



# Drug Utilization Review Board

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

Wednesday  
July 11, 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 – July 11, 2012

DATE: July 5, 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 July 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 Zioptan® – See Appendix C.

Action Item – Vote to Prior Authorize Keflex® 750mg – See Appendix D.

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

30 Day Notice to Prior Authorize Botulinum Toxin Products – See Appendix F.

60 Day Notice to Prior Authorize Select Gonadotropin-Releasing Hormone Analogs for Central Precocious Puberty – See Appendix G.

Questions Regarding 30 Day Notice to Prior Authorize Onasl™ – See Appendix H.

Questions Regarding 30 Day Notice to Prior Authorize Subsys™ – See Appendix I.

Questions Regarding 30 Day Notice to Prior Authorize Dymista™ – See Appendix J.

FDA and DEA Updates – See Appendix K.

Future Business

Adjournment

**Oklahoma Health Care Authority**  
**Drug Utilization Review Board**  
(DUR Board)  
**Meeting – July 11, 2012 @ 6:00 p.m.**

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

---

**AGENDA**

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

1. **Call To Order**
  - A. Roll Call – Dr. Cothran

Items to be presented by Dr. Muchmore, Chairman:

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

Items to be presented by Dr. Muchmore, Chairman:

3. **Action Item – Approval of DUR Board Meeting Minutes – See Appendix A.**
  - A. May 9, 2012 DUR Minutes – Vote
  - B. May 10, 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 for February 2012, March 2012
  - B. Retrospective Drug Utilization Review Response for December 2011, January 2012
  - C. Medication Coverage Activity for May 2012, June 2012
  - D. Pharmacy Help Desk Activity for May 2012, June 2012

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

5. **Action Item – Vote to Prior Authorize Zioptan<sup>®</sup> – See Appendix C.**
  - A. COP Recommendations

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

6. **Action Item – Vote to Prior Authorize Keflex<sup>®</sup> 750mg – See Appendix D.**
  - A. COP Recommendations

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

7. **Action Item – Vote to Prior Authorize Duexis<sup>®</sup> – See Appendix E.**
  - A. COP Recommendations

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

8. **30 Day Notice to Prior Authorize Botulinum Toxin Products – See Appendix F.**
  - A. Product Summary
  - B. Utilization Data
  - C. COP Recommendations
  - D. Product Details

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

9. **60 Day Notice to Prior Authorize Select Gonadotropin-Releasing Hormone Analogs for Central Precocious Puberty – See Appendix G.**
  - A. Overview
  - B. COP Recommendations

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

10. **Questions Regarding 30 Day notice to Prior Authorize Qnasl™ – See Appendix H.**
  - A. Overview
  - B. COP Recommendations
  - C. Product Details

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

11. **Questions Regarding 30 Day notice to Prior Authorize Suybsys™ – See Appendix I.**
  - A. Overview
  - B. COP Recommendations
  - C. Product Details

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

12. **Questions Regarding 30 Day notice to Prior Authorize Dymista™ – See Appendix J.**
  - A. Overview
  - B. COP Recommendations
  - C. Product Details

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

13. **FDA and DEA Updates – See Appendix K.**

14. **Future Business**
  - A. Annual Review of Synagis®
  - B. New Fiscal Year Annual Reviews
  - C. New Product Reviews
  - D. Medical Product Reviews

15. **Adjournment**





# Appendix A





OKLAHOMA HEALTH CARE AUTHORITY  
 DRUG UTILIZATION REVIEW BOARD MEETING  
 MINUTES of MEETING of MAY 9, 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	ABSENT
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	
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; Pharmacist Intern	X	
Graduate Students: Amany Hussein, Manish Mittal	X	
Visiting Pharmacy Student(s): Angie Quach	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:		
Jon Maguire, GSK	Jeff Himmelberg, GSK	Bryan Dillon, BMS
Tone Jones, Sunovion	Michael Tomcsanyi, Sunovion	Mark Declerk, Lilly
Sandra Manning, BMS	Linda Cantu, BMS	Brent Bumpas, Endo
Warren Tayes, Merck	Caroline Howard, Jazz	Ben Liniger, Alcon
Holly Turner, Merck	Anthony DeLeon, Shire	David Williams, Forest
Casey Cobb, Taro	Sharon Tonsett, AZ	Toby Thompson, Pfizer
Gregory Klingman, Pfizer	Richard Ponder, J&J	Brian Maves, Pfizer
Ron Schnare, Shire	Pam Davis, MHAT	Michael Hathaway, Otsuka

PRESENT FOR PUBLIC COMMENT:	
Agenda Item No. 6	Bill Clark, BMS
Agenda Item No. 10	Brent Bumpas, Endo

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. 6 Bill Clark, BMS

Agenda Item No. 10 Brent Bumpas, Endo

ACTION: NONE REQUIRED

AGENDA ITEM NO. 3: APPROVAL OF DUR BOARD MINUTES

3A: April 11, 2012 DUR Minutes

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

ACTION: MOTION CARRIED

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

4A: Retrospective Drug Utilization Review: January 2012

4B: Retrospective Drug Utilization Review Response: November 2011

4C: Medication Coverage Activity: April 2012

4D: Pharmacy Help Desk Activity: April 2012

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: VOTE ON NEW CITALOPRAM SAFETY ALERT LIMITATIONS

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

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: ANNUAL REVIEW OF ATYPICAL ANTIPSYCHOTICS

For Public Comment; Bill Clark, BMS.

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

Dr. Kuhls moved to accept current criteria, and track inpatient stabilization grandfathering data and bring back to September 2012 meeting; seconded by Dr. Preslar.

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: ANNUAL REVIEW OF MISCELLANEOUS ANTI-INFECTIVES AND 30-DAY NOTICE TO PRIOR AUTHORIZE KEFLEX®

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 8: ANNUAL REVIEW OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS AND 30-DAY NOTICE TO PRIOR AUTHORIZE DUEXIS®

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 9: ANNUAL REVIEW OF GLAUCOMA MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ZIOPTAN™

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

Dr. Feightner moved to approve moving Zalatan to Tier 1 and to change criteria from at least three Tier 1 trials at a minimum of 4 weeks each within the last 120 days; seconded by Dr. Winegardener.

ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: UTILIZATION REVIEW OF GONADOTROPIN RELEASING PRODUCTS

For Public Comment; Brent Bumpas, Endo.

Materials included in agenda packet; presented by Dr. 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: Utilization Review of Botulinum Toxin Products

B: Annual Review of Synagis®

C: New Product Reviews

D: Medical Product Reviews

ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: ADJOURNMENT

The meeting was adjourned at 7:30 p.m.



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

## Memorandum

Date: May 10, 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 May 9, 2012

Recommendation 1: Vote on New Citalopram Safety Alert Limitations

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends placement of a quantity limit of one tablet daily on all strengths of citalopram. An additional age restriction will also be placed on the 40 mg tablet to require a prior authorization for members age 60 years or greater.

Citalopram will also be placed in the Ingredient Duplication module of the Prospective DUR point-of-sale system to block any use of 20 mg and 40 mg concurrently without prior authorization.

The DUR Board recommends an informational letter be mailed to current prescribers of doses over the new maximum.

Recommendation 2: Annual Review of Atypical Antipsychotics Product Based Prior Authorization

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends continuation of the Atypical Antipsychotic Product Based Prior Authorization Program. The College recommends continued movement of Tier 3 products to Tier 1 as generics become available and SMAC pricing is applied (~~olanzapine will only be available as a Tier 2 product due to metabolic issues~~).

Proposed changes in January 2013:

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

<sup>a</sup>Mandatory Generic Plan Applies  
<sup>b</sup>Supplemental rebated Tier 3 products  
<sup>c</sup>May be rebated to Tier 2 status only  
<sup>d</sup>Includes Risperdal Consta

Approval Criteria for Tier 2 Medication:

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

Approval Criteria for Tier 3 Medication:

1. A trial of ~~risperidone~~ **two available Tier 1 products (not including clozapine)**, at least 14 days in duration, titrated to recommended dose, that did not yield adequate response or resulted in intolerable adverse effects.
2. A trial of two Tier 2 medications, at least 14 days in duration, titrated to recommended dose, that did not yield adequate response or resulted in intolerable adverse effects.

Approval Criteria for Use as Depression Adjunct:

1. For aripiprazole and 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. Tier structure still applies.

Clinical Exceptions:

1. Approvals will be granted for members with clinical conditions for which lower tiered drugs are contraindicated.
2. Approvals will be granted for members whose current regimen includes drugs known to adversely interact with all lowered tiered drugs.
3. Members being released from a hospital and stabilized on a higher tiered medication will be approved.

The DUR Board recommends review of the percent of prior authorizations approved based on inpatient stability. Once this information is collected it will be brought back to the Board for further discussion.

Recommendation 3: Annual Review of Miscellaneous Anti-Infectives

NO ACTION REQUIRED.

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

Recommendation 4: Annual Review of Non-Steroidal Anti-Inflammatory Drugs

NO ACTION REQUIRED.

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

Recommendation 5: Annual Review of Glaucoma Medications

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends latanoprost be moved to Tier 1.

The DUR Board recommends the following changes to the current criteria:

2. Member must attempt at least ~~one~~ **three** Tier 1 trial of a minimum of 4 weeks duration **each** within the last ~~90~~ **120** days. Tier 1 trials may be from any pharmacologic class.



OKLAHOMA MEDICAL RESEARCH FOUNDATION

Gabriel Pardo, MD  
Director  
MULTIPLE SCLEROSIS CENTER OF EXCELLENCE  
820 Northeast 15<sup>th</sup> Street  
Oklahoma City, OK 73104  
405-271-6242  
Fax 405-271-2887  
omrf.org/MSCenter

University of Oklahoma College of Pharmacy  
Pharmacy Management Consultants  
PO Box 26901; ORI W-4403  
Oklahoma City, OK 73190

I have become aware of your criteria for approval of dalfampridine (Ampyra®), which includes an EDSS of 4.0 to 7.5.

Allow me to be blunt: this is absurd. It shows a lack of understanding of the nature of the Kurtzke disability scale and the expected benefits of dalfampridine. A simple example is that a patient with moderate paraparesis who is still ambulatory and could benefit from this medication, would score 3.0 if he/she has no deficits in any other components of the scale. You would be denying access to an FDA approved medication to a patient who not only has a legitimate use for it fulfilling the approved indication but who happens to be the ideal candidate for it.

At our comprehensive Multiple Sclerosis Center of Excellence we follow approximately 3000 individuals with this chronic debilitating neurological condition. That task alone is monumental and it becomes even more difficult when ill-advised limitations are placed on proper access to services and medications.

I request you review this specific criterion and would be grateful if a response is given at your earliest convenience.

Sincerely,

Gabriel Pardo, MD  
Director  
OMRF Multiple Sclerosis Center of Excellence

cc:  
OHCA Pharmacy Director  
2401 NW 23<sup>rd</sup> St.  
Suite 1A  
Oklahoma City, OK 73107







# Appendix B



## RETROSPECTIVE DRUG UTILIZATION REVIEW REPORT

### February 2012

MODULE	DRUG INTERACTION	DUPLICATION OF THERAPY	DRUG-DISEASE PRECAUTIONS	DOSING & DURATION
Total # of <u>messages</u>	61,774	79,587	1,114,725	39,173
<u>Limits</u> applied	Established, Major, Males and Females, Age 19-35	Duplication of Benzodiazepines, Males and Females, Age 25-34	Safety alert issued, Diabetes utilizing Aliskiren and ACE or ARB medications, Males and Females, Ages 0-150	High Dose, Duration, Antihistamines-Non-sedating, Males and Females, age 0-1
Total # of <u>messages</u> after <u>limits</u> were applied	109	285	48	53
Total # of <u>members</u> reviewed	109	252	48	53
LETTERS				
Category	Prescribers	Pharmacies	Total Letters	
Drug Interaction	0	2	2	
Duplication of Therapy	99	42	141	
Drug-Disease Precautions	18	0	18	
Dosing & Duration	0	14	14	
Total Letters Sent	117	58	175	

# RETROSPECTIVE DRUG UTILIZATION REVIEW REPORT

## March 2012

MODULE	DRUG INTERACTION	DUPLICATION OF THERAPY	DRUG-DISEASE PRECAUTIONS	DOSING & DURATION
Total # of <u>messages</u>	60,208	78,177	1,120,103	36,523
<u>Limits</u> applied	Established, Major, Males and Females, Age 36-50	Long acting injectable antipsychotics, Males and Females, Age 0-150	Contraindicated, Females, Normal Pregnancy, Ages 30-35	High Dose, Duration, Proton Pump Inhibitors, Males, age 0-10
Total # of <u>messages</u> after <u>limits</u> were applied	97	23	223	52
Total # of <u>members</u> reviewed	97	23	221	52
LETTERS				
Category	Prescribers	Pharmacies	Total Letters	
Drug Interaction	1	2	3	
Duplication of Therapy	3	0	3	
Drug-Disease Precautions	0	0	0	
Dosing & Duration	15	1	16	
Total Letters Sent	19	3	22	

# Retrospective Drug Utilization Review Report

## Claims Reviewed for December 2011

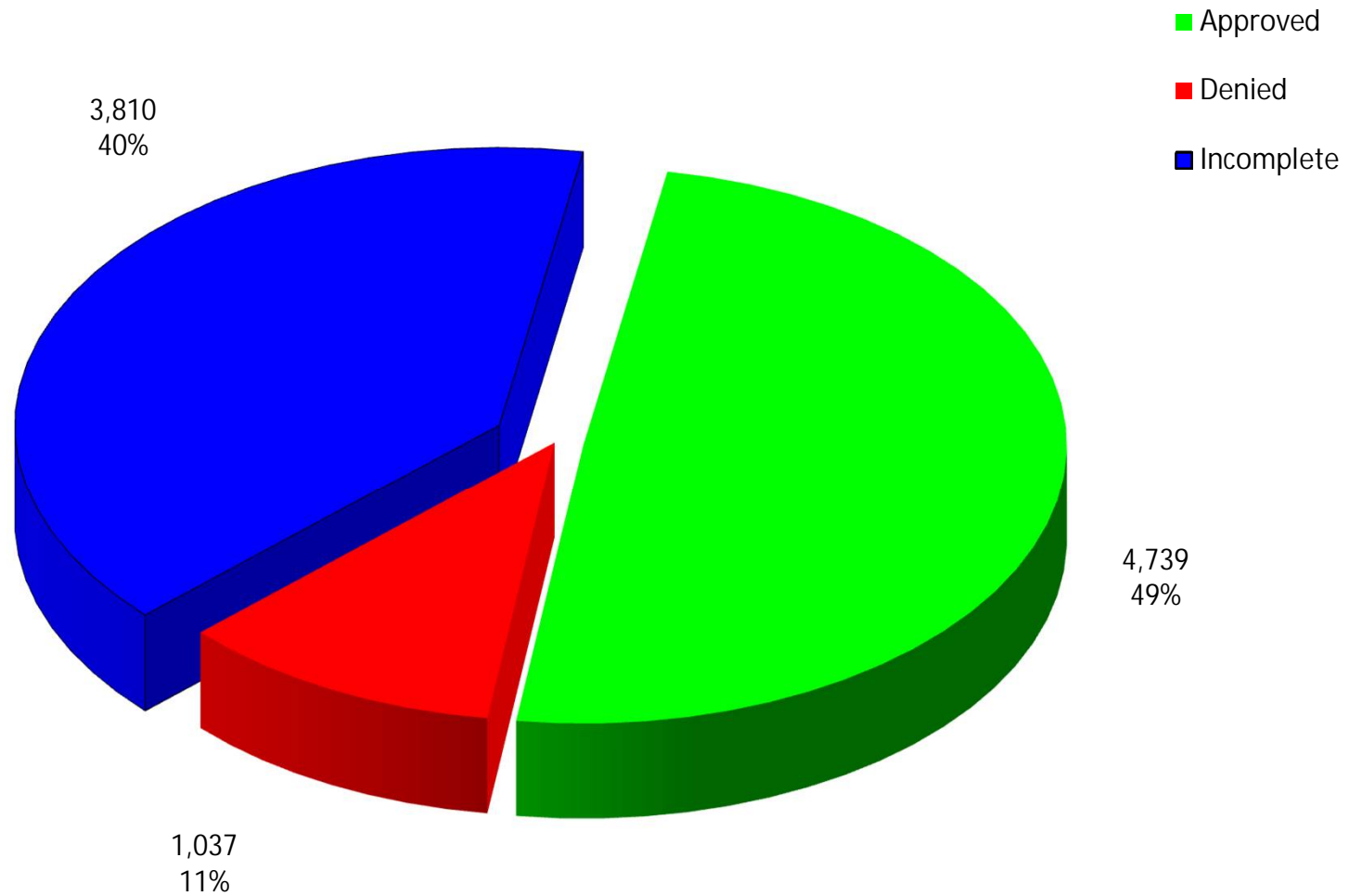
Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
<b>Limits which were applied</b>	Established, Major, Males and Females, Age 0-18	Duplication of Atypical Antipsychotics, Males and Females, Age 17-19	Contraindicated, Cardiac Dysrhythmias, Males and Females, Age 0-21	High Dose, Duration, Proton Pump Inhibitors, Males, Age 13-14
<b>Response Summary (Prescriber)</b> Letters Sent: 95 Response Forms Returned: 45  The response forms returned yielded the following results:				
1 (2%)	<i>Record Error—Not my patient.</i>			
6 (13%)	<i>No longer my patient.</i>			
2 (4%)	<i>Medication has been changed prior to date of review letter.</i>			
2 (4%)	<i>I was unaware of this situation &amp; will consider making appropriate changes in therapy.</i>			
28 (62%)	<i>I am aware of this situation and will plan to continue monitoring therapy.</i>			
6 (13%)	<i>Other</i>			
<b>Response Summary (Pharmacy)</b> Letters Sent: 0 Response Forms Returned: 0  The response forms returned yielded the following results:				
0	<i>Record Error—Not my patient.</i>			
0	<i>No longer my patient.</i>			
0	<i>Medication has been changed prior to date of review letter.</i>			
0	<i>I was unaware of this situation &amp; will consider making appropriate changes in therapy.</i>			
0	<i>I am aware of this situation and will plan to continue monitoring therapy.</i>			
0	<i>Other</i>			

# Retrospective Drug Utilization Review Report

## Claims Reviewed for January 2012

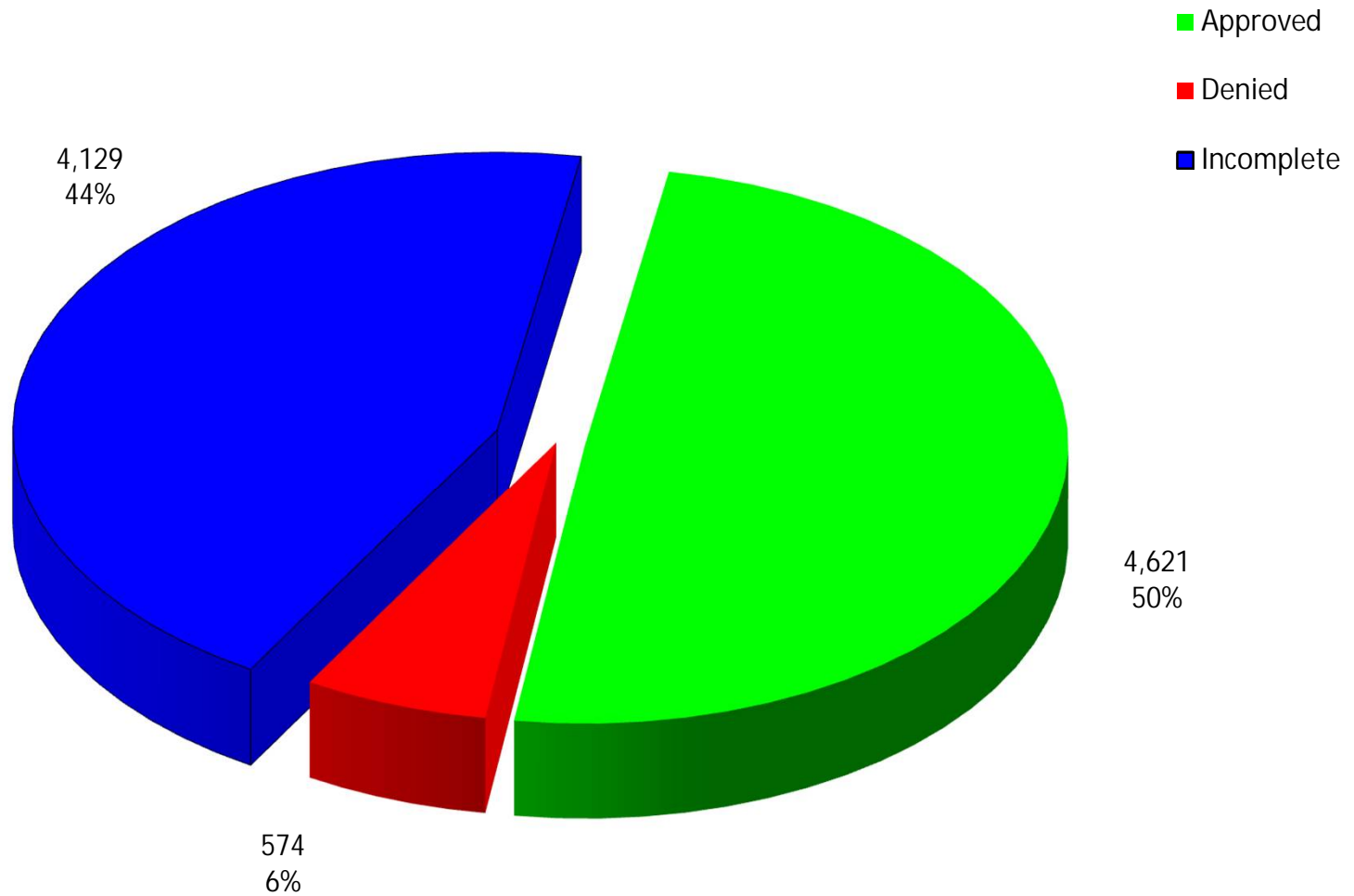
Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
<b>Limits which were applied</b>	Established, Major, Males and Females, Age 36-50	Duplication of Benzodiazepines, Males and Females, Age 35-45	Contraindicated, Ulcer, Males and Females, Age 0-150	High Dose, Duration, NSAIDs, Males and Females, Age 0-2
<b>Response Summary (Prescriber)</b> Letters Sent: 136 Response Forms Returned: 73  The response forms returned yielded the following results:				
1 (1%)	<i>Record Error—Not my patient.</i>			
16 (22%)	<i>No longer my patient.</i>			
6 (8%)	<i>Medication has been changed prior to date of review letter.</i>			
20 (27%)	<i>I was unaware of this situation &amp; will consider making appropriate changes in therapy.</i>			
16 (22%)	<i>I am aware of this situation and will plan to continue monitoring therapy.</i>			
14 (19%)	<i>Other</i>			
<b>Response Summary (Pharmacy)</b> Letters Sent: 49 Response Forms Returned: 43  The response forms returned yielded the following results:				
0 (0%)	<i>Record Error—Not my patient.</i>			
4 (9%)	<i>No longer my patient.</i>			
4 (9%)	<i>Medication has been changed prior to date of review letter.</i>			
16 (37%)	<i>I was unaware of this situation &amp; will consider making appropriate changes in therapy.</i>			
5 (12%)	<i>I am aware of this situation and will plan to continue monitoring therapy.</i>			
14 (33%)	<i>Other</i>			

# PRIOR AUTHORIZATION ACTIVITY REPORT: May 2012



PA totals include overrides

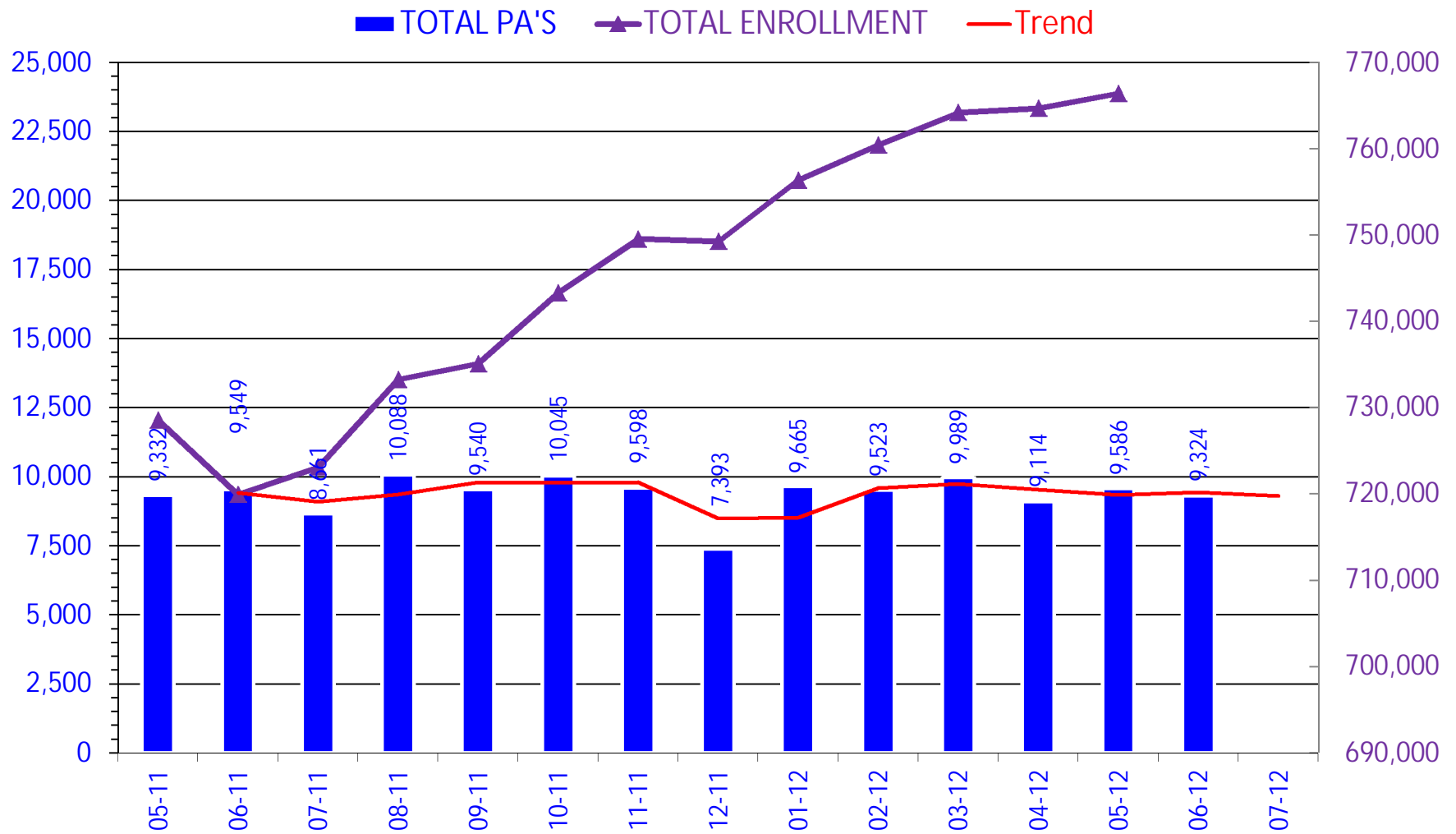
# PRIOR AUTHORIZATION ACTIVITY REPORT: June 2012



PA totals include overrides



# PRIOR AUTHORIZATION REPORT: May 2011 – June 2012



PA totals include overrides

## Prior Authorization Activity

5/1/2012 Through 5/31/2012

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort	356	149	26	181	354
Amitiza	23	9	2	12	118
Anti-Ulcer	374	103	116	155	97
Antidepressant	333	113	39	181	347
Antihistamine	253	164	14	75	351
Antihypertensives	65	17	7	41	325
Antimigraine	81	21	26	34	277
Atypical Antipsychotics	577	277	35	265	351
Benign Prostatic Hypertrophy	4	1	2	1	360
Benzodiazepines	68	45	2	21	230
Biologics	29	19	1	9	305
Bladder Control	69	13	13	43	358
Brovana (Arformoterol)	4	2	1	1	359
Byetta	14	6	0	8	360
Elidel/Protopic	44	21	2	21	86
ESA	134	64	11	59	99
Fibric Acid Derivatives	1	1	0	0	360
Fibromyalgia	136	34	38	64	336
Fortamet/Glumetza	5	0	0	5	0
Forteo	3	1	1	1	360
Glaucoma	12	3	1	8	360
Growth Hormones	64	48	2	14	166
HFA Rescue Inhalers	168	26	50	92	291
Insomnia	82	26	15	41	183
Insulin	12	6	1	5	271
Misc Analgesics	31	0	24	7	0
Multiple Sclerosis	19	9	1	9	250
Muscle Relaxant	142	59	48	35	60
Nasal Allergy	246	69	70	107	130
NSAIDS	169	31	30	108	317
Ocular Allergy	99	20	23	56	113
Ocular Antibiotics	58	12	15	31	8
Opioid Analgesic	379	206	27	146	259
Other	1,008	382	102	524	285
Otic Antibiotic	49	12	3	34	23
Pediculicides	147	35	25	87	9
Plavix	223	142	3	78	342
Prenatal Vitamins	32	1	1	30	153
Singular	977	545	74	358	234
Smoking Cessation	77	25	3	49	29
Statins	134	68	13	53	356
Stimulant	700	358	43	299	334
Suboxone/Subutex	146	117	5	24	80
Topical Antibiotics	6	0	0	6	0
Topical Antifungals	10	0	3	7	0
Topical Corticosteroids	93	1	30	62	86
Ultram ER and ODT	8	1	2	5	178
Xolair	4	0	1	3	0
Xopenex Nebs	19	11	2	6	321
Zetia (Ezetimibe)	20	6	1	13	360
Emergency PAs	5	5	0	0	
<b>Total</b>	<b>7,712</b>	<b>3,284</b>	<b>954</b>	<b>3,474</b>	

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
<b>Overrides</b>					
Brand	66	41	2	23	271
Dosage Change	551	533	2	16	7
High Dose	3	2	0	1	183
Ingredient Duplication	8	6	0	2	8
Lost/Broken Rx	109	98	3	8	13
NDC vs Age	9	9	0	0	331
Nursing Home Issue	115	100	0	15	6
Other	43	34	0	9	16
Quantity vs. Days Supply	963	625	76	262	262
Stolen	7	7	0	0	5
<b>Overrides Total</b>	<b>1,874</b>	<b>1,455</b>	<b>83</b>	<b>336</b>	
<b>Total Regular PAs + Overrides</b>	<b>9,586</b>	<b>4,739</b>	<b>1,037</b>	<b>3,810</b>	

#### Denial Reasons

Unable to verify required trials.	3,274
Does not meet established criteria.	1,007
Lack required information to process request.	532
Drug Not Deemed Medically Necessary	2

Duplicate Requests: 702

Letters: 2,237

No Process: 416

Changes to existing PAs: 542

**Prior Authorization Activity**  
**6/1/2012 Through 6/30/2012**

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort	303	116	5	182	350
Amitiza	15	5	1	9	88
Anti-Ulcer	365	114	66	185	113
Antidepressant	338	103	14	221	325
Antihistamine	202	127	7	68	348
Antihypertensives	68	18	8	42	332
Antimigraine	76	28	3	45	333
Atypical Antipsychotics	473	254	8	211	341
Benign Prostatic Hypertrophy	3	0	0	3	0
Benzodiazepines	76	52	0	24	221
Biologics	30	15	1	14	301
Bladder Control	71	12	3	56	331
Brovana (Arformoterol)	3	2	0	1	359
Byetta	43	25	1	17	359
Elidel/Protopic	42	19	2	21	85
ESA	170	80	13	77	57
Fibric Acid Derivatives	6	2	0	4	360
Fibromyalgia	178	45	21	112	343
Fortamet/Glumetza	1	0	0	1	0
Forteo	3	1	1	1	360
Glaucoma	16	4	0	12	308
Growth Hormones	76	45	4	27	139
HFA Rescue Inhalers	139	36	17	86	295
Insomnia	79	18	7	54	151
Insulin	9	3	0	6	242
Misc Analgesics	45	3	34	8	99
Multiple Sclerosis	26	11	0	15	188
Muscle Relaxant	138	51	42	45	48
Nasal Allergy	177	38	32	107	114
NSAIDS	182	32	27	123	270
Ocular Allergy	77	15	8	54	92
Ocular Antibiotics	39	9	4	26	24
Opioid Analgesic	345	179	7	159	262
Other	1,519	738	109	672	268
Otic Antibiotic	48	5	0	43	18
Pediculicides	143	58	11	74	13
Plavix	50	2	0	48	286
Prenatal Vitamins	19	0	1	18	0
Qualaquin (Quinine)	1	0	1	0	0
Singular	752	384	18	350	235
Smoking Cessation	54	18	0	36	29
Statins	107	68	0	39	355
Stimulant	698	331	25	342	331
Suboxone/Subutex	116	95	2	19	79
Symlin	2	0	0	2	0
Topical Antibiotics	12	3	0	9	36
Topical Antifungals	14	0	1	13	0
Topical Corticosteroids	63	2	18	43	43
Ultram ER and ODT	6	1	0	5	58
Xolair	7	1	1	5	360
Xopenex Nebs	14	7	0	7	359
Zetia (Ezetimibe)	18	8	1	9	357
Emergency PAs	5	5	0	0	
<b>Total</b>	<b>7,462</b>	<b>3,188</b>	<b>524</b>	<b>3,750</b>	

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
<b>Overrides</b>					
Brand	90	58	0	32	272
Dosage Change	573	536	2	35	6
High Dose	4	3	0	1	299
Ingredient Duplication	8	7	0	1	7
Lost/Broken Rx	101	97	0	4	5
NDC vs Age	10	10	0	0	268
Nursing Home Issue	132	128	0	4	6
Other	24	19	0	5	8
Quantity vs. Days Supply	910	566	47	297	270
Stolen	8	7	1	0	6
Wrong D.S. on Previous Rx	2	2	0	0	6
<b>Overrides Total</b>	<b>1,862</b>	<b>1,433</b>	<b>50</b>	<b>379</b>	

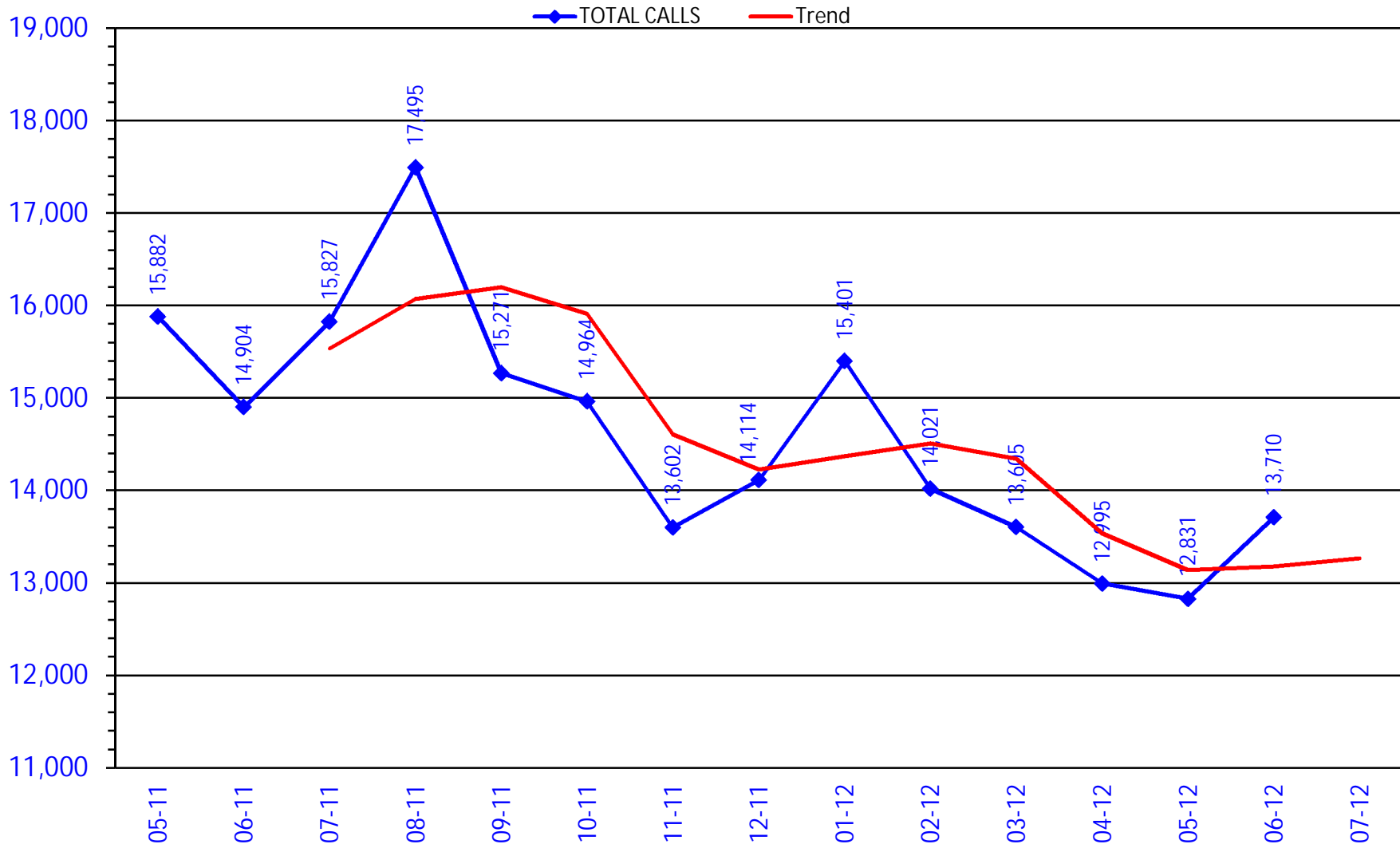
#### Denial Reasons

Unable to verify required trials.	3,598
Does not meet established criteria.	559
Lack required information to process request.	516

Duplicate Requests: 650

Changes to existing PAs: 742

# CALL VOLUME MONTHLY REPORT: May 2011 – June 2012





# Appendix C





## Vote to Prior Authorize Tafluprost (Zioptan®)

Oklahoma Health Care Authority, July 2012

### Recommendations

The College of Pharmacy recommends the following changes:

- Zioptan® (tafluprost) to be added to Tier 2.
- Member must have documented allergy to all Tier 1 preservatives to qualify for tafluprost.

Ophthalmic Glaucoma Medications	
Tier 1	Tier 2
<b>Beta-Blockers</b>	
betaxolol (Betoptic® 0.5%)	betaxolol (Betoptic-S®)
carteolol (Ocupress®)	brimonidine/timolol (Combigan®)
dorzolamide/timolol (Cosopt®)	timolol maleate (Timoptic® 0.5% dropperette)
levobunolol (Betagan®)	
metipranolol (OptiPranolol®)	
timolol maleate (Betimol®, Istalol®, Timoptic®, Timoptic Ocudose®, Timoptic-XE®)	
<b>Prostaglandin Analogs</b>	
travoprost (Travatan®, Travatan-Z®)*	bimatoprost (Lumigan®)
latanoprost (Xalatan®)	<b>tafluprost (Zioptan®)</b>
<b>Adrenergic Agonists</b>	
dipivefrin (Propine®)	
<b>Alpha-2 Adrenergic Agonists</b>	
brimonidine 0.2%	brimonidine (Alphagan-P® 0.1%, 0.15%)
	apraclonidine (Iopidine® 1%)
<b>Carbonic Anhydrase Inhibitors</b>	
dorzolamide/timolol (Cosopt®)	brinzolamide (Azopt®)
dorzolamide (Trusopt®)	
<b>Cholinergic Agonists/Cholinesterase Inhibitors</b>	
pilocarpine (Isopto Carpine®, Pilopine HS®, 0.5%, 1%, 2%, 4%, 6%)	carbachol (Isopto®, Miostat® 1.5%, 3%)
	echothiophate iodide (Phospholine Iodide®)

\*Supplemental Rebate





# Appendix D



## **Vote to Prior Authorize Keflex® 750 mg (cephalexin)**

*Oklahoma Health Care Authority, July 2012*

### **Recommendations**

---

The College of Pharmacy recommends the addition of Keflex® 750 mg to the miscellaneous anti-infectives category.

#### **Approval Criteria:**

For all these formulations member must have a clinically significant reason why the immediate release formulation and/or other cost effective therapeutic equivalent medication(s) cannot be used.

**Moxatag® (extended-release amoxicillin trihydrate)**

**Augmentin XR® (amoxicillin/clavulanate potassium)**

**Oracea® (extended-release doxycycline monohydrate 40mg)**

**Doryx® (extended-release doxycycline)**

**Solodyn® (extended-release minocycline)**

**Keflex® 750 mg (cephalexin)**





# Appendix E





## Vote to Prior Authorize Duexis® (ibuprofen/famotidine)

Oklahoma Health Care Authority, July 2012

### Recommendations

---

The College of Pharmacy recommends the addition of Duexis® (ibuprofen/famotidine) to the current NSAID product based prior authorization category.

Criteria for the non-steroidal, anti-inflammatory drugs in Tier 2 are demonstrated by the following conditions:

1. Previous use of at least two Tier 1 NSAIDs (from different product lines) plus a PPI.
2. For those with prior GI bleed who must have an NSAID, then a Tier 2 product may be approved (Celebrex should also be taken with a PPI).

Criteria for the NSAIDS in the Special PA Category are:

1. Special indications, such as the diagnosis of gout for indomethacin, OR
2. Previous use of at least two Tier 1 NSAIDs (from different product lines) AND
3. Reason why a special formulation is needed over a Tier 1 product.  
(History of severe ulcers or GI bleed may receive topical NSAIDs if currently on PPI.)

NSAIDs (Non-Steroidal Anti-Inflammatory Drugs)		
Tier 1	Tier 2	Special PA
diclofenac ER (Voltaren® XR)	celecoxib (Celebrex®)	diclofenac epolamine (Flector® patch)
diclofenac pot (Cataflam®)	diclofenac sodium/misoprostol (Arthrotec®)	diclofenac potassium (Zipsor® capsule)
diclofenac sodium (Voltaren®)	fenoprofen (Nalfon®)	diclofenac sodium (Voltaren Gel®)
etodolac (Lodine®)		diclofenac potassium (Cambia® pk)
etodolac ER (Lodine® XL)		diclofenac sodium (Pennsaid® drops)
flurbiprofen (Ansaid®)		indomethacin (Indocin®)+
ibuprofen (Motrin®)		mefanamic acid (Ponstel®)
ketoprofen (Orudis®)		naproxen sodium (Naprelan®)
ketoprofen ER (Oruvail®)		piroxicam (Feldene®)
meclofenamate (Meclomen®)		naproxen/esomeprazole (Vimovo®)
meloxicam (Mobic®)		<b>ibuprofen/famotidine (Duexis®)</b>
nabumetone (Relafen®)		
naproxen (Naprosyn®)		
naproxen sodium (Anaprox®)		
naproxen EC (Naprosyn® EC)		
oxaprozin (Daypro®)		
sulindac (Clinoril®)		
tolmetin (Tolectin®)		





# Appendix F



## 30 Day Notice to Prior Authorize Botulinum Toxin Products

Oklahoma Health Care Authority, July 2012

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.

### Product Summary

Botulinum toxin (BTX) is produced by a gram-positive anaerobic bacterium, *Clostridium botulinum*. This toxin is very potent and causes a condition called botulism in humans. Botulism can result from ingesting contaminated foods, from colonization of an infant's gastrointestinal tract, or from a wound infection. There are seven neurotoxins (A, B, C [C1, C2], D, E, F, and G) in BTX. All are antigenically and serologically different, but they maintain structural similarity. The main serotypes which cause human botulism are A, B, E, and F.<sup>1</sup>

Brand	Serological Type	Chemical Name	FDA Approved Indications	Off-Label Uses
*Botox <sup>®</sup> Cosmetic	Serotype A	OnabotulinumtoxinA	*Glabellar lines	
Botox <sup>®</sup>	Serotype A	OnabotulinumtoxinA	Axillary hyperhidrosis, cervical dystonia, chronic migraine, strabismus and blepharospasm associated with dystonia, upper limb spasticity	Achalasia, acquired nystagmus, cosmetic use (lines/wrinkles), gustatory sweating (Frey Syndrome), hand dystonia, headache (tension type), hyperhidrosis (palmar), sialorrhea (drooling in adults), Tourette's syndrome
Dysport <sup>®</sup>	Serotype A	AbobotulinumtoxinA	Cervical dystonia, *Glabellar lines	Same as above
Xeomin <sup>®</sup>	Serotype A	IncobotulinumtoxinA	Blepharospasm, Cervical dystonia	Same as above
Myobloc <sup>®</sup>	Serotype B	RimabotulinumtoxinB	Cervical dystonia	Sialorrhea (drooling)

\*Cosmetic indications not covered.

### Utilization Data for BTX: CY 2011 vs. 2010 from Pharmacy and Medical Claims

	Total Members	Total Claims	Total Cost	Cost per Claim
<b>Calendar Year 2010</b>				
Pharmacy	46	69	\$114,776.70	\$1,663.43
Medical	201	318	\$426,558.76	\$1,341.38
<b>Total</b>		<b>387</b>	<b>\$541,335.46</b>	<b>\$1,398.80</b>
<b>Calendar Year 2011</b>				
Pharmacy	28	27	\$51,182.66	\$1,895.65
Medical	173	330	\$412,183.48	\$1,249.04
<b>Total</b>		<b>357</b>	<b>\$463,366.14</b>	<b>\$1,297.94</b>
Percent Change		-7.8 %	-14.4%	
Absolute Change		-15-301	-\$77,969.32	

## Recommendations

In February 2011, payment through pharmacy claims was discontinued and these products are only payable through medical claims. 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 quadripareisis, C1-C4, complete
344.02	Quadriplegia and quadripareisis, C1-C4, incomplete
344.03	Quadriplegia and quadripareisis, 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

<sup>1</sup>Kedlaya, DK. (2010 August 6). *Botulinum Toxin, Overview*. Retrieved June 1, 2012, from <http://emedicine.medscape.com/article/325451-overview#showall>.



## Botox® Product Details

---

### Indication

Botox® is an acetylcholine release inhibitor and a neuromuscular blocking agent indicated for:

#### Chronic Migraine

- Botox® (onabotulinumtoxinA) for injection is indicated for the prophylaxis of headaches in adult patients with chronic migraine ( $\geq 15$  days per month with headache lasting 4 hours a day or longer).
- Safety and effectiveness have not been established for the prophylaxis of episodic migraine (14 headache days or fewer per month) in seven placebo-controlled studies.

#### Upper Limb Spasticity

- Botox® is indicated for the treatment of upper limb spasticity in adult patients, to decrease the severity of increased muscle tone in elbow flexors (biceps), wrist flexors (flexor carpi radialis and flexor carpi ulnaris) and finger flexors (flexor digitorum profundus and flexor digitorum sublimis).
- Safety and effectiveness of Botox® have not been established for the treatment of other upper limb muscle groups, or for the treatment of lower limb spasticity. Safety and effectiveness of Botox® have not been established for the treatment of spasticity in pediatric patients under age 18 years. Botox® has not been shown to improve upper extremity functional abilities, or range of motion at a joint affected by a fixed contracture. Treatment with Botox® is not intended to substitute for usual standard of care rehabilitation regimens.

#### Cervical dystonia

- Botox® is indicated for the treatment of adults with cervical dystonia, to reduce the severity of abnormal head position and neck pain associated with cervical dystonia.

#### Primary Axillary Hyperhidrosis

- Botox® is indicated for the treatment of severe primary axillary hyperhidrosis that is inadequately managed with topical agents.
- The safety and effectiveness of Botox® for hyperhidrosis in other body areas have not been established. Weakness of hand muscles and blepharoptosis may occur in patients who receive Botox® for palmar hyperhidrosis and facial hyperhidrosis, respectively. Patients should be evaluated for potential causes of secondary hyperhidrosis (e.g., hyperthyroidism) to avoid symptomatic treatment of hyperhidrosis without the diagnosis and/or treatment of the underlying disease.
- Safety and effectiveness of Botox® have not been established for the treatment of axillary hyperhidrosis in pediatric patients under age 18.

#### Blepharospasm and Strabismus

- Botox® is indicated for the treatment of strabismus and blepharospasm associated with dystonia, including benign essential blepharospasm or VII nerve disorders in patients 12 years of age and above.

## Dosage Forms

Single-use, sterile 50 Units, 100 Units, or 200 Units vacuum-dried powder for reconstitution only with sterile, non-preserved 0.9% Sodium Chloride Injection USP prior to injection.

## Contraindications

- Hypersensitivity to any botulinum toxin preparation or to any of the components in the formulation.
- Infection at the proposed injection site.

## Pregnancy Risk Factor C

## Precautions

- Potency Units of Botox® not interchangeable with other preparations of botulinum toxin products.
- Spread of toxin effects; swallowing and breathing difficulties can lead to death.
- Immediate medical attention may be required in cases of respiratory, speech or swallowing difficulties.
- Concomitant neuromuscular disorder may exacerbate clinical effects of treatment.
- Use with caution in patients with compromised respiratory function.
- Corneal exposure and ulceration due to reduced blinking may occur with treatment of blepharospasm.
- Retrobulbar hemorrhages and compromised retinal circulation may occur with treatment of strabismus.
- Bronchitis and upper respiratory tract infections may occur in patients treated for upper limb spasticity.
- Urinary retention: Post-void residual urine volume should be monitored in patients treated for detrusor overactivity associated with a neurologic condition who do not catheterize routinely, particularly patients with multiple sclerosis.

## Common Adverse Effect

In controlled studies, the most commonly observed adverse reactions ( $\geq 5\%$  and  $>$ placebo) were:

- Chronic Migraine: neck pain, headache.
- Spasticity: pain in extremity
- Cervical Dystonia: dysphagia, upper respiratory infection, neck pain, headache, increased cough, flu syndrome, back pain, rhinitis.
- Axillary Hyperhidrosis: injection site pain and hemorrhage, non-axillary sweating, pharyngitis, flu syndrome.

## Drug Interactions

- Patients receiving concomitant treatment of Botox® and aminoglycosides or other agents interfering with neuromuscular transmission (e.g., curare-like agents), or muscle relaxants, should be observed closely because the effect of Botox® may be potentiated.
- Use of anticholinergic drugs may potentiate systemic anticholinergic effects.
- The effect of administering different botulinum neurotoxins during the course of treatment with Botox® is unknown.

## REFERENCE

BOTOX® (onabotulinumtoxinA) Product Information. Allergan Pharmaceuticals Inc. June 1, 2012.

## Botox® Cosmetic Product Details

---

Botox® Cosmetic is not a covered product for SoonerCare members. Product details can be provided upon request.

## Dysport™ Product Details

---

### Indication

Dysport™ is an acetylcholine release inhibitor and a neuromuscular blocking agent indicated for:

- the treatment of adults with cervical dystonia to reduce the severity of abnormal head position and neck pain in both toxin-naïve and previously treated patients
- the temporary improvement in the appearance of moderate to severe glabellar lines associated with procerus and corrugator muscle activity in adult patients <65 years of age

### Dosage Forms

Dysport™ is supplied as:

- a single-use, sterile 500 Unit vial for reconstitution with 1 mL of 0.9% Sodium Chloride Injection USP (without preservative) to yield a solution of 500 Units per mL
- a single-use, sterile 300 Unit vial for reconstitution with 0.6 mL of 0.9% Sodium Chloride Injection USP (without preservative) to yield a solution equivalent to 250 Units per 0.5 mL

### Contraindications

- Dysport™ is contraindicated in patients with known hypersensitivity to any botulinum toxin preparation or to any of the components in the formulation.
- This product may contain trace amounts of cow's milk protein. Patients known to be allergic to cow's milk protein should not be treated with Dysport™.
- Dysport™ is contraindicated for use in patients with infection at the proposed injection site(s).

### Pregnancy Risk Factor C

### Warnings and Precautions

- The potency Units of Dysport™ are specific to the preparation and assay method utilized. They are not interchangeable with other preparations of botulinum toxin products.
- Post-marketing safety data from Dysport™ and other approved botulinum toxins suggest that botulinum toxin effects may, in some cases, be observed beyond the site of local injection.
- Treatment with Dysport™ and other botulinum toxin products can result in swallowing or breathing difficulties. Deaths as a complication of severe dysphagia have been reported after treatment with botulinum toxin.
- Caution should be exercised when administering Dysport™ to patients with surgical alterations to the facial anatomy, excessive weakness or atrophy in the target muscle(s), marked facial asymmetry,

inflammation at the injection site(s), ptosis, excessive dermatochalasis, deep dermal scarring, thick sebaceous skin or the inability to substantially lessen glabellar lines by physically spreading them apart. Do not exceed the recommended dosage and frequency of administration of Dysport™. In clinical trials, subjects who received a higher dose of Dysport™ had an increased incidence of eyelid ptosis.

- Individuals with peripheral motor neuropathic diseases, amyotrophic lateral sclerosis or neuromuscular junction disorders (e.g., myasthenia gravis or Lambert-Eaton syndrome) should be monitored particularly closely when given botulinum toxin. Patients with neuromuscular disorders may be at increased risk of clinically significant effects including severe dysphagia and respiratory compromise from typical doses of Dysport™.
- The possibility of an immune reaction when injected intradermally is unknown. The safety of Dysport™ for the treatment of hyperhidrosis has not been established.
- This product contains albumin, a derivative of human blood and carries an extremely remote risk for transmission of viral diseases.

## Common Adverse Effect

### Cervical Dystonia

Most commonly observed adverse reactions (>5% of patients) are: muscular weakness, dysphagia, dry mouth, injection site discomfort, fatigue, headache, neck pain, musculoskeletal pain, dysphonia, injection site pain, and eye disorders.

### Glabellar Lines

The most frequently reported adverse events (≥2%) are nasopharyngitis, headache, injection site pain, injection site reaction, upper respiratory tract infection, eyelid edema, eyelid ptosis, sinusitis and nausea.

## Drug Interactions

- Patients receiving concomitant treatment of Dysport™ and aminoglycosides or other agents interfering with neuromuscular transmission (e.g., curare-like agents), or muscle relaxants, should be observed closely because the effect of botulinum toxin may be potentiated.
- Use of anticholinergic drugs may potentiate systemic anticholinergic effects.
- The effect of administering different botulinum neurotoxins during the course of treatment with Dysport™ is unknown.

## REFERENCE

Dysport™ (abobotulinumtoxinA) Product Information. Ipsen Biopharm Ltd. June 13, 2011.

## Myobloc™ Product Details

---

### Indication

Myobloc™ is indicated for the treatment of adults with cervical dystonia to reduce the severity of abnormal head position and neck pain associated with cervical dystonia.

### Dosage Forms

Myobloc™ is provided as a clear and colorless to light-yellow sterile injectable solution in single use 3.5-mL glass vials. Each single-use vial of formulated Myobloc™ contains 5,000 Units of botulinum toxin type B per milliliter in 0.05% human serum albumin, 0.01 M sodium succinate, 0.1M sodium chloride at approximately pH 5.6.

Myobloc™ is available in the following three dosage strengths: 2,500, 5,000, and 10,000 units.

### Contraindications

Myobloc™ is contraindicated in patients with a known hypersensitivity to any botulinum toxin preparation or to any of the components in the formulation.

Myobloc™ is contraindicated for use in patients with infection at the proposed injection site(s).

### Pregnancy Risk Factor C

### Warnings

The potency Units of Myobloc™ are specific to the preparation and assay method utilized and is not interchangeable with other preparations of botulinum toxin products

- Post marketing safety data from Myobloc™ and other approved botulinum toxins suggest that botulinum toxin effects may, in some cases, be observed beyond the site of local injection
- Treatment with Myobloc™ and other botulinum toxin products can result in swallowing or breathing difficulties. Critical loss of breathing capacity in patients with respiratory disorders may occur. There have been post marketing reports of serious breathing difficulties, including respiratory failure, in cervical dystonia patients.
- Individuals with peripheral motor neuropathic diseases, amyotrophic lateral sclerosis, or neuromuscular junctional disorders (e.g., myasthenia gravis or Lambert-Eaton syndrome) should be monitored particularly closely when given botulinum toxin. Patients with neuromuscular disorders may be at increased risk of clinically significant effects including severe dysphagia and respiratory compromise from typical doses of Myobloc™.
- This product contains albumin, a derivative of human blood and carries a remote risk for transmission of viral diseases

### Precautions

Only 9 subjects without a prior history of tolerating injections of type A botulinum toxin have been studied. Treatment of botulinum toxin naïve patients should be initiated at lower doses of Myobloc™.

## Common Adverse Effects

The most common adverse effects reported by at least 5% of the treated population include neck pain not related to cervical dystonia, injection site pain, infection, pain, headache, dyspepsia, nausea, torticollis, rhinitis, dry mouth, and dysphagia.

## Drug Interactions

- Co-administration of Myobloc™ and aminoglycosides or other agents interfering with neuromuscular transmission (e.g., curare-like compounds) should only be performed with caution as the effect of the toxin may be potentiated.
- The effect of administering different botulinum neurotoxin serotypes at the same time or within less than 4 months of each other is unknown. However, neuromuscular paralysis may be potentiated by co-administration or overlapping administration of different botulinum toxin serotypes.

## REFERENCE

Myobloc™ (rimabotulinumtoxinB) Product Information. Solstice Neurosciences, Inc. June 14, 2011.

## Xeomin™ Product Details

---

### Indication

Xeomin™ is an acetylcholine release inhibitor and neuromuscular blocking agent indicated for the treatment of:

- Adults with cervical dystonia, to decrease the severity of abnormal head position and neck pain in both botulinum toxin-naïve and previously treated patients.
- Blepharospasm in adults previously treated with onabotulinumtoxinA (Botox®).

### Dosage Forms

- 50 Units, lyophilized powder in single-use vial
- 100 Units, lyophilized powder in single-use vial

### Contraindications

#### Hypersensitivity

Use in patients with a known hypersensitivity to the active substance botulinum neurotoxin type A, or to any of the excipients (human albumin, sucrose), could lead to a life-threatening allergic reaction. Xeomin™ is contraindicated in patients with known hypersensitivity to any botulinum toxin preparation or to any of the components in the formulation.

#### Infection at Injection Site

Use in patients with an infection at the injection site could lead to severe local or disseminated infection. Xeomin™ is contraindicated in the presence of infection at the proposed injection site(s).

## Pregnancy Risk Factor C

### Precautions

- Xeomin™ is not interchangeable with the other preparations of botulinum toxin products.
- Post-marketing safety data from Xeomin™ and other approved botulinum toxins suggest that botulinum toxin effects may, in some cases, be observed beyond the site of local injection.
- Hypersensitivity reactions have been reported with botulinum toxin products (anaphylaxis, serum sickness, urticaria, soft tissue edema, and dyspnea). If serious and/or immediate hypersensitivity reactions occur further injection of Xeomin™ should be discontinued and appropriate medical therapy immediately instituted.
- Treatment with Xeomin™ and other botulinum toxin products can result in swallowing or breathing difficulties that may result in critical loss of breathing capacity in patients with respiratory disorders. Individuals with peripheral motor neuropathic diseases, amyotrophic lateral sclerosis, or neuromuscular junctional disorders (e.g., myasthenia gravis or Lambert-Eaton syndrome) should be monitored particularly closely when given botulinum toxin. Patients with neuromuscular disorders may be at increased risk of clinically significant effects including severe dysphagia and respiratory compromise from typical doses of Xeomin™.
- Reduced blinking from injection of botulinum toxin products in the orbicularis muscle can lead to corneal exposure, persistent epithelial defect and corneal ulceration, especially in patients with VII nerve disorders. Because of its anticholinergic effects, Xeomin™ should be used with caution in patients at risk of developing narrow angle glaucoma.
- This product contains albumin, a derivative of human blood and carries a remote risk for transmission of viral diseases

### Common Adverse Effect

Cervical Dystonia: The most commonly observed adverse reactions ( $\geq 5\%$  of patients and  $>$  placebo) were: dysphagia, neck pain, muscle weakness, injection site pain, and musculoskeletal pain.

Blepharospasm: The most commonly observed adverse reactions ( $\geq 5\%$  of patients and  $>$  placebo) were: eyelid ptosis, dry eye, dry mouth, diarrhea, headache, visual impairment, dyspnea, nasopharyngitis, and respiratory tract infections.

### Drug Interactions

- No formal drug interaction studies have been conducted with Xeomin™.
- Coadministration of Xeomin™ and aminoglycoside antibiotics or other agents interfering with neuromuscular transmission, e.g., tubocurarine-type muscle relaxants, should only be performed with caution as these agents may potentiate the effect of the toxin.
- Use of anticholinergic drugs after administration of Xeomin™ may potentiate systemic anticholinergic effects.
- The effect of administering different botulinum toxin products at the same time or within several months of each other is unknown.
- Excessive neuromuscular weakness may be exacerbated by administration of another botulinum toxin prior to the resolution of the effects of a previously administered botulinum toxin. Excessive weakness

may also be exaggerated by administration of a muscle relaxant before or after administration of Xeomin™.

## REFERENCE

Xeomin<sup>(TM)</sup> (incobotulinumtoxinA) Product Information. Merz Pharmaceuticals, LLC. June 1, 2012.





# Appendix G



## 60 Day Notice to Prior Authorize Select Gonadotropin-Releasing Hormone Analogs for Central Precocious Puberty

Oklahoma Health Care Authority, July 2012

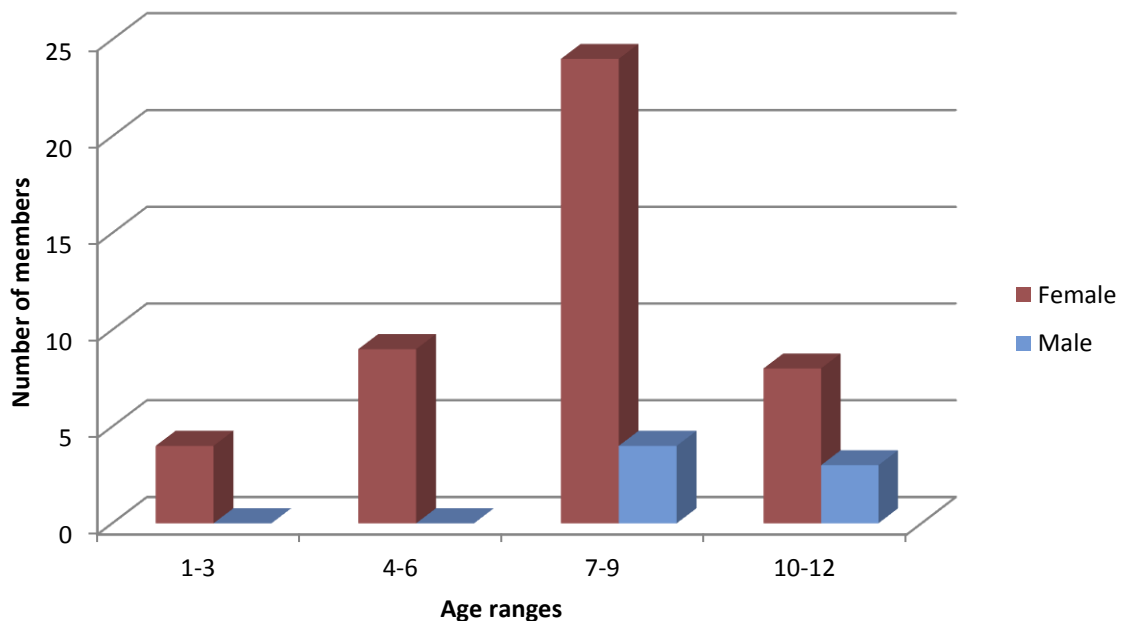
*This category was introduced for possible inclusion in the Product Based Prior Authorization program in May 2012. See the May DUR packet for a more complete discussion of the category. This notice and statement of potential economic impact are presented to meet the statutory requirements of 63 O.S. Sec. 5030.5.*

*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.*

### Member Demographics of Select Gonadotropin-Releasing Hormone Analogs

---

In fiscal year 2011, there were a total of 52 members utilizing the gonadotropin-releasing hormone analogs (Gn-RH) class of medications for central precocious puberty (CPP) through the pharmacy and medical benefit. Within this population there was 1 waiver patient.



### Market Share of Select Gonadotropin-Releasing Hormone Analogs

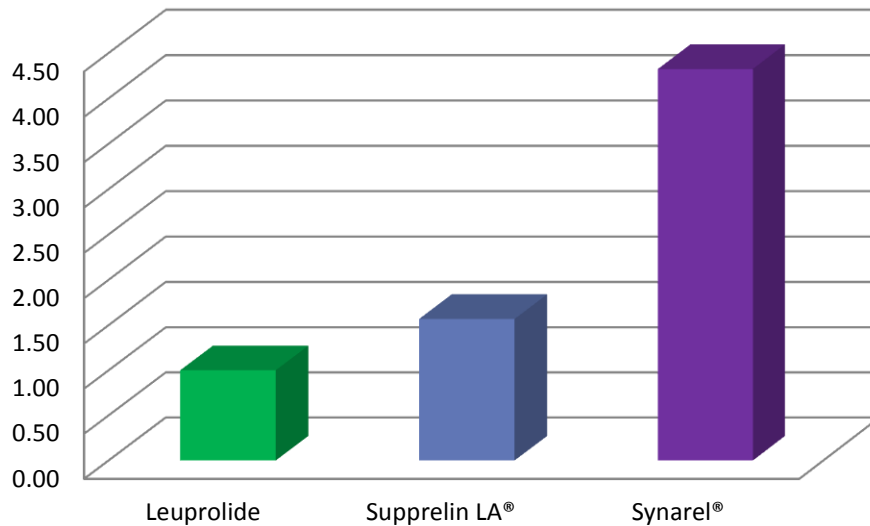
---

Currently the proposed Tier 1 product, leuprolide, has 100 percent of the market share for CPP.

## Cost Comparison of Select Gonadotropin-Releasing Hormone Analogs

---

The chart below shows a comparison of medication costs based on cost per month. The costs of the select Gn-Rh products for CPP are compared as a ratio to the medication with the lowest monthly cost.



## Comparison of Safety and Efficacy of Select Gonadotropin-Releasing Hormone Analogs<sup>i,ii,iii</sup>

---

Gonadotropin-releasing hormone analogs are the standard of care for treating central precocious puberty. Studies to date comparing the efficacy of the gonadotropin-releasing hormone analogs formulations have found no clear significant differences in efficacy. The most commonly used drugs worldwide are triptorelin depot and leuprorelin depot. However, triptorelin is only approved in the United States for palliative treatment of advanced carcinoma of the prostate. Depot preparations are superior to short-acting agonist preparation in terms of hormonal suppression and improvement of growth potential during the early phase of treatment and in terms of improvement of final height. However, 3-month leuprolide depot has not shown consistent suppression of sex hormones when compared with the monthly doses. Despite the improved efficacy, intramuscular depot injections are painful.

The potential for irregular compliance with daily administration, as well as the variable absorption of the intranasal route for nafarelin, can limit the long-term benefit of the latter preparations on adult height. An open-label trial introduced histrelin implants to patients who were treatment naïve and to patients who had been treated and suppressed with leuprolide, resulting in maintenance of the hypothalamic-pituitary-gonadal suppression in both groups for up to a year, indicating comparable efficacy.

## Economic Impact

---

### Potential Secondary Costs

Overall efficacy is considered to be similar across the products in this class for CPP, but drug selection requires individual patient history which includes, but is not limited to: other illnesses, disease risk factors, and current symptoms.

### Potential Administrative Costs

The potential number of petitions which might be required if a Tier 1 product was not chosen initially by the prescriber is estimated to be approximately 75. Currently no members will be affected by this new prior authorization as there is no utilization for the higher tiered products.

Previously, it has been theorized that the total cost per petition to the *healthcare system* (includes cost to physicians, pharmacists, and program) is between \$7.63 and \$14.82. Total cost for prior authorization to the *healthcare system* is estimated to be between \$1,000 and \$1,500 annually. Anticipated actual administrative cost to the program is projected to be less than \$1,500.

### Potential Program Savings

It is unknown what the program savings will be without current utilization of the higher tiered products. However based on net ingredient costs differences, the annual savings per member is estimated to be between \$5,000 and \$20,000.

## 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®)

<sup>i</sup> Partsch, C, Geger S, Sippel, W. Management and outcome of central precocious puberty. *Clinical Endocrinology* 2002; 56:129-148.

<sup>ii</sup> Garibaldi, Luigi. *Kliegman: Nelson Textbook of Pediatrics*. 19<sup>th</sup> ed, Elsevier 2011

<sup>iii</sup> Eugster E, Clarke W, Kletter G, et al, Efficacy and Safety of Histrelin Subdermal Implant in Children with Central Precocious Puberty: A Multicenter Trial. *J Clin Endocrin* 2007; 92(5): 1697-1704.





# Appendix H





## 30 Day Notice to Prior Authorize Qnasl™ (beclomethasone dipropionate)

Oklahoma Health Care Authority, July 2012

<b>Manufacturer</b>	Teva Respiratory, LLC.
<b>Classification</b>	Adrenal Glucocorticoid
<b>Status</b>	Prescription Only

### Allergic Rhinitis<sup>1</sup>

Allergic rhinitis affects roughly 10-20% of the US population yearly. This condition is more common in children and adults less than 20 years of age. Allergic rhinitis usually affects boys more than girls and can be linked to family history.

### Qnasl™ (beclomethasone dipropionate) Summary<sup>2</sup>

Qnasl™ (beclomethasone dipropionate) is indicated for rhinitis attributed to allergies, seasonal and perennial for ages 12 years and older. It is available as 80mcg per actuation in an 8.7g canister containing 120 actuations. Each actuation is delivered intranasally as two sprays in each nostril daily. The recommended dose of 2 actuations in each nostril daily is also the maximum dosage.

### Efficacy

The efficacy of Qnasl™ (beclomethasone dipropionate) in patients 12 years and above was evaluated in placebo-controlled clinical trials. Treatment doses ranged from 80-320mcg and from duration of 2-52 weeks. The most often reported adverse effects were epistaxis and headache.

	Qnasl™(beclomethasone)	Beconase™(beclomethasone)	Fluticasone
<b>Cost per canister(EAC)</b>	\$113.02	\$142.50	\$25.28
<b>Size of canister</b>	8.7g (120 doses)	25g (180 doses)	16g (120 doses)
<b>Day supply of canister*</b>	30	22	30
<b>Cost per day*</b>	\$3.77	\$6.48	\$0.85

\*at maximum doses (Qnasl™ 4 doses, Beconase™ 8 doses, Fluticasone 4 doses)

### Recommendations

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

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

## PRODUCT DETAILS OF QNASL™ (BECLOMETHASONE DIPROPIONATE)<sup>2</sup>

FDA APPROVED: 2012

**INDICATIONS:** Qnasl™ is indicated for rhinitis attributed to allergies, seasonal and perennial for ages 12 years and up.

**DOSAGE FORM:** 80mcg spray in aerosol container holding 120 actuations.

### ADMINISTRATION:

- 160mcg (two 80mcg sprays) per nostril daily.
- A maximum of 320mcg is recommended daily.

**CONTRAINDICATIONS:** hypersensitivity to Qnasl™ or any beclomethasone product.

### SPECIAL POPULATIONS:

- **Pregnancy Category C.** No sufficient data on pregnant women while on Qnasl™. World Health Organization (WHO) states Qnasl™ is compatible with breastfeeding.
- **Pediatric Use:** Safety and effectiveness in patients <12 years of age have not been established.
- **Geriatric Use:** Safety and effectiveness in patients >65 years of age have not been established.
- **Renal and Hepatic Impairment:** Qnasl™ was not extensively studied in these populations therefore monitoring is recommended.

### WARNINGS & PRECAUTIONS:

- **Nasal Discomfort, Epistaxis and Nasal Ulceration:** monitor for irritation if this occurs discontinue therapy until resolved.
- **Candida Infection:** monitor for signs and symptoms of infection, discontinue therapy and treat infection. Patients with continued use of Qnasl™ are at greater risk of infection.
- **Glaucoma and Cataracts:** monitor vision, ocular pressure, and avoid in patients with glaucoma and cataracts.
- **Hypersensitivity Reactions including Anaphylaxis:** Qnasl™ can cause hypersensitivity reactions, monitor and discontinue medication if occurs.
- **Immunosuppression:** Corticosteroids can be immunosuppressive.
- **Hypothalamic-Pituitary-Adrenal Axis Effect:** monitor for acute adrenal insufficiency.
- **Effects on Growth:** monitor growth velocity in pediatric population.

**ADVERSE REACTIONS:** (occurring ≥5% of subsequent to titration)

- Headache
- Pharyngitis

### DRUG INTERACTIONS:

Qnasl™ does not have any studies showing drug interaction.

<sup>1</sup>Flint et al. Cummings Otolaryngology: Head & Neck Surgery, 5<sup>th</sup> ed. Chapter 40: Immunology of the upper airway and pathophysiology and treatment of allergic rhinitis. 1986 Mosby, Inc.. Accessed online at: <http://www.mdconsult.com/books/page.do?eid=4-u1.0-B978-0-323-05283-2..X0001-8&isbn=978-0-323-05283-2&uniqId=336929213-3> Copyright 2010.

<sup>2</sup> Qnasl™ Highlights of Prescribing Information. Teva Respiratory, LLC. Accessed online at: [http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2012/202813s000lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/202813s000lbl.pdf) Last revised March 2012.



# Appendix I



## 30 Day Notice to Prior Authorize Subsys™ (fentanyl sublingual spray)

Oklahoma Health Care Authority, July 2012

**Manufacturer** Insys Therapeutics, Inc.  
**Classification** Opioid Analgesic  
**Status** Prescription Only: CII

### Breakthrough Oncological Pain<sup>1</sup>

Oncological pain is multifactorial encompassing procedural, diagnostic, therapeutic, and etiologic pain. When considering treatment options for cancer pain both chronic and acute pain medications should be applied. Adequate chronic pain management only minimizes breakthrough pain needs but not eliminate them due to issues (i.e. surgery, chemotherapy, or radiation) that may arise from disease progression.

### Subsys™ (fentanyl sublingual spray) Summary<sup>2</sup>

Subsys™ (fentanyl sublingual spray) is indicated for breakthrough cancer pain in patients age 18 years and older who have chronic analgesic therapy that needs augmentation. Although Subsys™ is a fentanyl product its dosage cannot be directly converted to other fentanyl products. Subsys™ is neither effective nor approved for patients without analgesia tolerance.

Subsys™ (fentanyl sublingual spray) is available as 100, 200, 400, 600, and 800mcg blister packs containing single sublingual spray units, and should be taken under the tongue at the maximum of 2 doses at once not more frequently than every four hours up to four doses daily. The dose should be reduced in patients when co-administered with drugs that are moderate or strong CYP3A inhibitors and titration should be done slowly in elderly patients and those with compromised respiratory or central nervous system to closely monitor for adverse events.

### Efficacy

The efficacy of Subsys™ (fentanyl sublingual spray) in patients with breakthrough cancer pain was evaluated in a randomized, double-blind, placebo-controlled crossover study. The trial evaluated adults that were opioid tolerant and not controlled with chronic opiates alone. The study showed significantly less pain with Subsys™ compared to placebo which was evaluated at the 30 minute mark.

### Cost

Subsys™ (fentanyl sublingual spray) comes in the following strengths:

Dose	Average Wholesale Price(EACW) <sup>+</sup>	Est. 30 day cost*	Fentanyl Citrate pop EACW (30 day)
100mcg	\$22.64	\$181.12	Not applicable
200mcg	\$28.61	\$228.88	\$14.30 (114.40)
400mcg	\$41.55	\$332.40	\$18.11 (144.88)
600mcg	\$53.94	\$431.52	\$22.19 (177.52)
800mcg	\$66.43	\$531.44	\$26.29 (210.32)
1200mcg	\$91.77	\$734.16	\$34.18 (273.44)
1600mcg	\$117.11	\$936.88	\$42.15 (337.20)

<sup>+</sup>not including 4.02 dispensing fee    <sup>\*</sup>Assuming 2 doses 4 times daily

## Recommendations

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 #240 individual spray blister packages per 30 days (8 of the #30 packages)
4. Reason why other forms of fentanyl breakthrough pain therapy cannot be used

Tier-1	Tier-2	Tier-3	Oncology Only
All immediate release narcotics not listed in a higher tier	<b>Long Acting</b>		
	fentanyl patches (Duragesic®)	morphine sulfate ER (Avinza®)	
	morphine ER	morphine sulfate ER (Kadian®)	
		morphine/naltrexone (Embeda®)	
		Oxycodone ER (OxyContin®)	
		oxymorphone (Opana® ER)	
		tramadol ER (Ultram ER®, Ryzolt®)	
		hydromorphone ER (Exalgo®)	
		buprenorphine patch (Butrans®)	
		Tapentadol ER (Nucynta® ER)	
	<b>Short Acting</b>		
	Tapentadol (Nucynta®)	hydrocodone/APAP (Xodol®, Zamicet®, Hycet®, Zolvit®, Liquicet®)	fentanyl (Actiq®)
	Oxymorphone (Opana® IR)	oxycodone/APAP (Primlev™, Xolox®)	fentanyl (Fentora®)
		tramadol ODT (Rybix®)	Fentanyl (Onsolis® buccal film)
	Oxycodone (Oxecta®)	Fentanyl (Abstral®, Lazanda®)	
		<b>Fentanyl (Subsys™) sublingual spray</b>	

## PRODUCT DETAILS OF SUBSYS™ (FENTANYL SUBLINGUAL SPRAY)<sup>2</sup>

FDA APPROVED: 2012

**INDICATIONS:** Subsys™ is indicated for the management of breakthrough pain in cancer patients 18 years and up that are opioid tolerant receiving continuous chronic pain medication.

**DOSAGE FORM:** 100mcg, 200mcg, 400mcg, 600mcg, 800mcg blister packs.

### ADMINISTRATION:

- Initial dose of 100mcg then titrate to effective dose.
- A maximum of 2 doses per event of pain with a 4 hours minimum between doses.
- Once effective dose found the maximum of 4 doses per day is recommended.

**CONTRAINDICATIONS:** Opioid non-tolerant patients, management of acute or postoperative pain including headache/migraine and dental pain, intolerance or hypersensitivity to fentanyl Subsys™ or its components.

### SPECIAL POPULATIONS:

- **Pregnancy Category C.** Excretion into human milk does occur, therefore it is not recommended to nurse while on Subsys™.
- **Pediatric Use:** Safety and effectiveness in patients <18 years of age have not been established.
- **Geriatric Use:** Clinical studies have shown Subsys™ to be safe in the elderly but monitoring respiratory depression is recommended.
- **Renal and Hepatic Impairment:** Subsys™ was not extensively studied in these populations therefore monitoring is recommended.

### WARNINGS & PRECAUTIONS:

- **Respiratory & CNS Depression:** monitor appropriately, and take caution in elderly, patients that are respiratory compromised i.e COPD, CNS depressants, and other comorbidities affecting respiration and CNS. Increase in CO<sub>2</sub> retention may occur in these patients therefore slow titration is recommended.
- **Use with CYP3A inhibitors:** Concomitant use with strong CYP3A inhibitors may substantially decrease respiration and increase sedation and hypotension. Therefore, co-administration may require dose adjustments and added monitoring.
- **Storage & disposal:** Subsys™ can be fatal, proper storage and disposal is required and provided from the manufacturer Insys Therapeutics, Inc.

### ADVERSE REACTIONS: (occurring ≥5% of subsequent to titration)

- Nausea/Vomiting
- Constipation
- Asthenia
- Dyspnea
- Anxiety

**DRUG INTERACTIONS:**

**CYP3A inhibitors:** Increase Subsys™ plasma levels when co-administered with strong CYP3A inhibitors (e.g., ketoconazole) increasing risk of adverse reactions of respiratory and CNS depression. Titrate conservatively and monitor extensively.

**CYP3A inducers:** Decrease Subsys™ plasma levels when co-administered with CYP3A inducers decreasing the efficacy of Subsys™.

<sup>1</sup>Baumann TJ, Strickland JM, Herndon CM. Chapter 69. Pain Management. In: Talbert RL, DiPiro JT, Matzke GR, Posey LM, Wells BG, Yee GC, eds. Pharmacotherapy: A Pathophysiologic Approach. 8th ed. New York: McGraw-Hill; 2011.

<http://www.accesspharmacy.com/content.aspx?aID=7986332>. Accessed May 2, 2012.

<sup>2</sup>Subsys™ Highlights of Prescribing Information. Insys Therapeutics, Inc. Accessed online at:

[http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2012/202788s000lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/202788s000lbl.pdf) Last revised January 2012.

<sup>3</sup>Subsys™ Medication Guide. Insys Therapeutics, Inc. Accessed online at:

[http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2012/202788s000mg.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/202788s000mg.pdf). Last revised January 2012.





# Appendix J



## 30 Day Notice to Prior Authorize Dymista™ (azelastine/fluticasone nasal spray)

Oklahoma Health Care Authority, July 2012

<b>Manufacturer</b>	Meda Pharmaceuticals, Inc.
<b>Classification</b>	Antihistamine/Adrenal Glucocorticoid
<b>Status</b>	Prescription Only

### Allergic Rhinitis<sup>1</sup>

Allergic rhinitis affects roughly 10-20% of the US population yearly. This condition is more common in children and adults less than 20 years of age. Allergic rhinitis usually affects boys more than girls and can be linked to family history.

### Dymista™ (azelastine hydrochloride and fluticasone propionate) Summary<sup>2</sup>

Dymista™ (azelastine/fluticasone) is indicated for rhinitis attributed to seasonal allergies for ages 12 years and older that require combination therapy. It is available as 137mcg of azelastine and 50mcg of fluticasone per spray of 0.137mL. Each actuation is delivered intranasally as one spray in each nostril twice daily and is available in a 23g bottle. Six sprays for initial priming and one spray if not used for a 14 day period is recommended. There are 120 metered sprays per canister after priming.

### Efficacy

The efficacy of Dymista™ (azelastine/fluticasone) in patients 12 years to 78 years were evaluated in placebo-controlled clinical trials. These trials showed a statistically significant decrease in reflective total nasal symptoms of rhinorrhea, nasal congestion, sneezing, and nasal itching which indicated Dymista™ was beneficial in seasonal allergic rhinitis.

	Dymista™ (azelastine/fluticasone)	Beconase™ (beclomethasone)	Fluticasone
<b>Cost per canister(EAC)</b>	\$146.97	\$142.50	\$25.28
<b>Size of canister</b>	23g (120 doses)	25g (180 doses)	16g (120 doses)
<b>Day supply of canister*</b>	30	22	30
<b>Cost per day*</b>	\$4.90	\$6.48	\$0.85

\*at maximum doses (Dymista™ 4 doses, Beconase™ 8 doses, Fluticasone 4 doses)

### Recommendations

The College of Pharmacy recommends placement of Dymista™ (azelastine/fluticasone) into Tier 3 of the Nasal Allergy Products PBPA category with the following criteria:

Nasal Allergy Products		
Tier 1	Tier 2	Tier 3
Fluticasone(Flonase®)	Beclomethasone(Beconase® AQ)	Ciclesonide (Omnaris™)
Flunisolide (Nasalide®, Nasarel™)	Triamcinolone (Nasacort® AQ)	Budesonide (Rhinocort® AQ)
	Olapatadine (Patanase®)	Fluticasone (Veramyst™) no alc
		Mometasone (Nasonex®)
		Azelastine (Astepro®)
		Azelastine (Astelin®)
		<b>Azelastine/fluticasone (Dymista®)</b>

## PRODUCT DETAILS OF DYMISTA™ (AZELASTINE/FLUTICASONE)<sup>2</sup>

FDA APPROVED: 2012

**INDICATIONS:** Dymista™ is indicated for Seasonal Allergic rhinitis for ages 12 years and up.

**DOSAGE FORM:** 137mcg/50mcg in 0.137mL suspension spray of 23g containing 120 sprays.

### ADMINISTRATION:

- 137mcg/50mcg (one spray) per nostril twice daily.

**CONTRAINDICATIONS:** None.

### SPECIAL POPULATIONS:

- **Pregnancy Category C.** No sufficient data on pregnant women while on Dymista™. Caution is advised when using Dymista™ while breastfeeding.
- **Pediatric Use:** Safety and effectiveness in patients <12 years of age have not been established.
- **Geriatric Use:** Safety and effectiveness in patients >65 years of age have not been established.
- **Renal and Hepatic Impairment:** Dymista™ was not influenced by hepatic impairment and renal impairment under 50mL/min changed the concentration so caution may be advised.

### WARNINGS & PRECAUTIONS:

- **Nasal Discomfort, Epistaxis and Nasal Ulceration:** monitor for irritation and if it occurs discontinue therapy until resolved.
- **Candida Infection:** monitor for signs and symptoms of infection, discontinue therapy and treat infection.
- **Glaucoma and Cataracts:** monitor vision, ocular pressure, and avoid in patients with glaucoma and cataracts.
- **Somnolence:** Dymista™ has a higher incidence, therefore caution should be advised when doing activities that require being alert.
- **Immunosuppression:** Corticosteroids can be immunosuppressive.
- **Hypothalamic-Pituitary-Adrenal Axis Effect:** monitor for acute adrenal insufficiency.
- **Effects on Growth:** monitor growth velocity in pediatric population.

### ADVERSE REACTIONS: (occurring ≥2%)

- dysgeusia
- epistaxis
- headache

### DRUG INTERACTIONS:

Dymista™ should not be used with ritonavir, and when potent cytochrome P450 3A4 are used concurrently, caution is recommended.

<sup>1</sup>Flint et al. Cummings Otolaryngology: Head & Neck Surgery, 5<sup>th</sup> ed. Chapter 40: Immunology of the upper airway and pathophysiology and treatment of allergic rhinitis. 1986 Mosby, Inc.. Accessed online at: <http://www.mdconsult.com/books/page.do?eid=4-u1.0-B978-0-323-05283-2..X0001-8&isbn=978-0-323-05283-2&uniqId=336929213-3> Copyright 2010.

<sup>2</sup> Dymista™ Highlights of Prescribing Information. Meda Pharmaceutical, Inc. Accessed online at: [http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2012/202236s000lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/202236s000lbl.pdf) Last revised April 2012.



# Appendix K



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

---

## FDA NEWS RELEASE

For Immediate Release: June 28, 2012  
FDA approves Myrbetriq for overactive bladder

The U.S. Food and Drug Administration today approved Myrbetriq (mirabegron) to treat adults with overactive bladder, a condition in which the bladder muscle cannot be controlled, squeezes too often or squeezes without warning.

An extended-release tablet taken once daily, Myrbetriq improves the storage capacity of the bladder by relaxing the bladder muscle during filling. Symptoms of overactive bladder include urinary frequency, urinary urgency, urge urinary incontinence.

Myrbetriq's safety and efficacy were demonstrated in three double-blind, placebo-controlled, multicenter clinical trials. A total of 4,116 patients with overactive bladder were randomly assigned to take Myrbetriq at doses of 25 milligrams, 50 mg, 100 mg, or a placebo once daily for 12 weeks.

Results showed that Myrbetriq 25 mg and 50 mg effectively reduced the number of times a patient urinated and the number of times a patient had wetting accidents during a 24-hour period. Patients taking Myrbetriq 50 mg also expelled a greater amount of urine, demonstrating the drug's effectiveness in improving the storage capacity of the bladder.

The most common side effects observed in the trials were increased blood pressure, common cold-like symptoms (nasopharyngitis), urinary tract infection, constipation, fatigue, elevated heart rate (tachycardia), and abdominal pain. Myrbetriq is not recommended for use in those with severe uncontrolled high blood pressure, end stage kidney disease or severe liver impairment.

Myrbetriq is marketed by Astellas Pharma US, Inc. of Northbrook, Ill.

## FDA NEWS RELEASE

For Immediate Release: June 27, 2012  
FDA approves Belviq to treat some overweight or obese adults

The U.S. Food and Drug Administration today approved Belviq (lorcaserin hydrochloride), as an addition to a reduced-calorie diet and exercise, for chronic weight management.

The drug is approved for use in adults with a body mass index (BMI) of 30 or greater (obese), or adults with a BMI of 27 or greater (overweight) and who have at least one weight-related condition such as high blood pressure (hypertension), type 2 diabetes, or high cholesterol (dyslipidemia).

Belviq works by activating the serotonin 2C receptor in the brain. Activation of this receptor may help a person eat less and feel full after eating smaller amounts of food.

The safety and efficacy of Belviq were evaluated in three randomized, placebo-controlled trials that included nearly 8,000 obese and overweight patients, with and without type 2 diabetes, treated for 52 to 104 weeks. All participants received lifestyle modification that consisted of a reduced calorie diet and exercise counseling. Compared with placebo, treatment with Belviq for up to one year was associated with average weight loss ranging from 3 percent to 3.7 percent.

About 47 percent of patients without type 2 diabetes lost at least 5 percent of their body weight compared with about 23 percent of patients treated with placebo. In people with type 2 diabetes, about 38 percent of patients treated with Belviq and 16 percent treated with placebo lost at least 5 percent of their body weight. Belviq treatment was associated with favorable changes in glycemic control in those with type 2 diabetes. The

approved labeling for Belviq recommends that the drug be discontinued in patients who fail to lose 5 percent of their body weight after 12 weeks of treatment, as these patients are unlikely to achieve clinically meaningful weight loss with continued treatment.

Belviq should not be used during pregnancy. Treatment with Belviq may cause serious side effects, including serotonin syndrome, particularly when taken with certain medicines that increase serotonin levels or activate serotonin receptors. These include, but are not limited to, drugs commonly used to treat depression and migraine. Belviq may also cause disturbances in attention or memory.

In 1997, the weight-loss drugs fenfluramine and dexfenfluramine were withdrawn from the market after evidence emerged that they caused heart valve damage. This effect is assumed to be related to activation of the serotonin 2B receptor on heart tissue. When used at the approved dose of 10 milligrams twice a day, Belviq does not appear to activate the serotonin 2B receptor.

Heart valve function was assessed by echocardiography in nearly 8,000 patients in the Belviq development program. There was no statistically significant difference in the development of FDA-defined valve abnormalities between Belviq and placebo-treated patients. Because preliminary data suggest that the number of serotonin 2B receptors may be increased in patients with congestive heart failure, Belviq should be used with caution in patients with this condition. Belviq has not been studied in patients with serious valvular heart disease.

The drug's manufacturer will be required to conduct six postmarketing studies, including a long-term cardiovascular outcomes trial to assess the effect of Belviq on the risk for major adverse cardiac events such as heart attack and stroke.

The most common side effects of Belviq in non-diabetic patients are headache, dizziness, fatigue, nausea, dry mouth, and constipation, and in diabetic patients are low blood sugar (hypoglycemia), headache, back pain, cough, and fatigue.

Belviq is manufactured by Arena Pharmaceuticals GmbH of Zofingen, Switzerland, and distributed by Eisai Inc. of Woodcliff Lake, N.J.

## Safety Announcements

FDA Drug Safety Communication: New information regarding QT prolongation with ondansetron (Zofran)  
This update is in follow-up to the [FDA Drug Safety Communication: Abnormal heart rhythms may be associated with use of Zofran \(ondansetron\)](#)<sup>1</sup> on 9/15/2011.

[06-29-2012] The U.S. Food and Drug Administration (FDA) is informing healthcare professionals and the public that preliminary results from a recently completed clinical study suggest that a 32 mg single intravenous dose of ondansetron (Zofran, ondansetron hydrochloride, and generics) may affect the electrical activity of the heart (QT interval prolongation), which could pre-dispose patients to develop an abnormal and potentially fatal heart rhythm known as Torsades de Pointes.

GlaxoSmithKline (GSK) has announced changes to the [Zofran drug label](#)<sup>2</sup> to remove the 32 mg single intravenous dose. The updated label will state that ondansetron can continue to be used in adults and children with chemotherapy-induced nausea and vomiting at the lower intravenous dose recommended in the drug label, a dose of 0.15 mg/kg administered every 4 hours for three doses; however, no single intravenous dose should exceed 16 mg. Information from the new clinical study will be included in the updated drug label.

FDA will evaluate the final study results when available, and will work with GSK to explore an alternative single dose regimen that is both safe and effective for the prevention of chemotherapy-induced nausea and vomiting in adults. The new information on QT prolongation does not change any of the recommended oral dosing regimens for ondansetron. It also does not change the recommended lower dose intravenous dosing of ondansetron to prevent post-operative nausea and vomiting.



As part of the ongoing safety review of ondansetron, FDA continues to assess data about the risk of QT prolongation and will update the public when more information becomes available.

#### Information for Healthcare Professionals (updated from 9/15/2011)

- i ECG changes including QT interval prolongation have been observed in patients receiving ondansetron. In addition, Torsade de Pointes, an abnormal, potentially fatal, heart rhythm, has been reported in some patients receiving ondansetron.
- i The use of a single 32 mg intravenous dose of ondansetron should be avoided. New information indicates that QT prolongation occurs in a dose-dependent manner, and specifically at a single intravenous dose of 32 mg.
- i Patients who may be at particular risk for QT prolongation with ondansetron are those with congenital long QT syndrome, congestive heart failure, bradyarrhythmias, or patients taking concomitant medications that prolong the QT interval
- i Electrolyte abnormalities (e.g., hypokalemia or hypomagnesemia) should be corrected prior to the infusion of ondansetron.
- i The lower dose intravenous regimen of 0.15 mg/kg every 4 hours for three doses may be used in adults with chemotherapy-induced nausea and vomiting. However, no single intravenous dose of ondansetron should exceed 16 mg due to the risk of QT prolongation.
- i The new information does not change any of the recommended oral dosing regimens for ondansetron, including the single oral dose of 24 mg for chemotherapy induced nausea and vomiting.
- i The new information also does not change the recommended lower dose intravenous dosing to prevent post-operative nausea and vomiting.
- i Report adverse events involving ondansetron to the FDA MedWatch program.

#### Data Summary

GlaxoSmithKline (GSK), the manufacturer of Zofran, was required by FDA to conduct a thorough QT study to assess the potential for the drug to prolong the QT interval. Preliminary review of the study results shows that QT prolongation occurs in a dose-dependent manner. Specifically, at the highest tested single intravenous dose of 32 mg, the maximum mean difference in QTcF from placebo after baseline-correction was 20 msec. At the lower tested single intravenous dose of 8 mg, the maximum mean difference in QTcF from placebo after baseline-correction was 6 msec.

### Safety Announcements

#### FDA Drug Safety Communication: Cefepime and risk of seizure in patients not receiving dosage adjustments for kidney impairment

[6-26-2012] The U.S. Food and Drug Administration (FDA) is reminding health care professionals about the need to adjust the dosage of the antibacterial drug cefepime in patients with renal (kidney) impairment. There have been cases of a specific type of seizure called nonconvulsive status epilepticus associated with the use of cefepime, primarily in patients with renal impairment who did not receive appropriate dosage adjustments of cefepime. The Warnings and Precautions and Adverse Reactions sections of the cefepime label are being revised to highlight this risk.

Cases of nonconvulsive status epilepticus associated with cefepime are documented in the medical literature and have been identified in FDA's Adverse Event Reporting System (AERS) database (see [Data Summary](#) below). Most cases occurred in patients with renal impairment who did not receive appropriate dosage adjustment; however, some cases occurred in patients receiving dosage adjustment appropriate for their degree of renal impairment. In the majority of cases, the seizures were reversible and resolved after discontinuing cefepime and/or after hemodialysis.

To minimize the risk of seizures, health care professionals should adjust the dosage of cefepime in patients with creatinine clearance less than or equal to 60 mL/min (see [product label](#)<sup>2</sup>). If seizures associated with

cefepime therapy occur, consider discontinuing cefepime or making appropriate dosage adjustments in patients with renal impairment.

#### Information for Health Care Professionals

- i The dosage of cefepime should be adjusted in patients with creatinine clearance less than or equal to 60 mL/min.
- i Nonconvulsive status epilepticus has been reported with cefepime. Most cases occurred in patients with renal impairment for whom the dosage was not appropriately adjusted.
- i In the majority of cases, the seizures were reversible and resolved after discontinuation of cefepime and/or after hemodialysis. If a patient experiences a seizure during cefepime therapy, health care professionals should consider discontinuing cefepime or making appropriate dosage adjustments in patients with renal impairment.
- i Health care professionals should report adverse events involving cefepime to the FDA MedWatch program.

#### Data Summary

A search of FDA's Adverse Event Reporting System (AERS) database, from the approval of cefepime, in 1996, through February 2012, identified 59 cases of nonconvulsive status epilepticus during cefepime administration; 56% of these cases involved patients >65 years of age (range: 7-95 years) and 69% of the 59 cases involved female patients. Renal dysfunction was present in 58/59 patients (renal status was unknown in one patient). In 56/59 patients, cefepime dosing was not appropriately adjusted for renal impairment as recommended in the cefepime label. Nonconvulsive status epilepticus resolved in 43 patients. Of the 16 patients who died, 13 deaths were caused by intercurrent illness (another illness that developed at the same time). Of the remaining three deaths, one involved a patient with central nervous system disease and a ventriculoperitoneal shunt who had ongoing seizure activity after discontinuing cefepime. The second death occurred in a patient who had concomitantly elevated amoxicillin levels possibly contributing to seizures, and insufficient data prevented determination of the cause of the third death.

FDA also reviewed case reports and case series in the medical literature. In general, patients who developed signs of neurotoxicity with cefepime were 50 years of age or older, had underlying renal dysfunction, and often did not receive appropriate dosage adjustments. Some patients had underlying central nervous system pathology or prior history of seizures on other beta-lactam antibacterial drugs or cephalosporins.

### Safety Announcements

FDA Drug Safety Communication: Revised recommendations for cardiovascular monitoring and use of multiple sclerosis drug Gilenya (fingolimod)

[05-14-2012] The U.S. Food and Drug Administration (FDA) has completed its evaluation of a report of a patient who died after the first dose of multiple sclerosis drug Gilenya (fingolimod). The agency also has evaluated additional clinical trial and postmarket data for Gilenya, including reports of patients who died of cardiovascular events or unknown causes. FDA could not definitively conclude that Gilenya was related to any of the deaths (see Data Summary, below). However, based on its reevaluation of the data, FDA remains concerned about the cardiovascular effects of Gilenya after the first dose. Data show that, although the maximum heart rate lowering effect of Gilenya usually occurs within 6 hours of the first dose, the maximum effect may occur as late as 20 hours after the first dose in some patients (See Data Summary).

For this reason, Gilenya is now contraindicated (FDA advises against its use) in patients with certain pre-existing or recent (within last 6 months) heart conditions or stroke, or who are taking certain antiarrhythmic medications. See CONTRAINDICATION section of the drug label<sup>3</sup>.

FDA continues to recommend that all patients starting Gilenya be monitored for signs of a slow heart rate (bradycardia) for at least 6 hours after the first dose. FDA is now recommending hourly pulse and blood pressure measurement for all patients starting Gilenya. Electrocardiogram (ECG or EKG) testing should be

performed prior to dosing and at the end of the observation period. Cardiovascular monitoring should continue until any symptoms resolve.

In addition, FDA is now also recommending that the time of cardiovascular monitoring be extended past 6 hours in patients who are at higher risk for or who may not tolerate bradycardia. Extended monitoring should include continuous ECG monitoring that continues overnight. See DOSAGE AND ADMINISTRATION section of the drug label<sup>4</sup>. These higher risk patients include those:

- i Who develop severe bradycardia after administration of the first dose of Gilenya
- i With certain pre-existing conditions in whom bradycardia may be poorly tolerated
- i Receiving therapy with other drugs that slow the heart rate or atrioventricular conduction
- i With QT interval prolongation (a type of heart rhythm abnormality) prior to starting Gilenya, or at any time during the cardiovascular monitoring period
- i Receiving therapy with other drugs that prolong the QT interval and that can cause a serious and life-threatening abnormal heart rhythm called Torsades de pointes

Healthcare professionals are encouraged to review the updated drug label for Gilenya<sup>5</sup> and note specific FDA recommendations for monitoring patients and the new contraindications for use in certain patients. Patients should not stop taking Gilenya without talking to their healthcare professional. They should contact their healthcare professional and seek immediate care if they develop dizziness, tiredness, irregular heart beat, or palpitations--signs of a slowing heart rate. FDA continues to believe that the benefits of treatment with Gilenya outweigh its potential risks when it is used as described in the updated drug label.

#### Data Summary

In December 2011<sup>6</sup>, FDA issued a Drug Safety Communication (DSC) concerning a patient with multiple sclerosis (MS) who died within 24 hours of taking the first dose of Gilenya (fingolimod). Based on the reported information, a cause of death could not be identified. The patient also had extensive brainstem MS lesions; such lesions have been associated with sudden death. The patient was also taking two blood pressure medications (metoprolol and amlodipine), which can also affect heart rate; whether they could have played a role in the patient's death is unknown. On the basis of the available data, a link between the first dose of Gilenya and the patient's death could not be ruled out, however, there is not clear evidence that the drug played any role in the death.

After receipt of this case, FDA re-evaluated clinical trial data related to the effects of Gilenya on heart rate and blood pressure, including data from trials that were ongoing at the time the drug was approved by FDA. Analyses of changes in heart rate by 24 hour Holter monitoring confirmed that the heart rate-lowering effect of Gilenya is biphasic, with an initial decrease within 6 hours, and a second decrease, in part related to a circadian rhythm, around 12 to 20 hours post-dose. In order to allow an adequate response to possible severe symptomatic bradycardia in the 6- to 24-hour period after the first dose, FDA concluded that it would be prudent to extend the monitoring period beyond 6 hours in patients who experience a heart rate of less than 45 beats per minute in the first 6 hours, or in those who had their lowest heart rate at 6 hours post-dose, as further bradycardia is still possible after 6 hours. In addition, in order to reduce the risks related to bradycardia or atrioventricular block, extended monitoring is now recommended in patients with certain pre-existing conditions, such as QT prolongation, and in patients receiving concurrent drugs that slow the heart rate or atrioventricular conduction.

FDA also reviewed postmarket data reported for Gilenya, including other deaths from apparent cardiovascular origin or of unknown origin. For each of these deaths, Gilenya's contribution to the death was unclear. The number of deaths of apparent cardiovascular origin or of unknown origin does not appear to be higher than in MS patients not treated with Gilenya.

In light of the findings of the clinical trial data and postmarketing data, including all reported deaths of cardiovascular or unknown origin, FDA has revised the Gilenya drug label with specific recommendations for monitoring patients and with new contraindications for use of Gilenya in certain patients.

FDA will communicate any important new information about the cardiovascular safety of Gilenya when it becomes available.

### Current Drug Shortages (as of June 26, 2012):

- i [Drug Shortages: Current Drug Shortages: Acetylcysteine Inhalation Solution](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Alfentanil Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Amino Acid Products](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Ammonium Chloride Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Aquasol A](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Atropine Sulfate Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Bumetanide Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Bupivacaine Hydrochloride Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Buprenorphine Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Chromic Chloride Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Diltiazem Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Epinephrine Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Epinephrine 1mg/mL \(Preservative Free\)](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Etomidate Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Fentanyl Citrate Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Fosphenytoin Sodium Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Hydromorphone Hydrochloride Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Intravenous Fat Emulsion](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Ketorolac Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Lidocaine Hydrochloride Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Lorazepam Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Magnesium Sulfate Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Mannitol Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Metoclopramide Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Midazolam Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Morphine Sulfate Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Morphine Sulfate Injection \(Preservative Free\)](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Nalbuphine HCl Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Naloxone Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Ondansetron Injection 32 mg/50 mL premixed bags](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Oxytocin Injection, USP \(synthetic\)](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Pancuronium Bromide Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Phytonadione Injectable Emulsion \(Vitamin K\)](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Potassium Chloride Injection 2 mEq/mL](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Potassium Phosphate Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Procainamide HCL Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Promethazine Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Protonix \(pantoprazole\) Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Sodium Bicarbonate Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Sufentanil Citrate Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Tobramycin Solution for Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Tromethamine Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Vecuronium Injection](#) (updated)
- i [Drug Shortages: Current Drug Shortages: Zinc Injection](#) (updated)
- i [Drug Shortages: Drugs to be Discontinued: Mytelase \(Ambenonium Chloride\)](#)