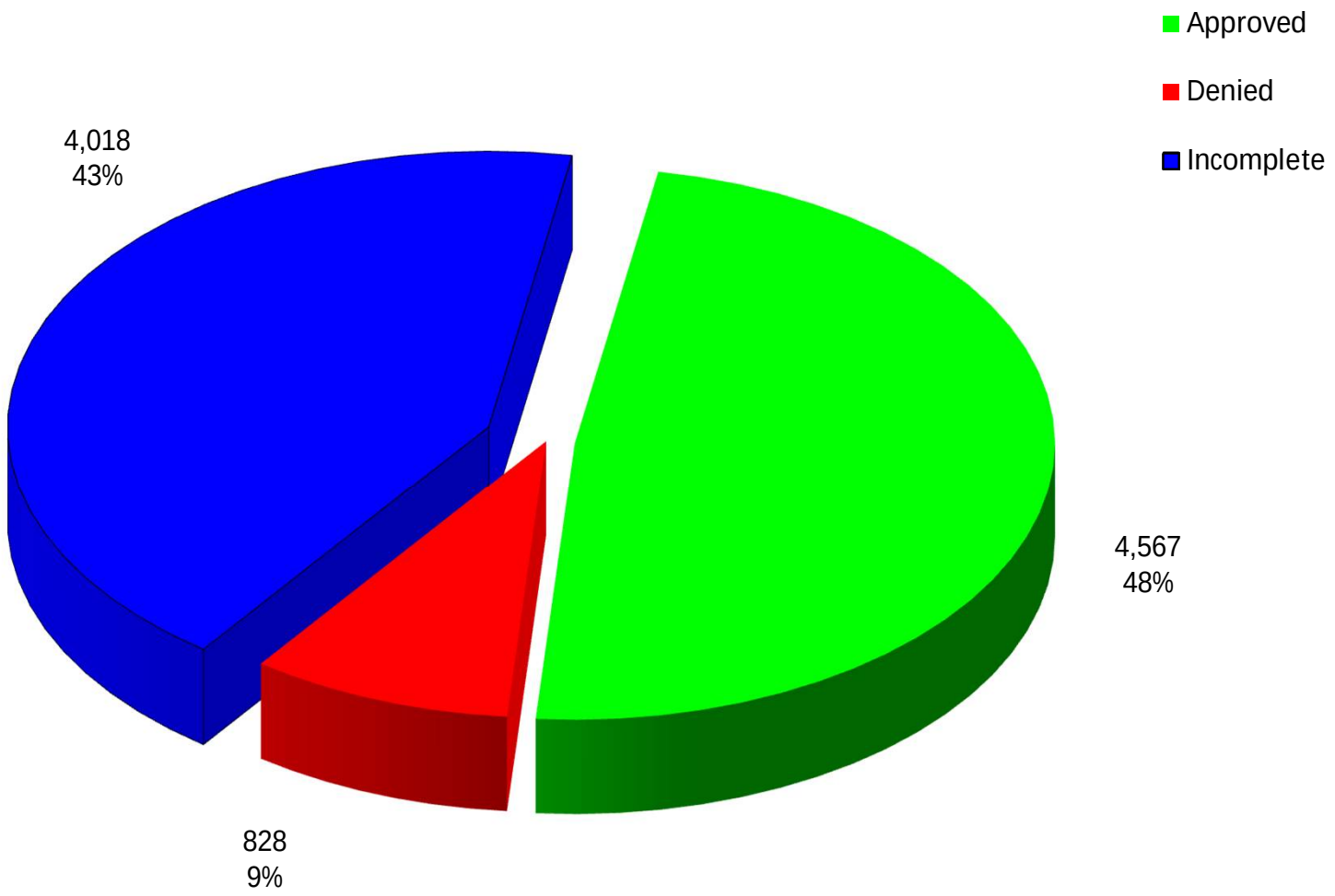
| | |
|---|---|
| *0 (0%)* | *Record Error—Not my patient.* |
| *0 (0%)* | *No longer my patient.* |
| *0 (0%)* | *Medication has been changed prior to date of review letter.* |
| *1 (8%)* | *I was unaware of this situation & will consider making appropriate changes in therapy.* |
| *10 (83%)* | *I am aware of this situation and will plan to continue monitoring therapy.* |
| *1 (8%)* | *Other* |

**Response Summary (Pharmacy)**
Letters Sent: 3
Response Forms Returned: 0

The response forms returned yielded the following results:

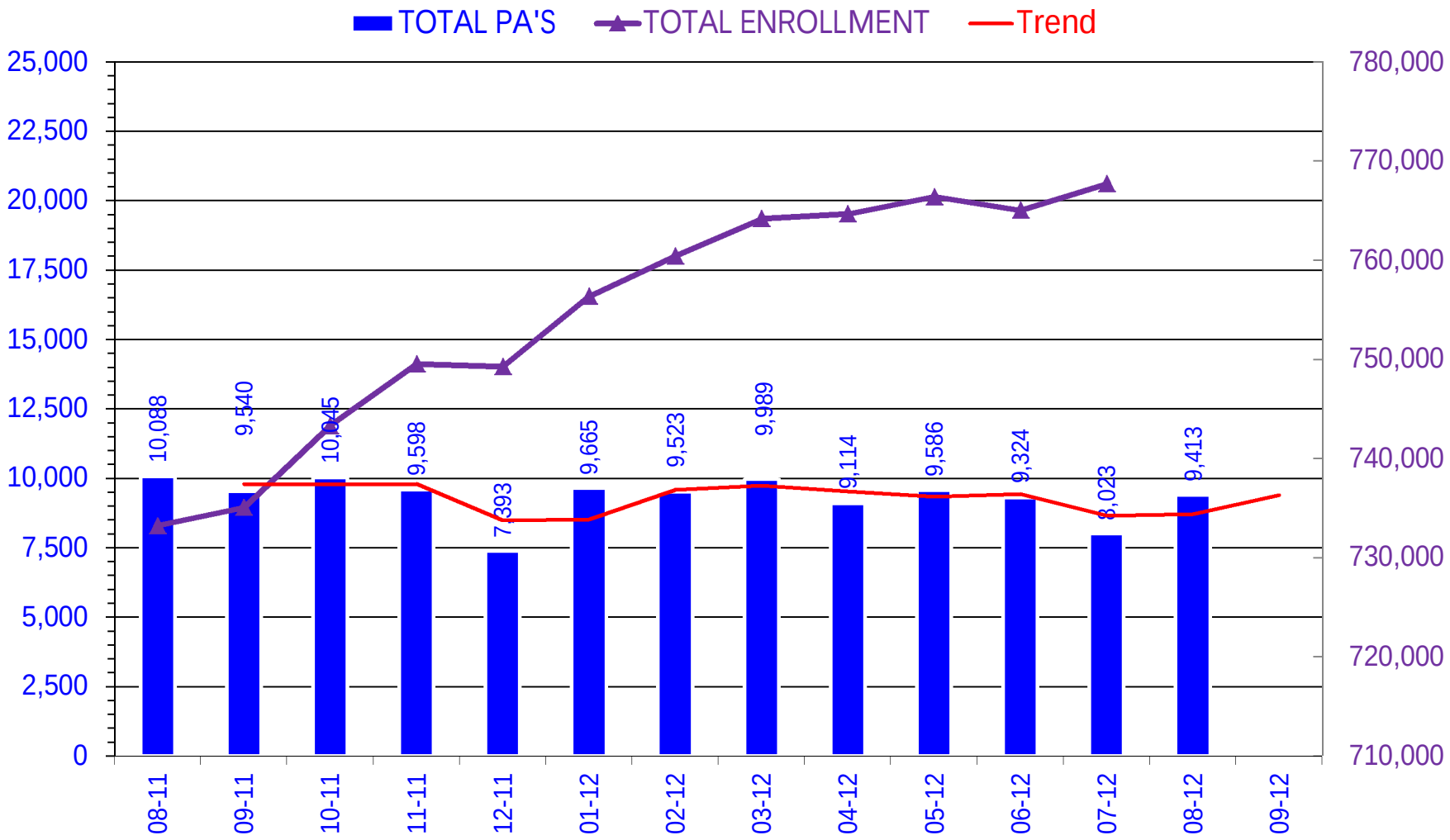
| | |
|---|---|
| *0 (0%)* | *Record Error—Not my patient.* |
| *0 (0%)* | *No longer my patient.* |
| *0 (0%)* | *Medication has been changed prior to date of review letter.* |
| *0 (0%)* | *I was unaware of this situation & will consider making appropriate changes in therapy.* |
| *0 (0%)* | *I am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

# PRIOR AUTHORIZATION ACTIVITY REPORT: August 2012




PA totals include overrides

# PRIOR AUTHORIZATION REPORT: August 2011 – August 2012




PA totals include overrides

# Prior Authorization Activity

## 8/1/2012 Through 8/31/2012

| | Total | Approved | Denied | Incomplete | Average Length of Approvals in Days |
|---|---|---|---|---|---|
| Advair/Symbicort/Dulera | 427 | 170 | 16 | 241 | 359 |
| Analgesic, Narcotic | 440 | 221 | 32 | 187 | 274 |
| Angiotensin Receptor Antagonist | 55 | 7 | 7 | 41 | 299 |
| Antiasthma | 1,013 | 399 | 57 | 557 | 242 |
| Antibiotic | 22 | 4 | 2 | 16 | 97 |
| Anticoagulant | 20 | 13 | 0 | 7 | 314 |
| Anticonvulsant | 94 | 33 | 4 | 57 | 320 |
| Antidepressant | 417 | 150 | 36 | 231 | 307 |
| Antidiabetic | 137 | 57 | 8 | 72 | 354 |
| Antigout | 12 | 3 | 1 | 8 | 360 |
| Antihistamine | 161 | 118 | 9 | 34 | 355 |
| Antihyperlipidemic | 25 | 2 | 8 | 15 | 344 |
| Antimigraine | 101 | 39 | 9 | 53 | 328 |
| Antiplatelet | 23 | 15 | 0 | 8 | 325 |
| Antiulcers | 387 | 115 | 92 | 180 | 103 |
| Anxiolytic | 128 | 91 | 3 | 34 | 231 |
| Atypical Antipsychotics | 538 | 308 | 17 | 213 | 346 |
| Biologics | 32 | 23 | 1 | 8 | 359 |
| Bladder Control | 65 | 15 | 4 | 46 | 347 |
| Cardiovascular | 28 | 13 | 7 | 8 | 273 |
| Contraceptive | 11 | 0 | 1 | 10 | 0 |
| Dermatological | 146 | 31 | 36 | 79 | 108 |
| Endocrine & Metabolic Drugs | 90 | 25 | 16 | 49 | 327 |
| Erythropoietin Stimulating Agents | 52 | 11 | 10 | 31 | 103 |
| Fibromyalgia | 165 | 35 | 36 | 94 | 331 |
| Gastrointestinal Agents | 92 | 49 | 6 | 37 | 193 |
| Genitourinary Agents | 14 | 2 | 2 | 10 | 12 |
| Glaucoma | 21 | 2 | 1 | 18 | 318 |
| Growth Hormones | 63 | 46 | 5 | 12 | 162 |
| HFA Rescue Inhalers | 143 | 25 | 28 | 90 | 344 |
| Insomnia | 86 | 16 | 18 | 52 | 256 |
| Multiple Sclerosis | 15 | 9 | 0 | 6 | 188 |
| Muscle Relaxant | 139 | 53 | 47 | 39 | 95 |
| Nasal Allergy | 108 | 8 | 30 | 70 | 120 |
| Neurological Agents | 48 | 34 | 1 | 13 | 357 |
| Non-Classified | 7 | 3 | 1 | 3 | 179 |
| Nsaids | 182 | 20 | 26 | 136 | 306 |
| Ocular Allergy | 56 | 12 | 10 | 34 | 126 |
| Ophthalmic | 43 | 12 | 5 | 26 | 11 |
| Osteoporosis | 30 | 7 | 2 | 21 | 356 |
| Other* | 154 | 32 | 11 | 111 | 172 |
| Otic Antibiotic | 52 | 9 | 1 | 42 | 10 |
| Pediculicide | 133 | 51 | 8 | 74 | 12 |
| Prenatal Vitamins | 14 | 0 | 0 | 14 | 0 |
| Smoking Cess. | 59 | 21 | 1 | 37 | 36 |
| Statins | 91 | 47 | 7 | 37 | 349 |
| Stimulant | 900 | 452 | 58 | 390 | 340 |
| Suboxone/Subutex | 157 | 129 | 3 | 25 | 87 |
| Topical Antibiotic | 15 | 1 | 1 | 13 | 13 |

| | | | | | |
|---|---|---|---|---|---|
| Topical Antifungal | 10 | 1 | 1 | 8 | 61 |
| Topical Corticosteroids | 62 | 0 | 22 | 40 | 0 |
| Vitamin | 35 | 7 | 22 | 6 | 361 |
| Pharmacotherapy | 132 | 106 | 3 | 23 | 209 |
| Emergency PAs | 5 | 5 | 0 | 0 | |
| **Total** | **7,455** | **3,057** | **732** | **3,666** | |
| **Overrides** | | | | | |
| Brand | 64 | 41 | 8 | 15 | 308 |
| Dosage Change | 592 | 555 | 5 | 32 | 7 |
| High Dose | 3 | 2 | 0 | 1 | 224 |
| Ingredient Duplication | 13 | 8 | 3 | 2 | 5 |
| Lost/Broken Rx | 156 | 145 | 4 | 7 | 9 |
| NDC vs Age | 4 | 4 | 0 | 0 | 193 |
| Nursing Home Issue | 102 | 99 | 0 | 3 | 7 |
| Other | 59 | 51 | 1 | 7 | 6 |
| Quantity vs. Days Supply | 948 | 588 | 75 | 285 | 290 |
| Stolen | 16 | 16 | 0 | 0 | 4 |
| Wrong D.S. on Previous Rx | 1 | 1 | 0 | 0 | 9 |
| **Overrides Total** | **1,958** | **1,510** | **96** | **352** | |
| **Total Regular PAs + Overrides** | **9,413** | **4,567** | **828** | **4,018** | |

| **Denial Reasons** | |
|---|---|
| Unable to verify required trials. | 3,455 |
| Does not meet established criteria. | 778 |
| Lack required information to process request. | 597 |

Duplicate Requests: 686

Letters: 2,590

No Process: 286

Changes to existing PAs: 476

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

# CALL VOLUME MONTHLY REPORT:
# August 2011 – August 2012

# SoonerCare Atypical Rx Program Update

*Oklahoma Health Care Authority*
*September 2012*

## Background

The Oklahoma Health Care Authority is engaged in a collaborative effort with five other states to improve the quality of care for children experiencing mental health difficulties. This effort is supported by a grant from the Agency for Healthcare Research and Quality (AHRQ) and its goal is to improve the utilization of antipsychotic medications in children receiving SoonerCare services. The Medicaid/Mental Health Network for Evidence Based Treatment (MEDNET) project brings together experts from Rutgers and Columbia Universities; staff from Academy Health to provide technical assistance; and six state Medicaid programs: Oklahoma, Missouri, Texas, California, Washington and Maine. Each state is launching multi-component initiatives to increase up-take of evidence-based practices in mental health treatment. Clinical areas targeted for measurement and intervention include poly-pharmacy, management of metabolic risks, high doses of antipsychotics, use of appropriate mental health services, and consistency between diagnoses and treatments. As part of this workgroup, Oklahoma will seek to improve treatment practices in these areas by developing and applying quality of care metrics and using a multi-stakeholder quality collaborative in order to implement a Continuous Quality Improvement (CQI) program. In Oklahoma, the Behavioral Health Advisory Committee (BHAC) at OHCA has been serving as the quality collaborative stakeholder group. The BHAC includes mental health professionals and providers as well as consumers. The program for Oklahoma has been titled SoonerCare Atypical Rx.

SoonerCare Atypical Rx will provide increased understanding of treatment patterns in SoonerCare and of variations that exist that do not always contribute to improved patient outcomes. It will facilitate increased use of evidence based practices for effective and safe use of psychotropic medications, in the context of overall improved clinical management of care including non-pharmacological psychosocial interventions.

As OHCA and the College of Pharmacy began to work on the plans to implement the MEDNET project, we purposefully considered the sustainability of any intervention beyond the three-year period of the MEDNET grant. Retrospective Drug Utilization Review (RetroDUR) is a required part of the pharmacy program and provides a vehicle for an ongoing initiative. RetroDUR is performed monthly on pharmacy claims and looks for doses, interactions, or other adverse events that may have been missed in the initial screening of pharmacy claims. Each month, letters are mailed to pharmacies and prescribers to alert them of potentially harmful reactions to medications.

By using the quality of care metrics that have been developed through MEDNET, COP is able to generate letters to prescribers via the existing RetroDUR process. The first of these letters was sent in June to over 300 prescribers representing over 700 children. The focus of this first letter was two-fold: (1) children receiving doses of AAP higher than recommended for their age, and (2) no diagnosis on file appropriate for prescription of AAP medication. Our target age range is 5-14 years.

With the letters, prescribers receive a list of their patients who have been flagged by either the dosing or diagnostic criteria. A dosing chart, broken out by age, is also included. The prescriber can also see

how they rank on each measure compared to their peers. For each patient included in the mailing, the prescriber receives a medication list from the past three months, so that they can determine if other providers are also prescribing mental health drugs. Finally, the packet includes a response form so that the prescriber can indicate whether they were aware of the situation and whether they plan to change the therapy or monitor the patient (see attachment 1). From the first mailing, we had a 32% response rate.

The next mailing is planned for September and will address poly-pharmacy in the 5-14 year old age range. For this project, poly-pharmacy will be defined as at least 90 days of two or more concurrent atypical antipsychotics. Including all ages, poly-pharmacy is very low in the SoonerCare program, at about 6% of those prescribed an AAP, and only 0.23% are taking three or more AAPs concurrently.

The project is meant to be educational for physicians: there is nothing punitive about it. This topic has been featured in a number of media articles, usually with negative connotations. However, OHCA understands the importance of these medications and the positive impact they can have for children with behavioral health issues. A child psychiatrist is available for consultation with prescribers that have questions regarding treatment options.

## Results of First Mailing

A total of 627 prescribers were listed on paid pharmacy claims for atypical antipsychotics between March 1, 2012 and May 31, 2012. A total of 6,628 members were reviewed for potential problems with dosing or appropriate diagnoses. There were 2,244 members flagged as having a potential problem. Packets were mailed to 338 prescribers in June of 2012. The packets included information regarding 713 of the individual patients flagged. 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 231 patients.

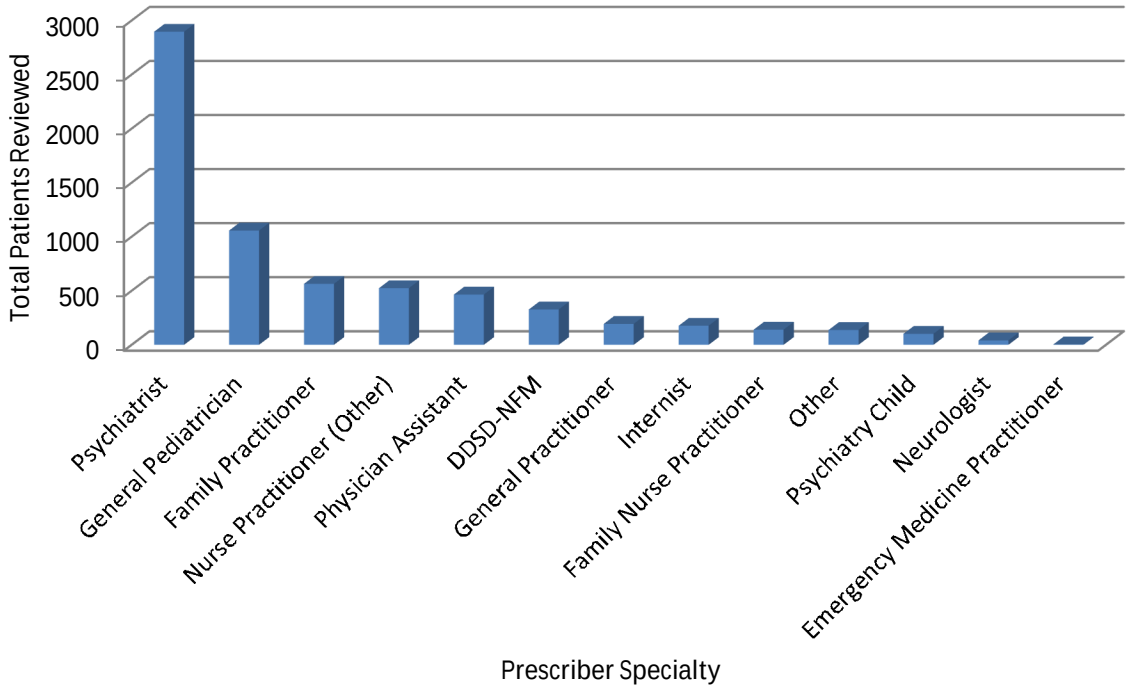
### Responses to Individual Patient Reports

| # | Response | Total |
|---|---|---|
| Q1 | Not my patient. | 12 |
| Q2 | No longer my patient. | 24 |
| Q3 | Medication has been changed prior to date of review letter. | 14 |
| Q4 | I was unaware of this situation and will consider making appropriate changes in therapy. | 22 |
| Q5 | I am aware of this situation and will plan to continue monitoring this therapy. | 125 |
| Q6 | I am continuing this medication from an original psychiatric prescription*. | 32 |
| Q7 | Other, comments. | 100 |

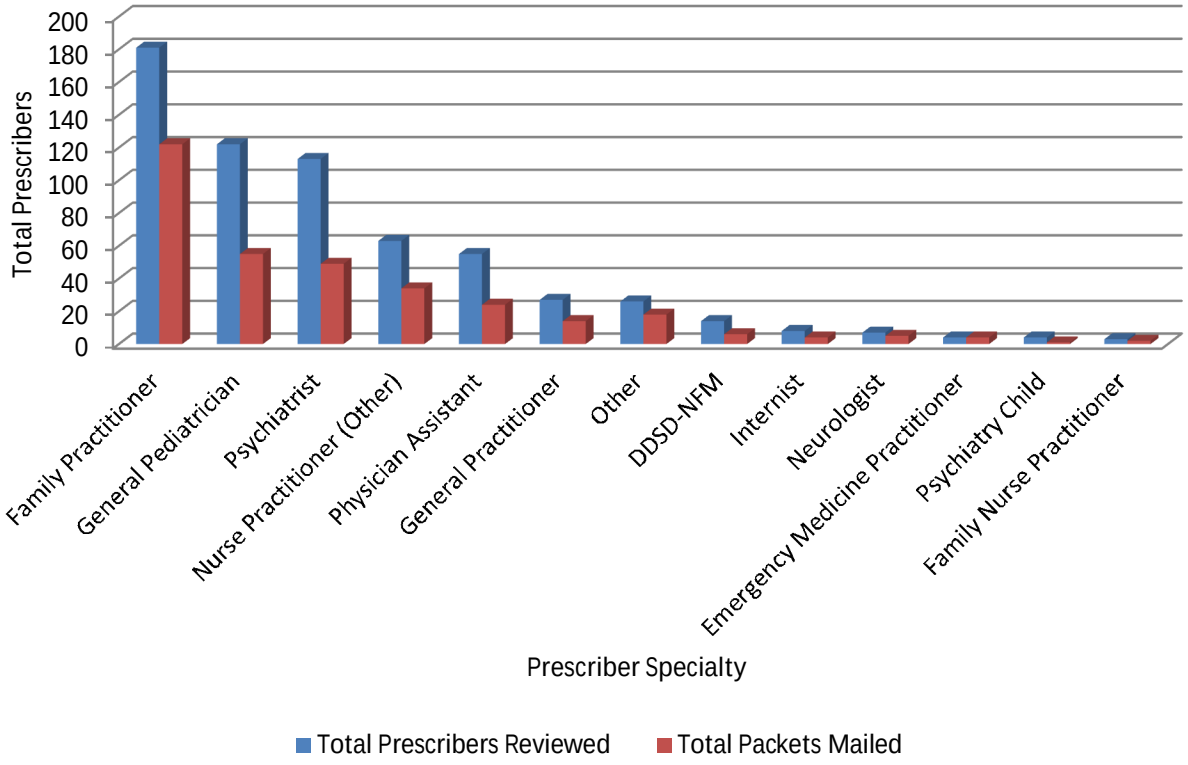
*No answers were marked for this question, however after reviewing comments the total number was imputed.

Comments were submitted for almost half of the responses. Most of the comments further detailed the diagnoses or symptoms being treated with the atypical antipsychotics. Some comments discussed where treatment was initiated or indicated members were being referred for more complex behavioral health therapy. Many of the additional diagnoses were supportive of atypical antipsychotic prescription, but were not located in the member's medical claims history.

## Total Patients Reviewed by Prescriber Specialties




## Total Prescribers Reviewed versus Packets Mailed



## Next Mailing – September 2012

The next mailing is planned for September and will address poly-pharmacy in the 5-14 year old age range (see attachment 2). For this project, poly-pharmacy will be defined as at least 90 days of two or more concurrent atypical antipsychotics. For this age range, only 2.4% have two concurrent atypical antipsychotics and none had 3 or more. All future mailings will be limited to 200 unique prescribers in order to alleviate intervention fatigue caused by multiple mailings. In order to bring the number of prescribers up to this limit, the diagnosis analysis will also be run and prescribers who did not receive a letter in the first mailing will be included up to the maximum for this mailing.

## Further Analysis

After three months, the metric will be run again for dosing and diagnosis indicators to see if any changes occurred in overall percentages of members flagged. Additional mailings will be scheduled for prescribers not included in the first mailing for each area of review.

## Attachment 1: Diagnosis and Dosing Sample Letter


# SoonerCare

## Pharmacy Services

June 25, 2012

Dear SoonerCare Provider,

The Oklahoma Health Care Authority is engaged in a collaborative effort with five other states to improve the quality of care for children experiencing mental health difficulties. This effort is supported by a grant from the Agency for Healthcare Research and Quality (AHRQ) and its goal is to improve the utilization of antipsychotic medications in children receiving SoonerCare services. Drug utilization review is a vital tool needed to meet this goal and ensure your patients are receiving optimal care.

We have recently completed a review of pharmacy and medical paid claims from the last three or twelve months respectively and have enclosed some information regarding specific patients whose prescriptions may represent potential differences from generally accepted evidence-based prescribing practices.

With this packet you will find the following:

1. Information related to atypical antipsychotic dosing and strongly indicated diagnoses.
2. Your Prescriber Summary Report which shows how your prescribing compares to other prescribers of atypical antipsychotics and a list of patients identified by one or both of the quality indicators. Patients were assigned to you based on the last prescriber of record on atypical antipsychotic pharmacy claim.
3. A Patient Detail Report listing the prescriptions which your identified patients received during the last three months.
4. A Patient Response Page for each identified patient. The response pages for each patient can be mailed together in the enclosed return envelope, faxed to the number at the bottom of the page, or your response can be entered on the Response Website using the patient's reference number or QR code.

This project, SoonerCare Atypical Rx, has been developed to look at atypical antipsychotic prescribing for SoonerCare children. Please review the attached information. Any errors can be reported on the response page or by calling the pharmacy help desk at the number below.

We hope that you find this information helpful when managing these complex patients. We appreciate your service to Oklahoma SoonerCare members.

# SoonerCare Atypical Rx Project

## How Much

Many atypical antipsychotic medications do not have established dosing guidelines from the FDA for children. Use the lowest effective dose.

## How Many

There are no studies indicating that multiple atypical antipsychotic medication regimens are effective for children. When switching between medications, taper the new drug up while simultaneously tapering the other down.

## How Long

Atypical antipsychotic medications can cause a number of metabolic conditions. Be sure to monitor weight, waist circumference, blood glucose, and lipid levels during treatment with these medications when appropriate. Limit treatment duration to the shortest effective time period.

## How Young

None of the atypical antipsychotics have been approved for children less than 5 years old. Please consider other treatment modalities before beginning treatment in a very young child with one of these medications.

## SoonerCare Support Options

A consultation with a child psychiatrist is available. If you would like to speak to the psychiatrist, please call 405-522-7597.

If additional services are needed for SoonerCare members, please contact:

- Care Management: 1-877-252-6002
- Behavioral Health Care Management: 1-800-652-2010

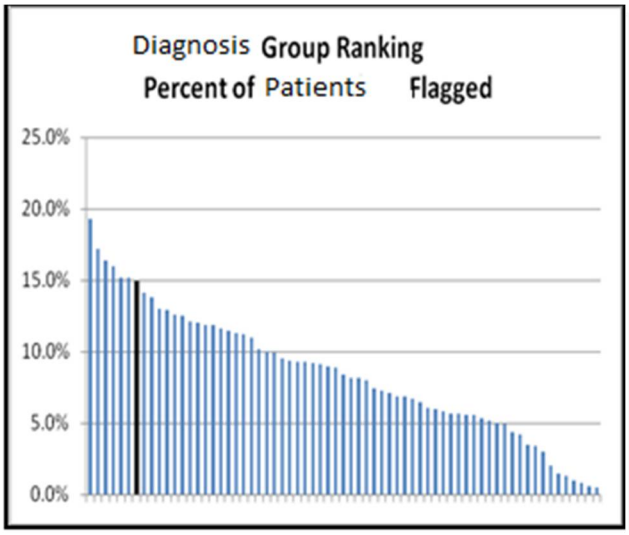
References:

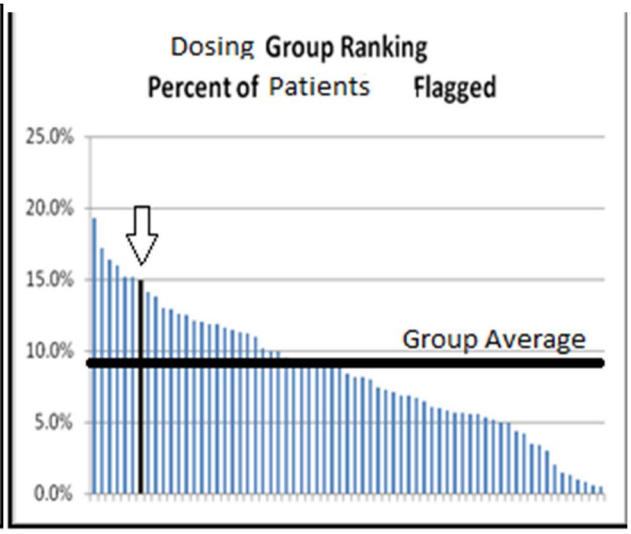
1. Children's Bureau, U.S. Department of Health and Human Services. Promoting the safe, appropriate, and effective use of psychotropic medications for children in foster care. [cited June 12, 2012] Available from: http://www.childwelfare.gov/systemwide/mentalhealth/effectiveness/psychotropic.cfm.
2. Haas, M., Unis, A.S., et al. A 6-week, randomized, doubleblind, placebo-controlled study of the efficacy and safety of risperidone in adolescents with schizophrenia. J Child Adolesc Psychopharm. 2009;19(6): 611-621.
3. Schooler, N., Rabinowitz, J., Davidson, M. Risperidone and Haloperidol in first-episode psychosis: A long-term randomized trial. Am J of Psychiatry. 2005;162(5): 947-959.
4. Goren JL, Parks, JJ, Ghinassi FA, et.al. When is antipsychotic polypharmacy supported by research evidence? Implications for QI. JCAHO. 2008;34(10):571-582.
5. Safer, D.J., J.M. Zito, and S. DosReis, Concomitant psychotropic medication for youths. Am J Psychiatry. 2002;160(3): 438-49.
6. McIntyre RS, Jerrell JM.: Metabolic and cardiovascular adverse events associated with antipsychotic treatment in children and adolescents. Arch of Ped and Adolesc Med. 2008;162(10):929-935.

# Prescriber Summary Report

Dates of Service: <Start Date> to <End Date>

Prescriber: <Prescriber Name> NPI: <Prescriber NPI>
Prescriber Percent of Patients Flagged*:
Dosing: XXX versus an average of XXXX
Diagnosis: XXX versus an average of XXXX




| SoonerCare ID | Reference Number | Patient Name | Dosing Indicator | Diagnosis Indicator |
|---|---|---|---|---|
| <UCI> | <Ref #> | <member name> | x | |
| <UCI> | <Ref #> | <member name> | | x |
| <UCI> | <Ref #> | <member name> | x | x |
| <UCI> | <Ref #> | <member name> | x | |
| <UCI> | <Ref #> | <member name> | x | |
| <UCI> | <Ref #> | <member name> | | x |
| <UCI> | <Ref #> | <member name> | | x |
| <UCI> | <Ref #> | <member name> | x | x |
| <UCI> | <Ref #> | <member name> | x | x |

Report Key:

Dosing: Patient prescribed an atypical antipsychotic at a dosing greater than or equal to 1.5 times the FDA maximum dose.

Diagnosis: Patients prescribed an atypical antipsychotic where recent twelve month medical claims history does not include a diagnosis with a strong indication for prescribing an antipsychotic medication.

The maximum number of listed patients for each mailing is 10 regardless of the number of actual patients flagged for review. These 10 patients were chosen at random for inclusion.

*100% and 0% are only represented once on the graphs regardless of the actual number in these categories.

# Dosing of Atypical Antipsychotics in Children and Adolescents

| Children 5-17 Maximum Oral Dosing | | |
|---|---|---|
| **Drug Name Generic (Brand)** | **Ages 5-12** | **Ages 13-17** |
| aripiprazole (Abilify®) | 15 mg | 30 mg |
| asenapine (Saphris®) | 10 mg | 10 mg |
| clozapine (Clozaril®, Fazaclo®) | 300 mg | 600 mg |
| iloperidone (Fanapt™ ) | 24 mg | 24 mg |
| lurasidone (Latuda®) | 80 mg | 80 mg |
| olanzapine (Zyprexa®) | 12.5 mg | 20 mg |
| olanzapine/fluoxetine (Symbyax®) | 12.5 mg | 18 mg |
| paliperidone (Invega®) | 15 mg | 15 mg |
| quetiapine (Seroquel®/Seroquel XR®) | 300 mg | 600 mg |
| risperidone (Risperdal®) | 3 mg | 6 mg |
| ziprasidone (Geodon®) | 160 mg | 160 mg |

PSYCKES Dose Indicators Documentation, July 2010

The dosing table above was used to determine potential high dosing concerns. Only solid dosing formulations were included in the review.

Oklahoma SoonerCare has approximately 7% of its atypical antipsychotic prescribing for children 5-12 years of age at a dose higher than the maximum. This percent is greater than for adolescents (1.6%) or adults (4.5%).

Best practice considerations include:

- Using the lowest possible dose
- Considering a tapering of dose every six months
- Monitoring for potential side effects

AACAP Work Group on Quality Issues. Practice parameters on the use of psychotropic medication in children and adolescents. J Am Acad Child Adolesc Psychiatry. 2009;48(9):961-973.

***Post this page for future reference!***

## Diagnosis Consistent with Antipsychotic Prescription

Diagnoses consistent with a strong indication for antipsychotic use:

- Schizophrenia
- Bipolar disorders
- Severe depression with or without psychotic features
- Delusional disorders
- Other nonorganic psychoses
- Obsessive-compulsive disorders
- Autistic disorder

All other mental health-related diagnoses or non-mental health-related diagnoses are considered weak or not-indicated.

> Oklahoma SoonerCare has >70% of its atypical prescribing for children 5 to 14 years of age in the weak diagnosis category!

The two most common diagnoses inconsistent with receipt of antipsychotics for SoonerCare were Attention Deficit Hyperactivity Disorder and Conduct/Disruptive Behavioral Disorders.

Medications indicated for treatment of ADHD:

- Psychostimulants: Methylphenidate HCl, Dextroamphetamine sulfate, and D- and L-amphetamine racemic mixture.
- Non-stimulants: Atomoxetine HCl, Imipramine HCl and Bupropion HCl.[1]

Medications indicated for treatment of Conduct/Disruptive Behavioral Disorders:

- Methylphenidate, Dextroamphetamine sulfate, Bupropion HCl, Fluoxetine HCl, Phenytoin, Carbamazepine, Valproic Acid, Lithium Carbonate, and Clonidine HCl.[2]

1. Pliszka S. Practice parameter for the assessment and treatment of children and adolescents with attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry. 2007; 46(7):894-921

2. Searight HR, Rottnek F, & Abby SL. Conduct disorder: diagnosis and treatment in primary care. Am Fam Physician. 2001; 63(8):1579-1588.

***Post this page for future reference!***

# Patient Detail Report

Prescriber: <Prescriber Name> NPI: <Prescriber NPI>

Patient: <Patient Name> Patient ID: <UCI> Reference #: <Ref #>

Date of Birth: <DOB>

Screening Date: <Start Date> through <End Date>

Report Type: _____ Dosing _____ Diagnosis _____ Both

Total Distinct Mental Health Medications: <#>

Total Distinct Prescribers: <#>

| Date of Fill | Drug | Quantity | Day Supply | NPI | Pharmacy ID |
|---|---|---|---|---|---|
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |

Please keep this patient profile for your records.

## Patient Response Page

Prescriber: <Prescriber Name> NPI: <Prescriber NPI>

Patient: <Patient Name> Patient ID: <UCI> Reference #: <Ref #>

Screening Date: <Start Date> through <End Date>

Report Type: ____ Dosing ____ Diagnosis ____ Both

This information is communicated strictly in confidence to the provider for evaluation and response (check all that apply):

- € Not my patient.
- € No longer my patient.
- € Medication has been changed prior to date of review letter.
- € I was unaware of this situation and will consider making appropriate changes in therapy.
- € I am aware of this situation and will plan to continue monitoring this therapy.
- € I am continuing this medication from an original psychiatric prescription.
- € Other, comments.

| |
|---|
| |

- € I am placing the Patient Detail Report in the patient's medical record.

_____ _____

Name (please print) Signature

You may enter your responses at the following website: www.XXXXXXXX.edu\ResponsePage, or scan the QR Code located at the bottom of this page (please note each QR Code is unique for each response page). You may also return each response page in the enclosed business reply envelope or fax to 866-335-3331.

Confidential Confidential

# Attachment 2: Poly-Pharmacy Sample Letter (Changes to Above Attachment)

## Duplication of Therapy of Atypical Antipsychotics (Poly-pharmacy)

Defined as:

1. Two or more concurrent antipsychotic medications for more than 90 days.
2. Three or more concurrent antipsychotic medications for more than 90 days.

Poly-pharmacy has been shown to be a frequent practice in the treatment of youth with mental health disorders. The rates of poly-pharmacy in children and adolescents have been reported to be as high as 70% according to studies by many payer groups such as Medicaid, private insurance, and SCHIP. For children in foster care, poly-pharmacy rates have been found to be especially high, with no evidence of therapeutic advantage. The use of multiple concurrent atypical antipsychotics has been shown to significantly increase the risk of severe negative outcomes such as serious drug interactions, serious behavioral changes, delirium, cardiac arrhythmias, and death.

> For SoonerCare children aged 5-14 years, approximately X% of atypical antipsychotic utilization meets the definition of poly-pharmacy.

The treatment of behavioral symptoms such as impulsivity and aggression may be challenging, and might contribute to poly-pharmacy. The American Academy of Child and Adolescent Psychiatry has published practice guidelines on poly-pharmacy. They detail the importance of a high quality diagnostic assessment, and then, utilizing the evidence base for psychopharmacological and psychosocial treatments in children and adolescents. Doses should be titrated to effect whenever possible, instead of adding medications. Also, appropriate psychosocial interventions should be attempted. This includes treating the specific disorders with psychological therapies that utilize an evidence-based treatment (EBT) approach, social skills training, parenting skills training, and Trauma-Focused Cognitive Behavioral Therapy (TF-CBT) for children suffering from trauma.

Remember, a consultation with a child psychiatrist is available. If you would like to speak to the psychiatrist, please call 405-522-7597. If additional services are needed for SoonerCare members, please contact Care Management at 1-877-252-6002 or Behavioral Health Care Management at 1-800-652-2010.


1. Safer, D.J., J.M. Zito, and S. DosReis, Concomitant psychotropic medication for youths. Am J Psychiatry, 2003. 160(3): p. 438-49.
2. Martin, A., et al. Multiple psychotropic pharmacotherapy among child and adolescent enrollees in Connecticut Medicaid managed care. Psychiatric Services, 2003. 54(1): p. 72-77.
3. Zito, J.M., et al., Psychotropic medication patterns among youth in foster care. Pediatrics, 2008. 121(1): p. e157-63.
4. Breland-Noble, A.M., et al., Use of psychotropic medications by youths in therapeutic foster care and group homes. Psychiatr Serv, 2004. 55(6): p. 706-8.
5. Bickford, C., Child's Ordeal Shows Risks of Psychosis Drugs for Young, in New York Times. 2010: New York.
6. Gleason, M.M., et al., Psychopharmacological treatment for very young children: contexts and guidelines. J Am Acad Child Adolesc Psychiatry, 2007. 46(12): p. 1532-72.
7. Pappadopulos, E., et al., Treatment recommendations for the use of antipsychotics for aggressive youth (TRAAY). Part II. J Am Acad Child Adolesc Psychiatry, 2003. 42(2): p. 145-61.

# Appendix C

# Vote to Prior Authorize Select Gonadotropin-Releasing Hormone Analogs for Central Precocious Puberty

*Oklahoma Health Care Authority, September 2012*

*This category was introduced for possible inclusion in the Product Based Prior Authorization program in May 2012. See the May, July, and August DUR packets for a more complete discussion of the category. This notice is presented to meet the statutory requirements of 63 O.S. Sec. 5030.5.*

*Under Oklahoma state law, the OHCA DUR Board must review and make recommendations for any drug subject to prior authorization, whether covered under the pharmacy benefit, the medical benefit, or both. Accordingly, physician administered drugs are brought through the same DUR process as those dispensed by pharmacies*.

## Recommendations

The College of Pharmacy recommends medical and pharmacy prior authorization of select gonadotropin-releasing hormone analogs for central precocious puberty.

**Criteria for Approval**

1. FDA approved indication – central precocious puberty (ICD-9 –CM Diagnosis Code 259.1) confirmed by submitting:
    - Documentation of onset of symptoms at ages less than 8 years of age in females and 9 years of age in males.
    - Documentation that bone age is advanced 1 year beyond the chronological age.
    - Lab assessment:
        - Documentation of abnormal basal gonadotropin levels, OR
        - Documentation of pubertal response to a gonadotropin releasing hormone analog stimulation test.

2. Documentation of a failed trial of lower tiered products or FDA approved indication not covered by a lowered tiered product.

| Tier 1 | Tier 2 | Tier 3 |
|---|---|---|
| Leuprolide (Lupron® Depot, Lupron Depot-Ped) | Histrelin (Supprelin LA®) | Nafarelin (Synarel®) |

# Appendix D

# ATYPICAL ANTIPSYCHOTICS ANNUAL REVIEW FOLLOW-UP

**OKLAHOMA HEALTH CARE AUTHORITY**
**SEPTEMBER 2012**

## BACKGROUND

At the August DUR Board meeting it was proposed the College evaluate the utilization of Seroquel® and Seroquel XR® to make appropriate recommendations regarding special criteria for the extended release formulation.

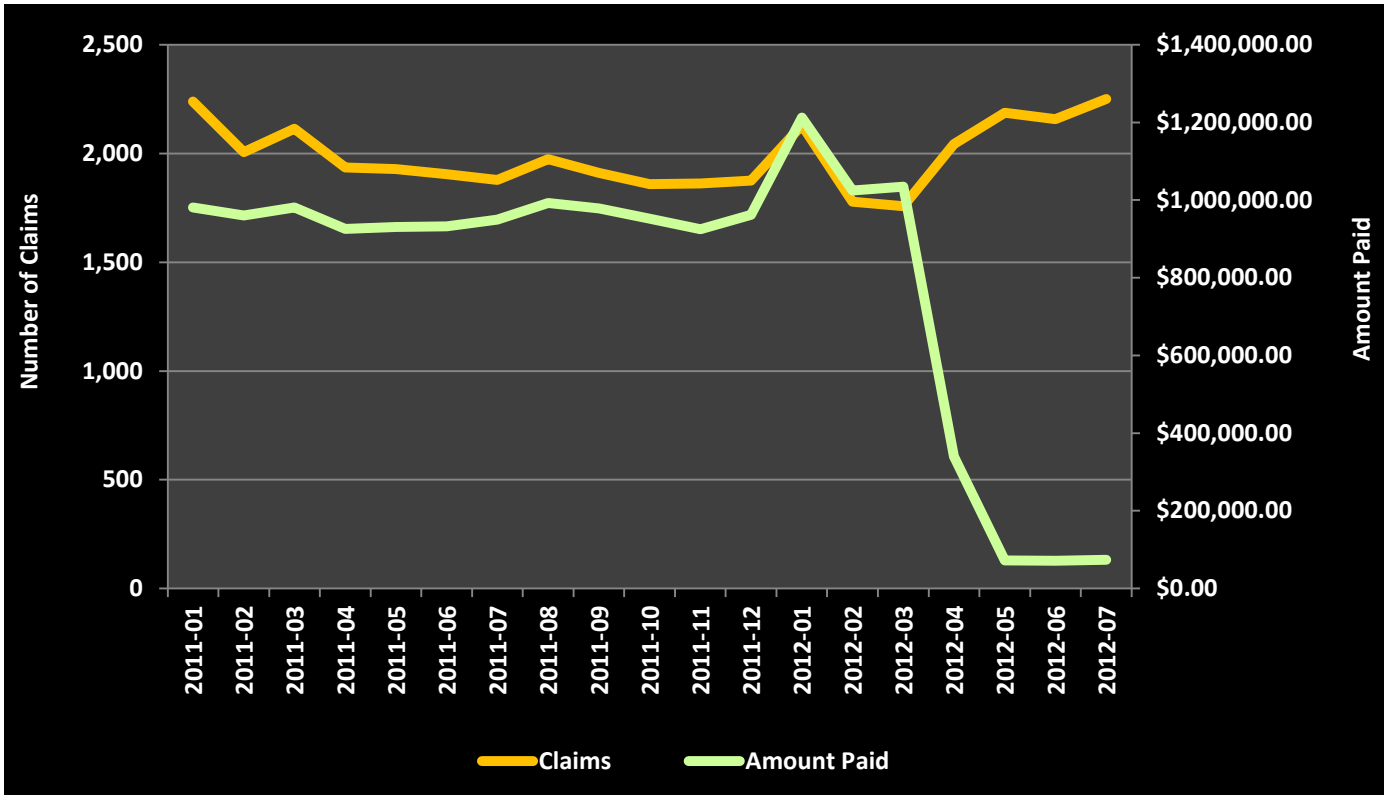
Clinical considerations consist of differences in efficacy and safety that may exist. Although the FDA approved indications are slightly different, the two formulations consist of quetiapine fumarate as the active chemical, and their pharmacokinetic profiles are very similar. The terminal half-life of the IR formulation is 6 hours and that of the XR is 7 hours. Steady state concentrations are expected to be achieved within two days for both formulations. A pharmacokinetic study[1] found that modifying the formulation of quetiapine IR to the XR does not change the overall absorption or elimination. Quetiapine IR may be switched to quetiapine XR at the equivalent total daily dose although individual dosage adjustments may be required. The IR formulation is indicated to be dosed once daily and up to three times daily while the XR formulation is indicated to be dosed once daily.

As for adverse effects, one head to head comparison trial[2] evaluated the time course and intensity of sedation after administration of IR and XR quetiapine in healthy subjects during dose initiation. The tolerability of the formulations was also evaluated. The results showed that in healthy subjects, quetiapine XR was associated with a lower intensity of self-reported sedation compared with quetiapine IR. The trial was only 5 days in duration for each drug, which is not enough time for meaningful evaluation of adverse effects because many adverse effects such as sedation often diminish with use in a couple of weeks. Furthermore, post dose sedation is considered a desired attribute of quetiapine, especially in the treatment of psychosis or mania. Quetiapine is typically dosed at night due to the expected sedation. The trial showed there were no significant differences in sedation between formulations at 7 hours after dosing, but may still require multiple tablets per day based on desired target dose.

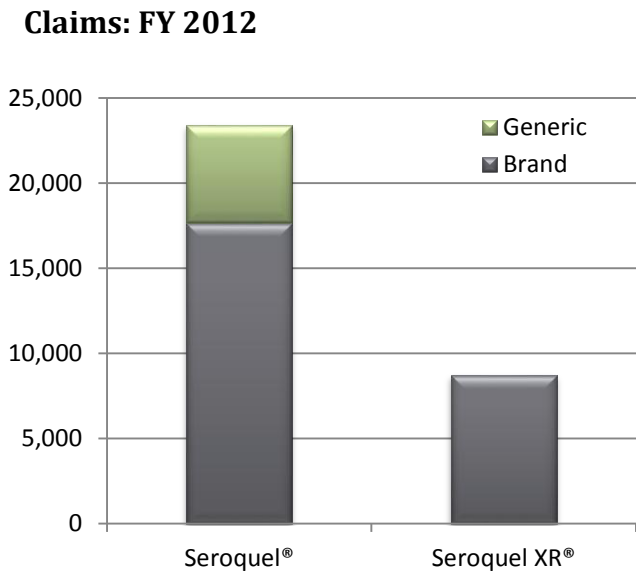
Currently the quetiapine immediate release product is on Tier-1 and available without a prior authorization. The generic of the quetiapine IR became available in the U.S. on March 26, 2012 and a state maximum allowable cost was applied in April 2012. The current tier structure of the Atypical Antipsychotics PBPA category is as follows:

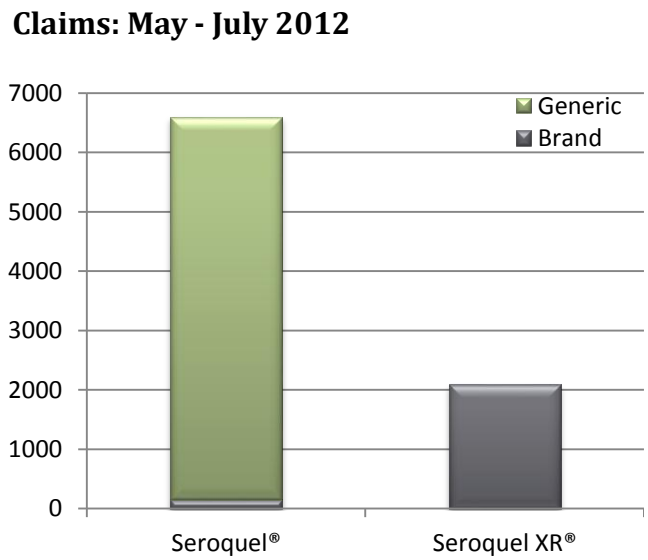
| Tier 1 | Tier 2 | Tier 3[†] |
|---|---|---|
| risperidone **(Risperdal®)**[₸] | aripiprazole **(Abilify®)** | paliperidone **(Invega®)** |
| quetiapine **(Seroquel®)** | iloperidone **(Fanapt™)** | clozapine **(Fazaclo®)** |
| olanzapine **(Zyprexa®)** | quetiapine ER **(Seroquel XR®)** | olanzapine/fluoxetine **(Symbyax®)** |
| clozapine **(Clozaril®)** | ziprasidone **(Geodon®)** | lurasidone **(Latuda®)** |
| | asenapine **(Saphris®)** | |

The following chart shows the utilization trends of quetiapine IR in the past 19 months.




The following chart shows the utilization between the IR and the XR doses. The data shows there are currently three times more usage of the IR product than the XR product. Within the past three months, the utilization is nearly all generic for the quetiapine IR formulation. This is due to the mandatory generic plan design.



The following chart shows a cost comparison between the products:

| Medication | Cost/Tab: SMAC | Cost/Tab: EACW | Avg Units/Day* |
|---|---|---|---|
| Seroquel 25mg | $0.39 | | 1.7 |
| Seroquel 50mg | $0.48 | | 1.5 |
| Seroquel 100mg | $0.49 | | 1.4 |
| Seroquel 200mg | $0.66 | | 1.4 |
| Seroquel 300mg | $0.75 | | 1.6 |
| Seroquel 400mg | $0.81 | | 1.6 |
| Seroquel XR 50mg | | $5.98 | 1.3 |
| Seroquel XR 150mg | | $10.74 | 1.0 |
| Seroquel XR 200mg | | $11.82 | 1.0 |
| Seroquel XR 300mg | | $15.49 | 1.3 |
| Seroquel XR 400mg | | $18.21 | 1.4 |

SMAC = State Maximum Allowable Cost
EACW = Estimated Wholesale Acquisition Cost
*SoonerCare specific data for FY 2012

## RECOMMENDATIONS

The College of Pharmacy recommends an addition to the Atypical Antipsychotics prior authorization criteria to be effective January 1, 2013:

- In addition to applicable tier trials, petitions for Seroquel XR® require a clinically significant reason why member cannot use the quetiapine immediate release.

Members currently stabilized on Seroquel XR® will be grandfathered.

1. Figueroa C, Brecher M, Hamer-Maansson JE, Winter H. **Pharmacokinetic profiles of extended release quetiapine fumarate compared with quetiapine immediate release.** Neuropsychopharmacol Biol Psychiatry. 2009 Mar 17;33(2):199-204. Epub 2008 Oct 9

2. Datto C, Berggren L, Patel JB, Eriksson H. **Self-reported sedation profile of immediate-release quetiapine fumarate compared with extended-release quetiapine fumarate during dose initiation: a randomized, double-blind, crossover study in healthy adult subjects.** Clin Ther. 2009 Mar;31(3):492-502.

# Appendix E

# Annual Review of Benign Prostatic Hyperplasia Medications- Fiscal Year 2012
# And 30 day Notice to Prior Authorize Cialis® (tadalafil)

Oklahoma HealthCare Authority

September 2012

## Current Prior Authorization Criteria

Prior Authorization Criteria:

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

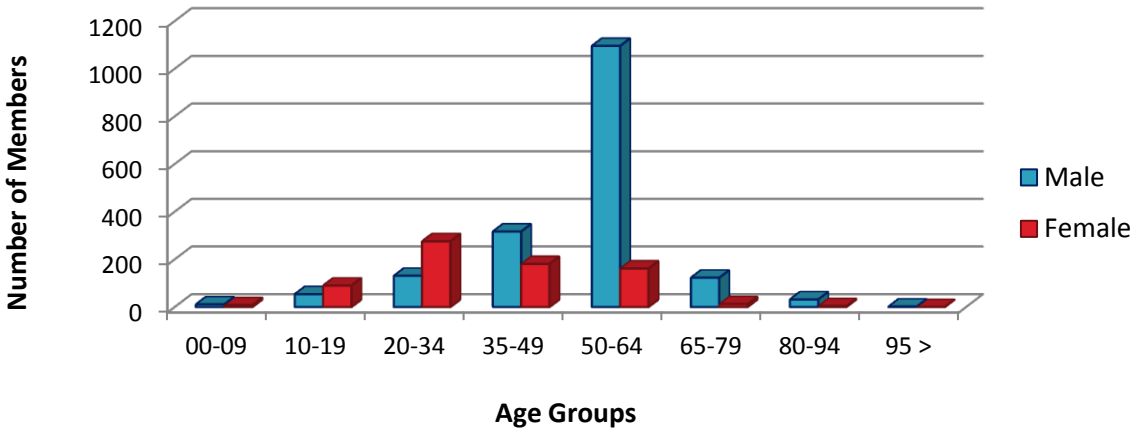
| Tier 1 | Tier 2 |
|---|---|
| Uroxatral® (Alfuzosin) | Rapaflo® (Silodosin) |
| Hytrin® (Terazosin) | Cardura XL® (Doxazosin) |
| Cardura® (Doxazosin) | Avodart® (Dutasteride) |
| Flomax® (Tamsulosin) | Jalyn® (Dutasteride/Tamsulosin) |
| Proscar® (Finasteride) | |

## Utilization of Benign Prostatic Hyperplasia Medications

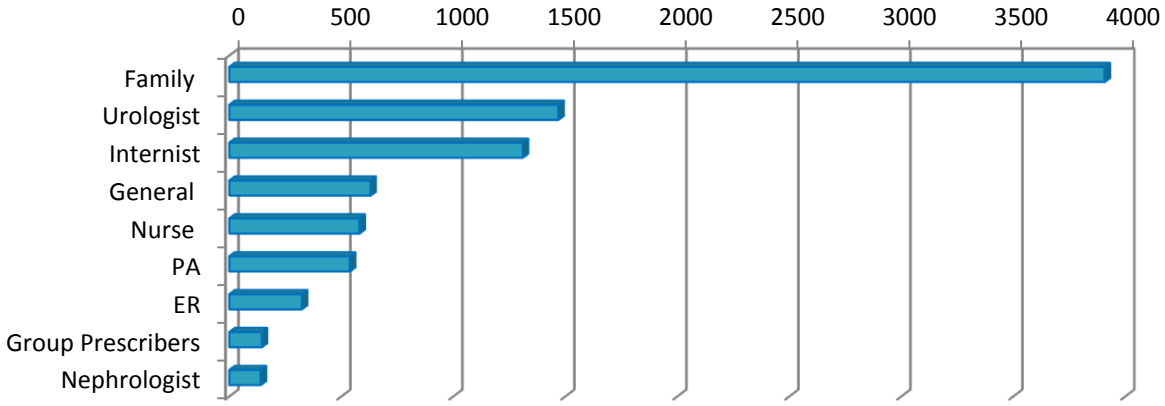
**Comparison of Fiscal Years**

| Fiscal Year | Total Members | Total Claims | Total Cost | Cost/Claim | Per-Diem Cost | Total Units | Total Days |
|---|---|---|---|---|---|---|---|
| **2011** | 2,178 | 8,716 | $253,142.20 | $29.04 | $0.80 | 343,389 | 316,870 |
| **2012** | 2,501 | 9,728 | $181,482.46 | $18.66 | $0.51 | 388,367 | 357,305 |
| **% Change** | **14.8%** | **11.6%** | **-28.3%** | **-35.7%** | **-36.3%** | **13.1%** | **12.8%** |
| **Total Change** | **323** | **1,012** | **$71,659.74** | **$10.38** | **$0.29** | **44,978** | **40,435** |

**Demographics of Members Utilizing Benign Prostatic Hyperplasia Medications: FY 2012**



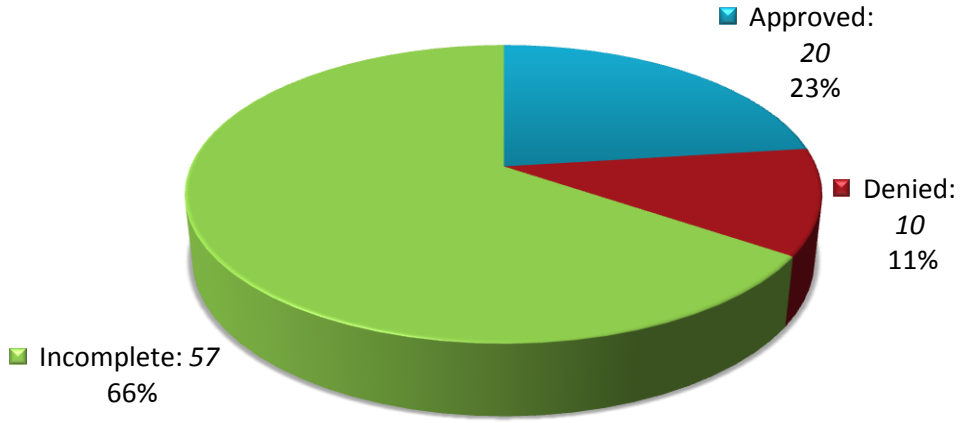
**Prescribers of Benign Prostatic Hyperplasia Medications by Number of Claims: FY 2012**




## Prior Authorization of Benign Prostatic Hyperplasia Medications

There were a total of 87 petitions submitted for this PBPA category during fiscal year 2012. Computer edits are in place to detect tier-1 medication in member's recent claims history and generate automated prior authorization where possible. The following chart shows the status of the submitted petitions.

**Status of Petitions for Benign Prostatic Hyperplasia: FY 2012**




## Market News and Update

- Uroxatral® (alfuzosin) – patent expired July 2011
  (Generic is available and a SMAC price has been applied)
- Avodart® (Dutasteride) – anticipated patent expiration September 2013
- Jalyn® (Dutasteride/Tamsulosin) - anticipated patent expiration September 2013
- Rapaflo® (Silodosin) – anticipated exclusivity expiration in October 2013

## Cialis® (tadalafil) Summary[2]

Cialis® (tadalafil) is indicated for erectile dysfunction. In October of 2011, the FDA approved two additional indications: the treatment of the signs and symptoms of benign prostatic hyperplasia and the combination of both erectile dysfunction and benign prostatic hyperplasia. For the indications involving benign prostatic hyperplasia Cialis® should be dosed once daily.

Cialis® (tadalafil) is available as 2.5, 5, 10, and 20 mg tablets, and should be taken by mouth once daily at approximately the same time every day. The recommended initial strength of Cialis® for once daily use for the indication of BPH should be 5mg. There are no well-established maximum doses for the approved indications according to the prescribing information. Cialis® tablets should not be split. Tablets may be taken without regard to food, however alcohol should be avoided. The dose should be evaluated in patients when co-administered with drugs that are potent CYP3A inhibitors.

## Efficacy

The efficacy of Cialis® (tadalafil) in patients with benign prostatic hyperplasia with lower urinary tract symptoms were evaluated in 2 randomized, multinational, double-blind, placebo-controlled, parallel-design studies of 12 week duration. The trials evaluated men ages 44 to 87 years of age with BPH by using the International Prostate Symptom Score (IPSS) which assesses irritative and obstructive symptoms. Scores for the IPSS questionnaire range from 0-35 with 35 being the most severe. Both studies showed with statistical significance improvement in IPSS compared to placebo at the dose of 5mg once daily.

Cialis® (tadalafil) comes in the following strengths:

| **Cialis® (tadalafil)** | **EACW[+]** |
|---|---|
| **2.5mg** | $3.97 |
| **5mg** | $3.97 |
| **10mg** | $25.58 |
| **20mg** | $12.69 |

[+]price per tablet

## Conclusion and Recommendations

The College of Pharmacy recommends the addition of a Tier-3 and placement of Cialis® (tadalafil) into Tier-3 of the Benign Prostatic Hyperplasia PBPA category with the following criteria:

| Tier 1 | Tier 2 | Tier 3 |
|---|---|---|
| Uroxatral® (Alfuzosin) | Rapaflo® (Silodosin) | **Cialis® (tadalafil)** |
| Hytrin® (Terazosin) | Cardura XL® (Doxazosin) | |
| Cardura® (Doxazosin) | Avodart® (Dutasteride) | |
| Flomax® (Tamsulosin) | Jalyn® (Dutasteride/Tamsulosin) | |
| Proscar® (Finasteride) | | |

Tier-2 Prior Authorization Criteria:

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

Tier-3 Prior Authorization Criteria:

1. FDA approved diagnosis.
2. Trial of at least two Tier 1 medications from different pharmacological classes.
3. A 4-week trial of each Tier 2 medication within the past 5 months.
4. Documented adverse effect, drug interaction, or contraindication to all available Tier 2 products.

## Utilization Details of Benign Prostatic Hypertrophy Medications: Fiscal Year 2012

| GENERIC NAME | BRAND NAME | CLAIMS | UNITS | DAYS | MEMBERS | COST | UNITS/ DAY | CLAIMS/ MEMBER | COST/ DAY | % COST |
|---|---|---|---|---|---|---|---|---|---|---|
| Alfuzosin 10mg | Uroxatral 10mg | 28 | 977 | 947 | 14 | $3,854.70 | 1.03 | 2.00 | $4.07 | 2.12% |
| Alfuzosin 10mg | Alfuzosin 10mg | 111 | 4,567 | 4,297 | 27 | $1,637.88 | 1.06 | 4.11 | $0.38 | 0.90% |
| | Subtotal | 139 | 5,544 | 5,244 | 41 | $5,492.58 | 1.05 | 3.39 | $1.05 | |
| Doxazosin 1mg | Doxazosin 1mg | 286 | 14,733 | 12,888 | 123 | $2,850.23 | 1.14 | 2.33 | $0.22 | 1.57% |
| Doxazosin 2mg | Doxazosin 2mg | 519 | 24,634 | 20,653 | 163 | $4,610.76 | 1.19 | 3.18 | $0.22 | 2.54% |
| Doxazosin 4mg | Doxazosin 4mg | 861 | 34,788 | 30,862 | 205 | $7,297.49 | 1.13 | 4.20 | $0.24 | 4.02% |
| Doxazosin 8mg | Doxazosin 8mg | 318 | 14,002 | 13,717 | 83 | $2,935.59 | 1.02 | 3.83 | $0.21 | 1.62% |
| Doxazosin 8mg | Cardura 8mg | 6 | 90 | 180 | 1 | $34.20 | 0.5 | 6.00 | $0.19 | 0.02% |
| | Subtotal | 1,990 | 88,247 | 78,300 | 575 | $17,728.27 | 1.13 | 3.46 | $0.23 | |
| Tamsulosin 0.4mg | Tamsulosin 0.4mg | 5,507 | 206,024 | 190,492 | 1,662 | $76,742.43 | 1.08 | 3.31 | $0.40 | 42.29% |
| Tamsulosin 0.4mg | Flomax 0.4mg | 3 | 90 | 90 | 1 | $44.18 | 1 | 3.00 | $0.49 | 0.02% |
| | Subtotal | 5,510 | 206,114 | 190,582 | 1,663 | $76,786.61 | 1.08 | 3.31 | $0.40 | |
| Terazosin 1mg | Terazosin 1mg | 205 | 7,615 | 7,255 | 64 | $1,429.27 | 1.05 | 3.20 | $0.20 | 0.79% |
| Terazosin 10mg | Terazosin 10mg | 102 | 4,912 | 4,132 | 27 | $718.52 | 1.19 | 3.78 | $0.17 | 0.40% |
| Terazosin 2mg | Terazosin 2mg | 332 | 16,947 | 13,371 | 109 | $2,908.32 | 1.27 | 3.05 | $0.22 | 1.60% |
| Terazosin 5mg | Terazosin 5mg | 346 | 13,303 | 12,403 | 77 | $2,501.14 | 1.07 | 4.49 | $0.20 | 1.38% |
| | Subtotal | 985 | 42,777 | 37,161 | 277 | $7,557.25 | 1.15 | 3.56 | $0.20 | |
| Dutasteride 0.5mg | Avodart 0.5mg | 283 | 13,068 | 12,828 | 58 | $50,602.46 | 1.02 | 4.88 | $3.94 | 27.88% |
| Dutasteride/Tamsulosin | Jalyn 0.5-0.4mg | 39 | 1,590 | 1,590 | 8 | $6,160.66 | 1 | 4.88 | $3.87 | 3.39% |
| Finasteride Tab 5mg | Finasteride 5mg | 759 | 30,217 | 30,790 | 171 | $13,768.52 | 0.98 | 4.44 | $0.45 | 7.59% |
| Silodosin Cap 8mg | Rapaflo 8mg | 23 | 810 | 810 | 5 | $3,386.11 | 1 | 4.60 | $4.18 | 1.87% |
| | **Total** | **9,728** | **388,367** | **357,305** | | **$181,482.46** | **1.09** | **3.89** | **$0.51** | **100.00%** |

## PRODUCT DETAILS OF CIALIS® (tadalafil)[2]

**INDICATIONS:** Cialis® is indicated for the following:

- treatment of erectile dysfunction
- signs and symptoms of benign prostatic hyperplasia (BPH)
- erectile dysfunction and the signs and symptoms of BPH

**DOSAGE FORM:** 2.5 mg, 5 mg, 10 mg, 20 mg.

**ADMINISTRATION:** BPH - one 5 mg tablet oral taken at the same time every day without regard to food.

**CONTRAINDICATIONS:** Cialis® administered in conjunction with any form of organic nitrate.

**SPECIAL POPULATIONS:**

- **Pregnancy Category B.** Cialis® is not intended for use in women. There are no adequate and well controlled studies in pregnant women; animal studies revealed no evidence of fetal harm.
- **Pediatric Use:** Cialis® is not indicated for use in pediatric patients. Safety and effectiveness in patients <18 years of age have not been established.
- **Geriatric Use:** No dose adjustment is needed for age alone.
- **Renal Impairment:** Creatinine clearance 30 to 50mL/min: starting dose of 5mg once per day is recommended, and the max dose is 10mg once in every 48 hours. Creatinine clearance less than 30mL/min or on hemodialysis the max dose is 5mg once in every 72 hours.
- **Hepatic Impairment:** Cialis® is not recommended in patients with severe (Child Pugh Class C) hepatic impairment. Mild to moderate impairment has not been extensively studied.

**WARNINGS & PRECAUTIONS:**

- **Cardiovascular status:** Cialis® is not recommended in: myocardial infarction, unstable angina or angina, ≥NYHA II, stroke, uncontrolled arrhythmias, hypotension, or uncontrolled hypertension.
- **Drug Interactions:** nitrates, alpha-blockers, anti-hypertensives, potent CYP3A4 inhibitors, alcohol, and other PDE5 inhibitors or erectile dysfunction therapies.
- **Prolonged Erection**: erections lasting longer than 4 hours and priapism - should seek emergency medical attention.
- **Eye:** sudden loss of vision in one or both eyes - should seek medical attention. Individuals with Non-Arteritic Anterior Ischemic Optic Neuropathy should inform physicians prior to use.
- **Sudden Hearing Loss:** sudden decrease or loss of hearing needs prompt medical attention.
- **Other Prior Urological Conditions:** other urological conditions like prostate cancer have similar symptoms therefore consideration should be given when initiating Cialis®.
- **Effects on Bleeding:** treatment of patients with bleeding disorders or significant active peptic ulcerations should be based upon risk-benefit assessment and caution.

**ADVERSE REACTIONS:** (occurring >2%)

- headache
- dyspepsia
- back pain
- nasal congestion
- flushing
- pain in limb/myalgia

[1]Bushman W. Etiology, Epidemiology, and Natural History. *Urol Clin North Am*. 36(4): 405-15. Nov. 2009 V.
[2] Cialis® Prescribing Information. Lilly USA, LLC. Accessed online at: http://pi.lilly.com/us/cialis-pi.pdf Last revised October 2011.

# Appendix F

# Annual Review of Adcirca® (tadalafil) and Revatio® (sildenafil)
# Fiscal Year 2012

Oklahoma HealthCare Authority
September 2012

## Current Prior Authorization Criteria

Revatio® (sildenafil) criteria:

1. Diagnosis:
   - Pulmonary Arterial Hypertension (early stage; NYHA Class II.)
   - Medical supervision by a pulmonary specialist and/or cardiologist.
2. Quantity limit of #90 tablets per 30 days

Adcirca® (tadalafil) criteria:

1. FDA approved diagnosis of pulmonary arterial hypertension.
2. Medical supervision by a pulmonary specialist and/or cardiologist.
3. Quantity limit of #60 tablets per 30 days will apply.

## Utilization

### Adcirca® Comparison of Fiscal Years

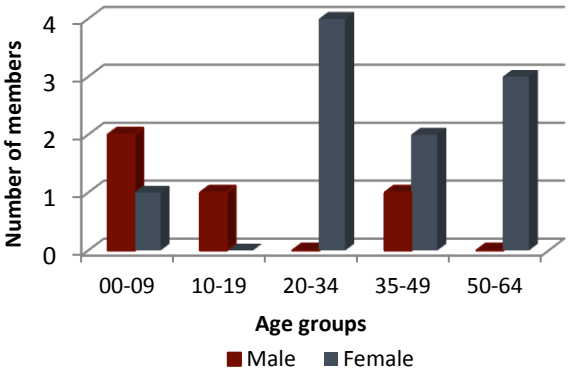
| Fiscal Year | Members | Claims | Cost | Cost/Claim | Perdiem | Units | Days |
|---|---|---|---|---|---|---|---|
| **2011** | 14 | 79 | $65,667.83 | $831.24 | $26.12 | 3,405 | 2,514 |
| **2012** | 14 | 90 | $85,054.48 | $945.05 | $28.64 | 3,842 | 2,970 |
| **Percent Change** | **0.00%** | **13.90%** | **29.50%** | **13.70%** | **9.60%** | **12.80%** | **18.10%** |
| **Change** | **0** | **11** | **$19,386.65** | **$113.81** | **$2.52** | **437** | **456** |

### Revatio® Comparison of Fiscal Years

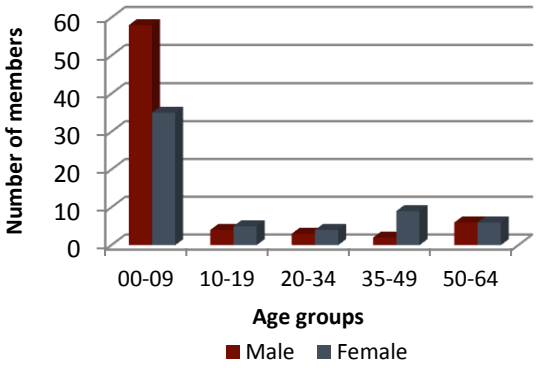
| Fiscal Year | Members | Claims | Cost | Cost/Claim | Perdiem | Units | Days |
|---|---|---|---|---|---|---|---|
| **2011** | 115 | 480 | $411,068.81 | $856.39 | $29.49 | 72,286 | 13,938 |
| **2012** | 132 | 561 | $579,519.15 | $1,033.01 | $34.12 | 73,255 | 16,984 |
| **Percent Change** | **14.80%** | **16.90%** | **41.00%** | **20.60%** | **15.70%** | **1.30%** | **21.90%** |
| **Change** | **17** | **81** | **$168,450.34** | **$176.62** | **$4.63** | **969** | **3,046** |

## Member Demographics: FY 2012

### Adcirca®

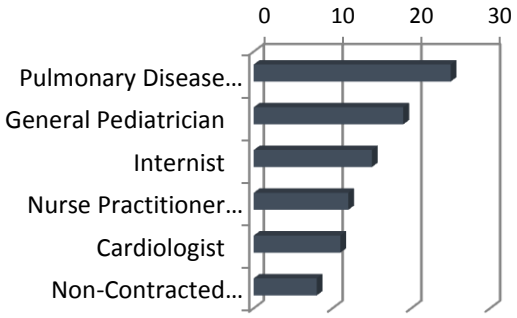



### Revatio®

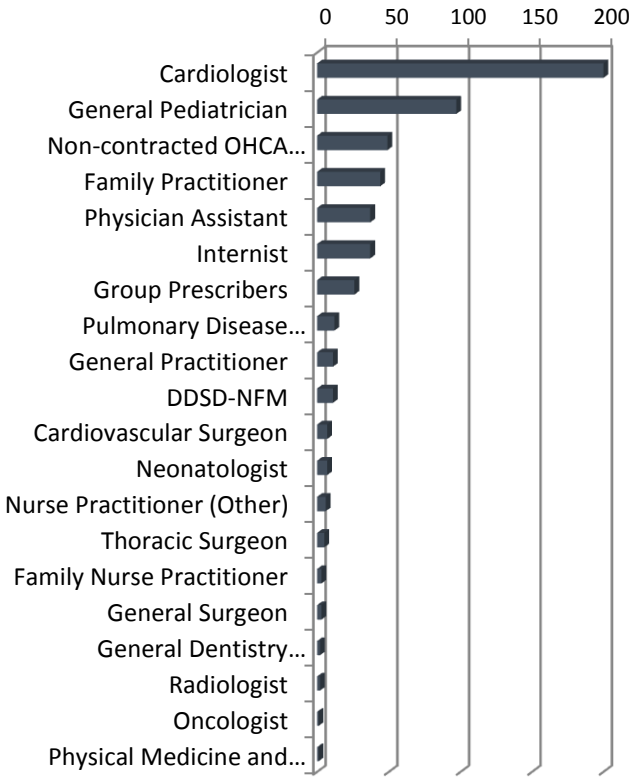



## Top Prescribers by Number of Claims: FY 2012

### Adcirca®




### Revatio®



## Utilization Details

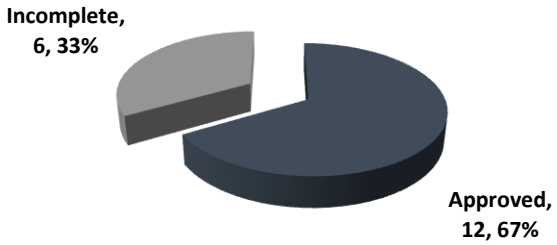
| BRAND NAME | CLAIMS | UNITS | DAYS | MEMBERS | COST | UNITS/ DAY | CLAIMS/ MEMBER | COST/ DAY | PERCENT COST |
|---|---|---|---|---|---|---|---|---|---|
| REVATIO TAB 20MG | 559 | 71,630 | 16,924 | 132 | $564,749.51 | 4.23 | 4.23 | $33.37 | 84.98% |
| ADCIRCA TAB 20MG | 90 | 3,842 | 2,970 | 14 | $85,054.48 | 1.29 | 6.43 | $28.64 | 12.80% |
| REVATIO INJ | 2 | 1,625 | 60 | 1 | $14,769.64 | 27.08 | 2 | $246.16 | 2.22% |
| **TOTALS:** | **651** | **77,097** | **19,954** | **145*** | **$664,573.63** | **3.86** | **4.49** | **$33.31** | **100.00%** |

***Total number of unduplicated members***

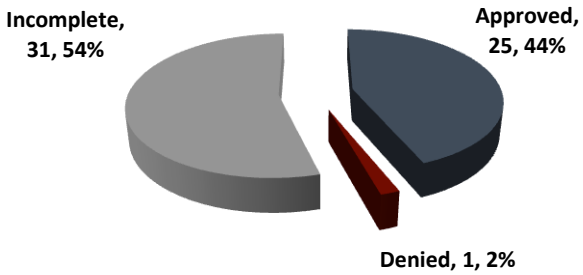
## Prior Authorization

There were 18 petitions submitted for Adcirca® and 57 petitions submitted for Revatio® during fiscal year 2012. The following charts show the status of the submitted petitions.

**Status of Petitions for Adcirca®: FY 2012**




**Status of Petitions for Revatio®: FY 2012**




## Market News and Updates

**Patent Expirations:**

- **Adcirca®:** November 21, 2017
- **Revatio®:** November 7, 2012
  - Several generic formulations of sildenafil have tentative FDA-approval and generic marketing is expected to begin around September 30, 2012.

**Safety alerts[1]:**

On August 30, 2012, the FDA recommended that Revatio® not be prescribed to children ages 1 through 17 for pulmonary arterial hypertension. This recommendation is based on a recent long-term clinical pediatric trial showing that:

1. Children taking a high dose of Revatio® had a higher risk of death than children taking a low dose.
2. Low doses of Revatio are not effective in improving exercise ability.

Most deaths were caused by pulmonary hypertension and heart failure, which are the most common causes of death in children with PAH. Revatio® has never been approved for the treatment of PAH in children, and in light of the new clinical trial information, off-label use of

the drug in pediatric patients is not recommended. The following new information is being added to the Revatio® drug label:

- A new warning stating the use of Revatio® is not recommended in pediatric patients.
- Results of the Revatio® trial in pediatric patients.

## Conclusion and Recommendations

The College of Pharmacy recommends the following changes to the criteria:

Revatio® (sildenafil) and Adcirca® (tadalafil) criteria:

1. **Member must be age 18 or older.**
2. FDA approved diagnosis of pulmonary arterial hypertension.
3. Medical supervision by a pulmonary specialist and/or cardiologist.
4. Quantity limits:
    - Adcirca® 20mg tabs: #60 tablets per 30 days.
    - Revatio® 20mg tabs: #90 tablets per 30 days.

[1] http://www.fda.gov/Drugs/DrugSafety/ucm317123.htm

# Appendix G

# Annual Review of Benlysta® (belimumab) - Calendar Year 2012

Oklahoma HealthCare Authority
September 2012

## Current Prior Authorization Criteria

1. FDA approved indication of adults with active, autoantibody-positive, systemic lupus erythematosus already receiving standard therapy.
2. Documented inadequate response to at least two of the following medications:
    a. High-dose oral corticosteroids
    b. Methotrexate
    c. Azathioprine
    d. Mycophenolate
    e. Cyclophosphamide
3. Member must not have severe active lupus nephritis or severe active central nervous system lupus.
4. No combination use with biologic therapies or intravenous cyclophosphamide.

## Utilization of Benlysta®: Jan 2012 – Jun 2012

### Utilization Summary

| Drug | Claims | Units | Days | Members | Cost | Claims/ Member | Cost/ Day |
|---|---|---|---|---|---|---|---|
| **Benlysta** | 21 | 1,874 | 540 | 5 | $64,271.91 | 4.2 | $119.02 |

### Utilization Details

| Member | Number of claims | Age range | Sex | Primary diagnosis |
|---|---|---|---|---|
| **1** | 3 | 41-50 | Female | Systemic lupus erythematosus |
| **2** | 2 | 41-50 | Female | Systemic lupus erythematosus |
| **3** | 5 | 41-50 | Female | Systemic lupus erythematosus |
| **4** | 4 | 31-40 | Female | Systemic lupus erythematosus |
| **5** | 7 | 41-50 | Female | Systemic lupus erythematosus |

## Market News and Updates

- A study accepted for publication in Arthritis & Rheumatism for 2012 suggests that when belimumab is added to standard therapy for SLE it is generally well-tolerated over a period of 4 years and has an acceptable safety profile for long-term use. This study was a long-term continuation of the original 52-week double-blind study and included 296 patients (out of 364 who completed the original study). Incidence rates of adverse events, including serious adverse events, were stable or declined during this 4-year period. The most common adverse events were arthralgia, upper respiratory tract infection, headache, fatigue, and nausea.

- Potential for off-label use based on clinical trials investigating the following conditions can be found at www.clinicaltrials.gov and are in various stages of research.
    - Prevention of kidney transplant rejection
    - Waldenstrom's Macroglobulinemia
    - Sjogren's syndrome
    - Wegener's granulomatosis
    - Membranous glomerulonephropathy
    - Rheumatoid arthritis
    - Myasthenia gravis
    - Idiopathic thromobocytopenia purpura
    - Systemic sclerosis

## Conclusion and Recommendations

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

# Appendix H

# 30 Day Notice to Prior Authorize Neupro® (Rotigotine Transdermal System)

**Oklahoma Health Care Authority**
**September 2012**

| | |
|---|---|
| **Manufacturer** | UCB, Inc. |
| **Classification** | Parkinson's Disease/Restless Leg Syndrome |
| **Status** | Prescription Only |

## Summary

**Parkinson's Disease**[1]

Parkinson's disease is a progressive neurodegenerative disorder that typically begins after the age of 50 years old and has a lifetime risk of 2% for men and 1.3% for women. The exact underlying cause of Parkinson's disease is unknown but the hallmark pathologic features of Parkinson's disease are the death of dopaminergic neurons in the brainstem. People with Parkinson's disease often exhibit a characteristic tremor, rigidity, and a masked facial expression as well as other motor and non-motor symptoms.

**Restless Leg Syndrome**[2]

Restless Leg syndrome (RLS) is a common neurological movement disorder affecting approximately 10 percent of adults of which about one third have severe enough symptoms to require medical treatment. RLS maybe be a primary condition, or it may be secondary to renal failure, iron deficiency, medications, or pregnancy. RLS presents with the urge to move the legs and is usually accompanied by an uncomfortable sensation. RLS symptoms typically occur at rest and improve with activity. These symptoms usually result in sleep disturbances which have a negative impact on quality of life.

**Indication and Dosing**[3]

Neupro® (Rotigotine Transdermal System) is FDA approved to treat signs and symptoms of Parkinson's disease and moderate-to-severe Restless Leg Syndrome. Rotigotine is a non-ergoline dopamine receptor agonist. The exact mechanism(s) of action in the treatment of Parkinson's disease and restless legs syndrome are unknown but are thought to be related to rotigotine's ability to stimulate dopamine receptors. In the treatment of Parkinson's disease, rotigotine is thought to stimulate dopamine receptors within the caudate-putamen in the brain.

Neupro® (Rotigotine Transdermal System) is available in 1 mg, 2 mg, 3 mg, 4 mg, 6 mg and 8 mg per 24 hours patch. The recommended dosing is as follows:

**Parkinson's disease:**

- Initially, 2 mg/24 hours for early-stage disease or 4 mg/24 hours for advanced-stage disease.
- Dose may be increased as needed by 2 mg/24 hours at weekly intervals, up to 6 mg /24 hours for early-stage disease and up to 8 mg/24 hours for advanced-stage disease.

**Restless Legs Syndrome:**

- Initially, 1 mg/24 hours.
- Increase as needed by 1 mg/24 hours at weekly intervals, up to 3 mg/24 hours.

The dose should be reduced gradually until complete withdrawal of Neupro® to discontinue treatment.

Neupro® (Rotigotine Transdermal System) contains sodium metabisulfite that may cause allergic reactions in patients with sulfite sensitivity. Neupro® is contraindicated in those who have a hypersensitivity to rotigotine or components of the transdermal patch. Neupro® can cause hallucinations, psychotic-like behavior, dyskinesia, falling asleep during activities of daily living such as operating a motor vehicle, symptomatic postural hypotension and syncope, application site reactions, elevation of blood pressure and heart rate, and intense urges that may cause impulse control and compulsive behaviors.

**Cost**
Neupro® (Rotigotine Transdermal System) comes in the following strengths:

| Dose | Average Wholesale Price Per Patch (EACW) | Est. 30 Day Cost |
|---|---|---|
| 1 mg/24 hours | $4.48 | $134.40 |
| 2 mg/24 hours | $4.48 | $134.40 |
| 3 mg/24 hours | $4.48 | $134.40 |
| 4 mg/24 hours | $13.20 | $396.00 |
| 6 mg/24 hours | $13.20 | $396.00 |
| 8 mg/24 hours | $13.20 | $396.00 |

Sinemet® (carbidopa/levodopa), the gold standard for Parkinson's disease and RLS treatment, dosed at the maximum dose indicated (carbidopa/levodopa 25 mg/250 mg tablets dosed at a maximum of 8 tablets per day) costs an estimated **$74.40** per 30 days.

## Recommendations

The College of Pharmacy recommends the prior authorization of Neupro® (Rotigotine Transdermal System) with the following criteria:

**Parkinson's Disease:**

1. FDA approved indication for the treatment of signs and symptoms of Parkinson's disease.
2. Must be 18 years old or older.
3. Prior use of or clinically significant reason why member cannot use oral dopamine agonists.

**Restless Leg Syndrome:**

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

# Product Information of Neupro® (Rotigotine Transdermal System)[3]
# FDA Approved: 2007

**INDICATIONS:** Neupro® is a dopamine agonist indicated for the treatment of signs and symptoms of Parkinson's disease and moderate-to-severe primary Restless Leg Syndrome.

**DOSAGE FORM:** Transdermal System: 1 mg, 2 mg, 3 mg, 4 mg, 6 mg, and 8 mg rotigotine per 24 hours.

**ADMINISTRATION:**

- **Parkinson's disease:** Initially, 2 mg/24 hours for early-stage disease or 4 mg/24 hours for advanced-stage disease. The dose may be increased as needed by 2 mg/24 hours at weekly intervals, up to 6 mg/24 hours for early-stage disease and up to 8 mg/24 hours for advanced-stage disease.
- **Restless Legs Syndrome:** Initially, 1 mg/24 hours, increased as needed by 1 mg/24 hours at weekly intervals, up to 3 mg/24 hours.
- Apply once a day to the skin; press firmly in place for 30 seconds, making good contact. Do not place Neupro® on oily, irritated, or damaged skin, or where it will be rubbed by tight clothing. Do not use the same site more than once every 14 days. The prescribed dose may be achieved using single or multiple patches.

**CONTRAINDICATIONS:** History of hypersensitivity to rotigotine or components of the transdermal patch.

**WARNINGS AND PRECAUTIONS:**

- Contains sodium metabisulfite that may cause allergic-type reactions in those with sulfite sensitivity.
- Falling asleep during activities of daily living, including the operation of motor vehicles and somnolence may occur.
- Hallucinations/psychotic-like behavior and dyskinesia may occur.
- Symptomatic postural hypotension and syncope may occur, especially during dose escalation.
- Application site reactions can occur, and may be severe.
- Elevation of blood pressure and heart rate may occur.
- Intense urges may cause impulse control and compulsive behaviors.
- Monitor patients for these adverse reactions. If these adverse reactions occur, lowering the dose or discontinuing Neupro may be beneficial.

**SPECIAL POPULATIONS**:

- **Pregnancy Category C**. Rotigotine decreases prolactin secretion in humans and could potentially inhibit lactation. It is unknown if rotigotine and/or its metabolites are excreted in human milk but use caution when administered to nursing women.

- **Pediatric Use**: Safety and effectiveness in pediatric patients for any indication have not been established.
- **Geriatric Use**: Clinical studies have shown Neupro® to be safe and effective in the elderly but greater sensitivity of some older individuals cannot be ruled out.
- **Renal and Hepatic Impairment**: No dosage adjustment is recommended in renal impairment and moderate impairment of hepatic function. No information is available on subjects with severe impairment of hepatic function.

**ADVERSE REACTIONS**: (≥ 5% greater than placebo)

- Nausea
- Vomiting
- Somnolence
- Application site reactions
- Dizziness
- Anorexia
- Hyperhidrosis
- Insomnia
- Peripheral edema
- Dyskinesia

**DRUG INTERACTIONS:** There is a low risk of inhibition of CYP2C19 and CYP2D6 catalyzed metabolism of other drugs at therapeutic concentrations.

References:


1. Simmons, Adam, MD. "Chapter 13 – Parkinson Disease." *Rakel: Integrative Medicine, 3rd ed.* n.pag. *MD Consult*. Web. 14 Aug 2012. <http://www.mdconsult.com/books/page.do?eid=4-u1.0-B978-1-4377-1793-8..00013-3&isbn=978-1-4377-1793-8&uniqId=351389500-9>.
2. Avonda, Thomas, MD, and James Wadzinski, MD. "Restless Legs Syndrome." *American Family Physician*. By Max Bayard, MD. Vol. 78. N.p.: n.p., n.d. N. pag. *MD Consult*. Web. 17 Aug. 2012. <http://http://www.mdconsult.com/das/article/body/351991831-3/jorg=journal&source=&sp=20847352&sid=0/N/651687/1.html?issn=0002-838X>.
3. "NEUPRO HIGHLIGHTS OF PRESCRIBING INFORMATION." . N.p., 04/2012. Web. 14 Aug 2012. <http://www.neupro.com/pdf/Neupro-PI.pdf>.

# Appendix I

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

## FDA NEWS RELEASE

For Immediate Release: Sept. 4, 2012
FDA approves new orphan drug for chronic myelogenous leukemia

The U.S. Food and Drug Administration today approved Bosulif (bosutinib) to treat chronic myelogenous leukemia (CML), a blood and bone marrow disease that usually affects older adults.

An estimated 5,430 men and women will be diagnosed with CML in 2012. Most people with CML have a genetic mutation, called the Philadelphia chromosome, which causes the bone marrow to make an enzyme called tyrosine kinase. This enzyme triggers the development of too many abnormal and unhealthy white blood cells called granulocytes. Granulocytes fight infection.

Bosulif is intended for patients with chronic, accelerated or blast phase Philadelphia chromosome positive CML who are resistant to or who cannot tolerate other therapies, including imatinib. Bosulif works by blocking the signal of the tyrosine kinase that promotes the development of abnormal and unhealthy granulocytes. Other drugs recently approved by FDA to treat various forms of CML include imatinib (2001), dasatinib (2006) and nilotinib (2007).

The safety and effectiveness of Bosulif was evaluated in a single clinical trial that enrolled 546 adult patients who had chronic, accelerated or blast phase CML. All patients had disease that progressed after treatment with imatinib or imatinib followed by dasatinib and/or nilotinib, or who could not tolerate the side effects of prior therapy. All patients in the trial were treated with Bosulif.

In patients with chronic phase CML, efficacy was determined by the number of patients who experienced a major cytogenetic response (MCyR) within the first 24 weeks of treatment. Results showed 34 percent of patients who had been previously treated with imatinib achieved MCyR after 24 weeks. Of the patients who achieved MCyR at any time, 52.8 percent had their response last at least 18 months. Among patients previously treated with imatinib followed by dasatinib and/or nilotinib, about 27 percent achieved MCyR within the first 24 weeks of treatment. Of those who achieved MCyR at any time, 51.4 percent had their MCyR last at least nine months.

In patients with accelerated CML previously treated with at least imatinib, 33 percent had their blood counts that returned to normal range (complete hematologic response) and 55 percent achieved normal blood counts with no evidence of leukemia (overall hematologic response) within the first 48 weeks of treatment. Meanwhile, 15 percent and 28 percent of patients with blast phase CML achieved complete hematologic response and overall hematologic response, respectively.

The most common side effects observed in those receiving Bosulif were diarrhea, nausea, a low level of platelets in the blood (thrombocytopenia), vomiting, abdominal pain, rash, low red blood cell count (anemia), fever and fatigue.

Bosulif is marketed by New York City-based Pfizer.

## FDA NEWS RELEASE

For Immediate Release: Aug. 31, 2012
FDA approves new treatment for a type of late stage prostate cancer

The U.S. Food and Drug Administration today approved Xtandi (enzalutamide) to treat men with late-stage (metastatic) castration-resistant prostate cancer that has spread or recurred, even with medical or surgical therapy to minimize testosterone.

Approved for prostate cancer patients previously treated with docetaxel, another anti-cancer treatment, Xtandi was reviewed under the FDA's priority review program. The program provides for an expedited six-month review for drugs that may offer major advances in treatment or that provide a treatment when no adequate therapy exists. Xtandi received FDA approval three months ahead of the product's prescription drug user fee goal date of Nov. 22, 2012.

Prostate cancer forms in a gland in the male reproductive system found below the bladder and in front of the rectum. The male sex hormone testosterone stimulates the prostate tumors to grow. According to the National Cancer Institute, an estimated 241,740 men will be diagnosed with prostate cancer and 28,170 will die from the disease in 2012.

The safety and effectiveness of Xtandi was evaluated in a study of 1,199 patients with metastatic castration-resistant prostate cancer who had received prior treatment with docetaxel. The study was designed to measure overall survival (the length of time before death) in men receiving Xtandi compared with men receiving a placebo (sugar pill). The median overall survival for patients receiving Xtandi was 18.4 months, compared with 13.6 months for the patients who received placebo.

The most common side effects observed in study participants taking Xtandi were weakness or fatigue, back pain, diarrhea, joint pain, hot flush, tissue swelling, musculoskeletal pain, headache, upper respiratory infections, dizziness, spinal cord compression and cauda equina syndrome, muscular weakness, difficulty sleeping, lower respiratory infections, blood in urine, tingling sensation, anxiety, and high blood pressure. Seizures occurred in approximately 1 percent of those receiving Xtandi. Patients in the study who had a seizure stopped Xtandi therapy. The clinical study excluded patients with a history of seizure, an underlying brain injury with loss of consciousness, a temporary decrease in blood to the brain within the past 12 months, a stroke, brain metastases, an abnormal connection of the arteries and veins in the brain, or patients taking medications that may lower the seizure threshold. The safety of Xtandi is unknown in patients with these conditions.

Xtandi will be co-marketed by Astellas Pharma U.S., Inc. of Northbrook, IL and Medivation, Inc. of San Francisco, CA.

## FDA NEWS RELEASE

For Immediate Release: Aug. 30, 2012

FDA approves Linzess to treat certain cases of irritable bowel syndrome and constipation

The U.S. Food and Drug Administration today approved Linzess (linaclotide) to treat chronic idiopathic constipation and to treat irritable bowel syndrome with constipation (IBS-C) in adults.

According to the National Institutes of Health, an estimated 63 million people are affected by chronic constipation. Chronic idiopathic constipation is a diagnosis given to those who experience persistent constipation and do not respond to standard treatment. Additionally, an estimated 15.3 million people are affected by IBS. IBS-C is a subtype characterized mainly by abdominal pain and by hard or lumpy stools at least 25 percent of the time and loose or watery stools less than 25 percent of the time.

Linzess is a capsule taken once daily on an empty stomach, at least 30 minutes before the first meal of the day. Linzess helps relieve constipation by helping bowel movements occur more often. In IBS-C, it may also help ease abdominal pain.

The safety and effectiveness of Linzess for the management of IBS-C were established in two, double-blind studies. A total of 1,604 patients were randomly assigned to take 290 micrograms of Linzess or a placebo for

at least 12 weeks. Results showed Linzess was more effective in reducing the amount of abdominal pain and increasing the number of complete spontaneous bowel movements compared with placebo.
The safety and effectiveness of Linzess for the management of chronic idiopathic constipation also were established in two, double-blind studies. A total of 1,272 patients were randomly assigned to take Linzess at doses of 145 mcg or 290 mcg or a placebo for 12 weeks. Results from these studies showed patients taking Linzess experienced more complete spontaneous bowel movements than those taking the placebo. The 290 mcg dose is not approved for chronic constipation because studies indicated it was no more effective than the 145 mcg dose.
Linzess is approved with a Boxed Warning to alert patients and health care professionals that the drug should not be used in patients 17 years of age and younger. The most common side effect reported in during the clinical studies was diarrhea.
Linzess is co-marketed by Ironwood Pharmaceuticals Inc., based in Cambridge, Mass., and Forest Pharmaceuticals Inc., based in St. Louis, Mo.

## FDA NEWS RELEASE

For Immediate Release: Aug. 10, 2012
FDA approves Lucentis to treat diabetic macular edema

The U.S. Food and Drug Administration today approved Lucentis (ranibizumab injection) for the treatment of diabetic macular edema (DME), a sight-threatening eye disease that occurs in people with diabetes.
An injection administered once a month by a health care professional, Lucentis is intended to be used along with good diabetic blood sugar control.
DME is a condition in which fluid leaks into the macula, the center part of the retina where sharp, straight-forward vision occurs. The fluid makes the macula swell, causing vision to blur.
According to the Centers for Disease Control and Prevention, diabetes (type 1 and type 2) affects about 26 million people in the United States and is the leading cause of new blindness among people ages 20 to 74 years. In 2010, 3.9 million adults diagnosed with diabetes reported trouble with their vision.
The drug's safety and effectiveness to treat DME were established in two clinical studies involving 759 patients who were treated and followed for three years. Patients were randomly assigned to receive monthly injections of Lucentis at 0.3 milligrams (mg) or 0.5 mg, or no injections during the first 24 months of the studies. After 24 months, all patients received monthly Lucentis either at 0.3 mg or 0.5 mg.
The studies measured the number of patients who gained vision, as measured on an eye chart. Results showed that between 34 percent and 45 percent of those treated with monthly Lucentis 0.3 mg gained at least three lines of vision compared with 12 percent to 18 percent of those who did not receive an injection. No additional benefit was observed with the higher monthly Lucentis dose of 0.5 mg.
The most common side effects reported in patients treated with Lucentis include bleeding of the conjunctiva, the tissue that lines the inside of the eyelids and covers the white part of the eye; eye pain; floaters; and increased pressure inside the eye (intraocular pressure).
The FDA previously had approved Lucentis to treat wet (neovascular) age-related macular degeneration (AMD), a condition in which abnormal blood vessels grow and leak fluid into the macula. Lucentis also is approved to treat macular edema following retinal vein occlusion, a blockage of the small veins that carry blood away from the retina that can cause fluid to leak into the macula.
Lucentis is marketed by South San Francisco, Calif.-based Genentech.

## FDA NEWS RELEASE

For Immediate Release: Aug. 27, 2012
FDA approves new combination pill for HIV treatment for some patients

The U.S. Food and Drug Administration today approved Stribild (elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil fumarate), a new once-a-day combination pill to treat HIV-1 infection in adults who have never been treated for HIV infection.

Stribild contains two previously approved HIV drugs plus two new drugs, elvitegravir and cobicistat. Elvitegravir is an HIV integrase strand transfer inhibitor, a drug that interferes with one of the enzymes that HIV needs to multiply. Cobicistat, a pharmacokinetic enhancer, inhibits an enzyme that metabolizes certain HIV drugs and is used to prolong the effect of elvitegravir. The combination of emtricitabine and tenofovir disoproxil fumarate, approved in 2004 and marketed as Truvada, blocks the action of another enzyme that HIV needs to replicate in a person's body. Together, these drugs provide a complete treatment regimen for HIV infection.

Stribild's approval is the latest HIV/AIDS-related action taken by the FDA this year. Other actions include approval of the first over-the-counter home-use rapid HIV test; approval of the first drug for pre-exposure prophylaxis in combination with safer sex practices to reduce the risk of sexually acquired HIV infection in adults at high risk; and commemoration of the full or tentative approvals of more than 150 antiretroviral products for the President's Emergency Plan for AIDS Relief (PEPFAR) to treat those in countries most affected by the HIV/AIDS epidemic.

The safety and effectiveness of Stribild was evaluated in 1,408 adult patients not previously treated for HIV in two double-blind clinical trials. Patients were randomly assigned to receive Stribild or Atripla, an HIV drug that contains Truvada and efavirenz, once daily in the first trial; and Stribild or Truvada plus atazanavir and ritonavir once daily in the second trial.

The studies were designed to measure the percentage of patients who had an undetectable amount of HIV in their blood at 48 weeks. Results showed between 88 percent and 90 percent of patients treated with Stribild had an undetectable amount of HIV in their blood, compared with 84 percent treated with Atripla and 87 percent treated with Truvada plus atazanavir and ritonavir.

Like labels of many other drugs used to treat HIV, Stribild's label carries a Boxed Warning alerting patients and health care professionals that the drug can cause a build up of lactic acid in the blood and severe liver problems, both of which can be fatal. The Boxed Warning also states that Stribild is not approved to treat chronic hepatitis B virus infection.

Common side effects observed in clinical trials include nausea and diarrhea. Serious side effects include new or worsening kidney problems, decreased bone mineral density, fat redistribution and changes in the immune system (immune reconstitution syndrome). Stribild's label gives advice to health care providers on how to monitor patients for kidney or bone side effects.

Gilead Sciences, Stribild's manufacturer, is required to conduct additional studies to help further characterize the drug's safety in women and children, how resistance develops to Stribild, and the possibility of interactions between Stribild and other drugs.

Gilead Sciences is based in Foster City, Calif.

## FDA NEWS RELEASE

For Immediate Release: Aug. 17, 2012
FDA approves first generic Actos to treat type 2 diabetes

The U.S. Food and Drug Administration today approved the first generic version of Actos (pioglitazone hydrochloride) tablets. Along with diet and exercise, pioglitazone is used to improve blood glucose control in adults with type 2 diabetes.

Mylan Pharmaceuticals, based in Morgantown, W.Va., gained FDA approval for 15 milligram, 30 mg and 45 mg pioglitazone tablets.

Diabetes is a disease in which blood glucose, or sugar, levels are too high. Glucose comes largely from the food we eat. Insulin is a hormone that helps move glucose into the body's cells to help them produce energy. In people with type 2 diabetes the body does not make or use insulin well. Without enough insulin, glucose stays in the blood. Over time, too much glucose in the blood can cause serious health problems such as damage to eyes, kidneys, and nerves. Diabetes can also contribute to heart disease, and stroke.

Pioglitazone is dispensed with a patient Medication Guide that provides important instructions about its use and drug safety information. The drug has a Boxed Warning to emphasize that pioglitazone may cause or worsen heart failure, particularly in certain patient populations. Careful monitoring of patients when starting the drug or increasing the dose is recommended. The product label also notes that the use of pioglitazone for more than one year may be associated with an increased risk of bladder cancer.

The most common side effects reported by patients using pioglitazone include cold-like symptoms, headache, sinus infection, muscle pain, and sore throat. Information about the availability of generic pioglitazone can be obtained from the manufacturer.

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

## Safety Announcements

Revatio (sildenafil): Drug Safety Communication - Recommendation Against Use in Children

[Posted 08/30/2012]

AUDIENCE: Pediatrics, Cardiology, Pulmonology

ISSUE: FDA notified healthcare professionals and their medical care organizations that Revatio (sildenafil) should not be prescribed to children (ages 1 through 17) for pulmonary arterial hypertension (PAH).This recommendation against use is based on a recent long-term clinical pediatric trial showing that: (1) children taking a high dose of Revatio had a higher risk of death than children taking a low dose and (2) the low doses of Revatio are not effective in improving exercise ability. Treatment of PAH in children with this drug is an off-label use (not approved by FDA) and a new warning, stating the use of Revatio is not recommended in pediatric patients has been added to the Revatio labeling.

BACKGROUND: Revatio is a phosphodiesterase-5 inhibitor used to treat pulmonary arterial hypertension by relaxing the blood vessels in the lungs to reduce blood pressure and is approved to improve exercise ability and delay clinical worsening of PAH in adult patients (WHO Group I).

RECOMMENDATION: Patients and caregivers are advised to not change the Revatio dose or stop taking Revatio without talking to a health care professional. Healthcare professionals were reminded that use of this product, particularly chronic use, in children is an off-label indication, not approved by FDA, and is not recommended. See the Drug Safety Communication for the Data Summary from the randomized, double-blind, placebo-controlled clinical trial of 234 patients with PAH, 1 to 17 years of age with mild to moderate symptoms at baseline.

## Safety Announcements

FDA Drug Safety Communication: Codeine Use in Certain Children After Tonsillectomy and/or Adenoidectomy: Drug Safety Communication - Risk of Rare, But Life-Threatening Adverse Events or Death

[Posted 08/15/2012]
AUDIENCE: Pediatricians, Surgery, Consumer
ISSUE: The FDA is reviewing reports of children who developed serious adverse effects or died after taking codeine for pain relief after tonsillectomy and/or adenoidectomy for obstructive sleep apnea syndrome. Recently, three pediatric deaths and one non-fatal but life-threatening case of respiratory depression were documented in the medical literature.
These children (ages two to five) had evidence of an inherited (genetic) ability to convert codeine into life-threatening or fatal amounts of morphine in the body. All children had received doses of codeine that were within the typical dose range.
BACKGROUND: When codeine is ingested, it is converted to morphine in the liver by an enzyme called cytochrome P450 2D6 (CYP2D6). Some people have DNA variations that make this enzyme more active, causing codeine to be converted to morphine faster and more completely than in other people. These "ultra-rapid metabolizers" are more likely to have higher than normal amounts of morphine in their blood after taking codeine. High levels of morphine can result in breathing difficulty, which may be fatal. Taking codeine after tonsillectomy and/or adenoidectomy may increase the risk for breathing problems and death in children who are "ultra-rapid metabolizers." See the FDA Drug Safety Communication for additional information, including a Data Summary.
RECOMMENDATION: Health care professionals should be aware of the risks of using codeine in children, particularly in those who have undergone tonsillectomy and/or adenoidectomy for obstructive sleep apnea syndrome. If prescribing codeine-containing drugs, the lowest effective dose for the shortest period of time should be used on an as-needed basis (i.e., not scheduled around the clock).
Parents and caregivers who observe unusual sleepiness, confusion, or difficult or noisy breathing in their child should seek medical attention immediately, as these are signs of overdose.

## Current Drug Shortages Index (as of September 5, 2012):

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

- Acetylcysteine Inhalation Solution UPDATED 9/5/2012
- Alfentanil Injection UPDATED 8/31/2012
- Amino Acid Products UPDATED 8/31/2012
- Ammonium Chloride Injection UPDATED 8/31/2012
- Aquasol A UPDATED 8/31/2012
- Atropine Sulfate Injection UPDATED 9/5/2012
- Bumetanide Injection UPDATED 8/31/2012
- Bupivacaine Hydrochloride Injection UPDATED 8/31/2012
- Buprenorphine Injection UPDATED 9/5/2012
- Butorphanol Injection UPDATED 8/31/2012
- Caffeine, anhydrous (125 mg/mL) and Sodium benzoate (125 mg/mL) UPDATED 9/5/2012
- Cardiolite, Kit for the Preparation of Technetium Tc99m Sestamibi for Injection UPDATED 8/30/2012
- Chromic Chloride Injection UPDATED 9/5/2012

Diazepam Injection UPDATED 8/31/2012
Epinephrine Injection UPDATED 8/31/2012
Epinephrine 1mg/mL (Preservative Free) UPDATED 9/5/2012
Erythromycin Lactobionate Injection UPDATED 8/31/2012
Esomeprazole (Nexium) For Delayed-Release Oral Suspension UPDATED 9/5/2012
Etomidate Injection UPDATED 9/5/2012
Fentanyl Citrate Injection UPDATED 8/31/2012
Fospropofol disodium (Lusedra) Injection UPDATED 8/30/2012
Furosemide Injection UPDATED 9/5/2012
Heparin Sodium Premixes UPDATED 8/31/2012
Hydromorphone Hydrochloride Injection UPDATED 8/31/2012
Ketorolac Injection UPDATED 9/5/2012
Leucovorin Calcium Lyophilized Powder for Injection UPDATED 8/31/2012)
Leuprolide Acetate Injection UPDATED 8/28/2012
Lidocaine Hydrochloride Injection UPDATED 9/5/2012
Lidocaine HCL, 4% Topical Solution UPDATED 8/31/2012)
Magnesium Sulfate Injection UPDATED 9/5/2012
Mannitol Injection UPDATED 9/5/2011)
Methotrexate Injection UPDATED 8/31/2012
Methyldopate Injection UPDATED 9/5/2012
Metoclopramide Injection UPDATED 9/5/2012
Midazolam Injection UPDATED 8/31/2012
Morphine Sulfate Injection UPDATED 8/31/2012
Morphine Sulfate Injection (Preservative Free) UPDATED 8/31/2012
Multi-Vitamin Infusion (Adult and pediatric) UPDATED 8/31/2012
Mustargen (mechlorethamine HCl) injection UPDATED 8/31/2012
Nalbuphine HCl Injection UPDATED 8/31/2012
Naloxone Injection UPDATED 8/31/2012
Neurolite, Kit for the Preparation of Technetium Tc99m Bicisate for Injection UPDATED 8/30/2012
Ondansetron Injection 2 mg/mL UPDATED 8/31/2012
Ondansetron Injection 32 mg/50 mL premixed bags UPDATED 8/30/2012
Pancuronium Bromide Injection UPDATED 8/31/2012
Pentamidine isethionate inhalant (NebuPent) (initial posting 8/27/2012)
Pentamidine isethionate for injection (Pentam 300) (initial posting 8/27/2012)
Pentostatin for Injection (Nipent) UPDATED ) 8/31/2012
Perflutren Lipid Microsphere (DEFINITY ) Injection UPDATED 8/31/2012
Phytonadione Injectable Emulsion (Vitamin K) UPDATED 8/31/2012
Pilocarpine HCL Opthalmic Gel 4% (Pilopine HS) (initial posting 6/1/2012)
Potassium Chloride Injection 2 mEq/mL UPDATED 8/31/2012
Potassium Phosphate Injection UPDATED 8/31/2012
Procainamide HCL Injection UPDATED 8/31/2012
Prochlorperazine Injection UPDATED 8/31/2012
Propofol Injection UPDATED 8/31/2012
Sodium Acetate Injection UPDATED 8/31/2012
Sodium Bicarbonate Injection UPDATED 8/31/2012
Sodium Chloride 0.9% (5.8mL and 20mL) UPDATED 8/30/2012
Sodium Chloride 23.4% UPDATED 8/31/2012
Sodium Lactate Injection UPDATED 8/31/2012

Succinylcholine Injection (initial posting 8/17/2012)
Sufentanil Citrate Injection UPDATED 8/31/2012
Ticarcillin disodium/Clavulanic Potassium Injection (Timentin) (initial posting 8/16/12)
Tobramycin Solution for Injection UPDATED 8/31/2012
Tromethamine Injection UPDATED 8/31/2012
Vinblastine Sulfate Injection UPDATED 8/31/2012
Zinc Injection UPDATED 8/31/2012