Drug Utilization Review Board

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

Wednesday
January 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 – January 11, 2012

DATE: January 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 January 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 Brilinta™ – See Appendix C.

Action Item - Vote to Prior Authorize Xarelto® – See Appendix D.

30 Day Notice to Prior Authorize Select Prenatal Vitamin Products – See Appendix E.

30 Day Notice to Prior Authorize Soliris® – See Appendix F.

30 Day Notice to Prior Authorize Onfi™ – See Appendix G.

Action Item – Annual Review of Ribavirin Miscellaneous Products – See Appendix H.

Action Item – Annual Review of Nasal Allergy Products – See Appendix I.

FDA and DEA Updates – See Appendix J.

Future Business

Adjournment

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

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

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. December 14, 2011 DUR Minutes – Vote
- B. December 15, 2011 DUR Recommendation Memorandum

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 September 2011
- B. Retrospective Drug Utilization Review Response for August 2011
- C. Medication Coverage Activity Audit for December 2011
- D. Pharmacy Help Desk Activity Audit for December 2011
- E. Pharmacy Lock-In Program Report for Calendar Year 2011

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

5. Action Item – Vote to Prior Authorize Brilinta™– See Appendix C.
- A. Product Summary
- B. COP Recommendations

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

6. Action Item – Vote to Prior Authorize Xarelto® – See Appendix D.
- A. Product Summary
- B. COP Recommendations

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

7. 30 Day Notice to Prior Authorize Select Prenatal Vitamin Products – See Appendix E.

A. Utilization Review
B. COP Recommendations

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

8. 30 Day Notice to Prior Authorize Soliris® – See Appendix F.

A. Introduction
B. COP Recommendations
C. Product Details

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

9. 30 Day Notice to Prior Authorize Onfi™ – See Appendix G.

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

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

10. Action Item – Annual Review of Ribavirin Miscellaneous Products – See Appendix H.

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

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

11. Action Item – Annual Review of Nasal Allergy Products – See Appendix I.

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

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

12. FDA and DEA Updates – See Appendix J.

13. Future Business

A. Annual Review of Narcotics
B. Annual Review of Erythropoiesis Stimulating Agents
C. New Product Reviews
D. Medical Product Reviews

14. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES of MEETING of DECEMBER 14, 2011

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

COLLEGE of PHARMACY STAFF:	PRESENT	ABSENT
Metha Chonlahan, D.Ph.; Clinical Pharmacist		X
Terry Cothran, D.Ph.	X	
Karen Egesdal, D.Ph.; SMAC-ProDUR Coordinator/OHCA Liaison	X	
Ronald Graham, D.Ph.; Pharmacy Director	X	
Shellie Keast, Pharm.D, M.S..; DUR Manager		X
Chris Le, Pharm.D.; Clinical Pharmacist/Coordinator	X	
Mark Livesay, Operations Coordinator	X	
Carol Moore, Pharm.D.; Clinical Pharmacist	X	
Neeraj Patel, Pharm.D.; Clinical Pharmacist	X	
Lester A. Reinke, Ph.D.; Associate Dean for Graduate Studies & Research	X	
Leslie Robinson, D.Ph.; PA Coordinator	X	
Jennifer Sipols, Pharm.D.; Clinical Pharmacist	X	
Visiting Pharmacy Student(s) n/a		

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

OTHERS PRESENT:		
Sandra Brazil, Depomed	Alan Kaye, Depomed	Wendy Smith, Depomed
Charlene Kaiser, Amgen	Jennifer Totten, Forest	David Williams, Forest
Andrea Johnson, AstraZeneca	Tone Jones, Sunovion	Michael Barber, Sunovion
Warren Tayes, Merck	Russ Wilson, Johnson & Johnson	Valerie Pennington, Novartis
Kathleen Karnik, Janssen	Deron Groth, Teva	John Omick, Novartis
Janie Huff, Takeda	Mark DeClerk, Lilly	Jim Chapman, Abbott

PRESENT FOR PUBLIC COMMENT:	
Agenda Item No. 8	Jennifer Totten, Pharm.D.; Forest
Agenda Item No. 10	Alan Kaye, M.D., Ph.D.; Depomed
Agenda Item No. 14	Andrea Johnson, Pharm.D.; AstraZeneca Kathleen Karnik, Pharm.D.; Janssen

AGENDA ITEM NO. 1: CALL TO ORDER

1A: Roll Call

Dr. Muchmore called the meeting to order. Roll call by Dr. Graham established the presence of a quorum.

ACTION: NONE REQUIRED

AGENDA ITEM NO. 2: PUBLIC COMMENT FORUM

Dr. Muchmore acknowledged the speakers for public comment:

Due to his schedule, Dr. Alan Kay, M.D., Ph.D. spoke at this time for Agenda Item No. 10 – see agenda item for transcription.

Agenda Item No. 8 Jennifer Totten, Pharm.D.; Forest

Agenda Item No. 14 Andrea Johnson, Pharm.D.; AstraZeneca

Kathleen Karnik, Pharm.D.; Janssen

ACTION: NONE REQUIRED

AGENDA ITEM NO. 3: APPROVAL OF DUR BOARD MINUTES

3A: November 9, 2011 DUR Minutes

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

ACTION: MOTION CARRIED

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

4A: Retrospective Drug Utilization Review: August 2011

4B: Retrospective Drug Utilization Review Response: July 2011

4A: Medication Coverage Activity Audit: November 2011

4B: Pharmacy Help Desk Activity Audit: November 2011

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: OVERVIEW OF OHCA ADVISORY GROUPS

Presented by Mr. Carter Kimble.

ACTION: NONE REQUIRED

AGENDA ITEM NO. 6: VOTE ON 2012 MEETING DATES

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

January 11, 2012	February 8, 2012	March 14, 2012	April 11, 2012
May 9, 2012	June 13, 2012	July 11, 2012	August 8, 2012
September 12, 2012	October 10, 2012	November 14, 2012	December 12, 2012

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: VOTE TO PRIOR AUTHORIZE MULTIPLE SCLEROSIS MEDICATIONS

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

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

ACTION: MOTION CARRIED

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

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

For Public Comment: Jennifer Totten, Pharm.D.: Good evening. My name is Jennifer Totten. I'm a pharmacist and I represent the scientific affairs department at Forest and thank you for the opportunity to provide comment on roflumilast, brand name Daliresp. Thank you, Dr. Le. I know that you have already gone over a summary of the product. I've looked that over as well as your criteria. Just to recap really quickly and address some of the criteria, roflumilast is the first phosphodiesterase for a PDE-4 inhibitor, FDA approved. It's indicated as a treatment to reduce the risk of exacerbation in patients with severe COPD who have chronic bronchitis and a history of exacerbations. It's an oral tablet, 500 mcg once a day.

Efficacy has been evaluated in eight clinical trials with over 9,000 patients. The first two trials were dose finding studies, the next two trials identified a population of patients who benefited most from therapy and those were the patients who had severe COPD, who had chronic bronchitis and who had a history of exacerbations. Then the pivotal trials were two identically designed one-year studies that looked at two primary endpoints; one being the incidence of moderate to severe COPD exacerbations and the other being FEV1, which is the measurement of lung function. And as you noted, these trials show roflumilast's ability to reduce the risk of exacerbations by 15% in one trial and 18% in the other trial for a mean of 17%. Although it's not a bronchodilator, it also did show some benefit on lung function. As far as safety, the safety of Daliresp has been evaluated in over 4,000 patients in those eight clinical trials and this is summarized in the P.I. Briefly, the most common adverse reactions were diarrhea, weight loss, nausea and headache. The most common that led to discontinuation were the diarrhea and nausea in 2.4% and 1.6% respectively. It does have one contraindication in patients with moderate to severe hepatic impairment and it has four warnings and precautions, the first being that it's not a bronchodilator; the second being an association with increased psychiatric events; the third being the weight loss which should be monitored; and the fourth is regarding drug interactions specifically with the use of strong cytochrome P450 inducers because they can reduce the effectiveness of the product. For more safety information I would refer you to the P.I. or the clinical summary. Finally I'd like to just comment briefly on proposed criteria. These obviously defined the target population which is severe COPD patients who have chronic bronchitis. This is consistent with the FDA approved label for roflumilast. The proposed criteria also require an FEV1 measurement as well as a specific smoking duration history. These are very useful criteria in the clinical trial setting; however in the real world practice setting these can be burdensome. Spirometry testing is encouraged but is often not routinely performed, especially in the primary care setting. Some data according to the NCQA 2010 stated health publications, spirometry testing rates in 2009 were less than 30% in Medicaid plans. It's also recognized in clinical practice as well as guidelines that patient symptoms impact on patient function as well as the history of exacerbations are important factors and can be used to define COPD severity. In addition you also have the criteria for the requirement of a trial of long-acting bronchodilator and that criteria may help identify patients who have severe disease or are inadequately controlled. Also in the United States, I'd like to point out that 80 to 90% of patients with COPD is due to cigarette smoking. Other causes could include occupational exposures or the use of solid fuels to either cook or heat the home although those are less common in the U.S. So given this information I would ask that you consider changing the verbiage in the criteria to a diagnosis of severe COPD associated with chronic bronchitis, removing FEV1 specific criteria and the smoking duration criteria. Thank you for this opportunity to talk about Daliresp and I'd be happy to answer any questions.

Dr. Kuhls: From my understanding and looking at the literature, the way you defined exacerbation was by one of the criteria not just being hospitalization but also by steroid use, right?

Dr. Totten: Yeah, so in this study, moderate exacerbations were those that required a systemic corticosteroid and severe were those that resulted in hospitalization or death. And the primary endpoint was the combined incidence of either moderate or severe exacerbations.

Dr. Kuhls: What was it in hospitalization alone?

Dr. Totten: If you look at the severe alone the reduction was about 18%; however it did not reach statistical significance because the study was powered to deduct that combined endpoint, moderate and severe, so there weren't enough numbers of severe exacerbations to be statistically significant, but it was trending and the trend was 18%.

Dr. Kuhls: So we don't know if there's a significant prevention of hospitalization which is significant cost or not?

Dr. Totten: We would need to see larger studies or longer duration studies, but … …

Dr. Kuhls: Is Forest doing that?

Dr. Totten: Forest is conducting additional studies. I'm not aware of one looking only at hospitalizations. They are also looking … .

Dr. Kuhls: Because that's where the money savings is if you use more patients but if you just look at steroid use I'm not sure there's a tremendous amount of … … 17% improvement or … … …

Dr. Totten: These are one-year studies.

Board members discussed the smoking history "pack years" criteria.

Dr. Kuhls moved to approve with the deletion of smoking history criteria; seconded by Dr. Feightner.

ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: VOTE TO PRIOR AUTHORIZE HORIZANT®

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

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: VOTE TO PRIOR AUTHORIZE GRALISE™

For Public Comment: Dr. Alan Kaye, M.D., Ph.D.: Thank you very much. I'm here to speak about Gralise. A little bit about my background. I have a Ph.D. pharmacology. I was the Chairman at Texas Tech in Lubbock in the anesthesia department. We had about a thousand pain patients a month. The last seven years I've been chairman of LSU med school in New Orleans. Again we have a very large pain practice. I'm happy and honored to speak about Gralise. I understand this Board is very aware of the efficacy and tolerability studies that have been presented in the past. Gabapentin TID and pregabalin pose significant side effects, the data indicates about one in three people who take these medications have significant clinical effects including somnolence following sedation and this is very impactful for individuals, such that the majority of these patients never receive a second refill of these drugs or they never receive the high end therapeutic or higher therapeutic doses because of these side effects. Gralise on the other hand, is a gastro retentive technology that's once a day rather than three times a day, which obviously would promote compliance. I think from a personal note I do see a lot of pain patients every day but my guinea pig patient for this was my own mother. My own mother has post herpetic neuralgia. We have a million cases a year in the United States. Shingles, 15% of those people get postherpetic neuralgia. She also had two rods put in her back after seven back operations, maybe a more common pain patient. Within three days on the Gralise starter pack she was off of

her sleeping pill. We had tried to cut her dose of gabapentin TID because she was falling. She was confused. She was not sharp. And this became very impactful for her when my stepfather passed away, leaving her by herself to drive and do all the errands of an older adult. Since that time three months ago, she is sharp, she's functional and it's just one example of a patient who's done real well with Gralise. This is similar to what I've seen in my practice and I'm happy to advocate for Gralise, not with requirements of having failed gabapentin TID or pregabalin TID or tricyclics which we all know have a lot of side effects. They're not tolerated very well. Seems to me that moving it to Tier 1 would make sense for Oklahoma and you know I think it's basically a better version of the drug that we're very familiar with and is very useful for a wide range of people. Because we know when people fail with gabapentin TID, when they fail with pregabalin, pain practitioner is left having to give opiates more often than not and we know that people on opiates have a whole list of side effects over time. They become dependent and it's a picture that we're all very familiar with. I think I've spoke as long as I can. Thank you for listening to me and if I can entertain any questions, I guess maybe I can't in this gap here. Thank you. Ms. Wendy Smith is here from Gralise; one of the science experts who is available and will be here for the remainder of the meeting. Again thank you, happy holidays, nice meeting you all.
Materials included in agenda packet; presented by Dr. Sipols.
Dr. Bell moved to approve as submitted; seconded by Dr. Kuhls.
ACTION: MOTION CARRIED

AGENDA ITEM NO. 11: ANNUAL REVIEW OF ANTIHISTAMINES
Materials included in agenda packet; presented by Dr. Sipols.
Dr. Feightner moved to approve with moving Allegra OTC to Tier 2; seconded by Dr. Winegardener.
ACTION: MOTION CARRIED

AGENDA ITEM NO. 12: ANNUAL REVIEW OF STATIN AND STATIN COMBINATION PRODUCTS
Materials included in agenda packet; presented by Dr. Le.
Dr. Feightner made a motion to move Atorvastatin to Tier 1 and to move Advicor and Simcor to Tier 3; seconded by Dr. Winegardener.
ACTION: MOTION CARRIED

AGENDA ITEM NO. 13: ANNUAL REVIEW OF LOVAZA®
Materials included in agenda packet; presented by Dr. Le.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: 30-DAY NOTICE TO PRIOR AUTHORIZE BRILINTA™ AND XARELTO™
Materials included in agenda packet; presented by Dr. Le.
For Public Comment: Andrea Johnson, Pharm.D.: Hello. Thank you for having me here today. I believe that there was a final report that was done on Brilinta. I'm here to just give you the overview of Brilinta as well. It's going to be brief. Excuse me for reading, but according to company rules there are things that I must say verbatim. So I will do that for you today. Thank you for the opportunity. Brilinta is indicated to reduce the rate of thrombotic cardiovascular events in patients with acute coronary syndrome including unstable angina, non-ST elevation, myocardial infarction or ST elevation myocardial infarction. When given the maintenance dose of aspirin at 100 mg or less, Brilinta has been shown to reduce the rate of a combined endpoint of CV, MI and stroke compared to clopidogrel and this was driven primarily by the cardiovascular death and MI with no difference in stroke rates. In patients treated with PCI, Brilinta also reduces the rate of stent thrombosis and Brilinta is contraindicated in patients with a history of intercranial hemorrhage, active pathological bleeding or severe hepatic impairment. I'd like to point out that ACCF and AHA and the SCAI have updated their guidelines to include Brilinta as a Class I recommendation for the management in patients with ACS undergoing PCI. In the PLATO trial which was a primary trial that compared Brilinta to clopidogrel for the reduction of CV, an event of over 18,000 patients with UA, NSTEMI, or STEMI. At 12 months the patients who received Brilinta versus clopidogrel had a 16% relative risk reduction or 1.9 ARR and the primary endpoint of cardiovascular death, MI or stroke compared to clopidogrel and this is driven again by the cardiovascular death and MI rates with no difference in stroke. In a North American subgroup, Brilinta was numerically inferior to clopidogrel. In PLATO, the use of more than 100 mg of aspirin decreased the effectiveness of Brilinta. So after initial dosing, aspirin should only be dosed in combination with Brilinta in 75 to 100 mg/day. So a maximum of 100 mg aspirin in combination with Brilinta. For adverse events PLATO defined major bleeding rates were similar between Brilinta and the clopidogrel groups. Brilinta was associated with a higher risk of non CABG-related bleeding and the most commonly reported adverse events were bleeding and dyspnea. Here is the box warning associated with Brilinta around the increased risk of bleeding that is known to be antiplatelet effect as well as the warning with the maintenance dose of 75 to 100 mg aspirin. Please refer to Brilinta prescribing for complete information as well as the boxed warning and precaution. Thank you for your time. If anyone has any questions I'd be glad to answer them.
For Public Comment: Kathleen Karnik, Pharm.D. Good evening. I'm here only to say that I've been working with Shellie and Chris and provided them with the clinical information regarding Xarelto. I'm here only to address any questions and we agree with the recommendations that the College has made.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 15: FDA & DEA UPDATES

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 16: FUTURE BUSINESS

Materials included in agenda packet; submitted by Dr. Graham.

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 17: ADJOURNMENT

The meeting was adjourned at 7:29 p.m.

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

Memorandum

Date: December 19, 2011

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

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

Subject: DUR Board Recommendations from Meeting of December 14, 2011

Recommendation 1: Vote on 2012 Meeting Dates

MOTION CARRIED by unanimous approval.

Meetings are held the second Wednesday of each month.

January 11, 2012
February 8, 2012
March 14, 2012
April 11, 2012
May 9, 2012
June 13, 2012
July 11, 2012
August 8, 2012
September 12, 2012
October 10, 2012
November 14, 2012
December 12, 2012

Recommendation 2: Vote to Prior Authorize Multiple Sclerosis Medications

MOTION CARRIED by unanimous approval.

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

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

Interferon Prior Authorization Criteria:

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

Glatiramer Acetate (Copaxone®) Prior Authorization Criteria:

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

Fingolimod (Gilenya®) Prior Authorization Criteria:

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

Recommendation 3: Vote to Prior Authorize Dalisrep® (roflumilast)

MOTION CARRIED by unanimous approval.

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

1. Diagnosis of COPD with history of chronic bronchitis; and
2. FEV </= 50% of predicted; and
3. ~~Smoking history >/= 20 pack-years; and~~

4. Inadequately controlled on long acting brochodilator therapy (must have 3 or more claims for long acting brochodilators in the previous 6 months)

Recommendation 4: Vote to Prior Authorize Horizant® (gabapentin enacarbil)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends prior authorizing Horizant® (gabapentin enacarbil) using the following criteria:

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

Recommendation 5: Vote to Prior Authorize Gralise™ (gabapentin extended-release)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends prior authorization of Gralise™ (gabapentin extended-release) with the following criteria:

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

Recommendation 6: Annual Review of Antihistamines

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends moving levocetirizine (Xyzal) into tier 2 of the PBPA criteria and fexofenadine (Allegra OTC®) into Tier 2 ~~3~~ of the PBPA criteria. ~~The status of~~

~~fexofenadine (Allegra OTC®) may be reconsidered when pricing is comparable to OTC loratadine and cetirizine.~~ Current criteria will remain the same.

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

Recommendation 7: Annual Review of Statins

MOTION CARRIED by unanimous approval.

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

Additionally, the Drug Utilization Board made the following recommendation:

HMG-CoA Reductase Inhibitors (Statins) and Statin Combination Products		
Tier 1	Tier 2	Tier 3
Fluvastatin (Lescol> & Lescol> XL)	Atorvastatin (Lipitor>)	Lovastatin (brand Altoprev>)
Lovastatin (Mevacor>)	Rosuvastatin (Crestor>)	Simvastatin/Ezetimibe (Vytorin>)
Pravastatin (Pravachol>)	Pitavastatin (Livalo>)	Ezetemibe (Zetia>)
Simvastatin (Zocor>)		Lovastatin/Niacin CR (Advicor>)
		Simvastatin/Niacin CR (Simcor>)
~~Statin/Niaspan® Combination Products~~		
~~Tier 1 Statins and/or Niaspan>~~	~~Lovastatin/Niacin CR (Advicor>)~~ ~~Simvastatin/Niacin CR (Simcor>)~~	

Recommendation 8: Annual Review of Lovaza® (omega-3-acid ethyl esters)

NO ACTION REQUIRED.

The College of Pharmacy recommends no changes at this time.

Appendix B

RETROSPECTIVE DRUG UTILIZATION REVIEW REPORT
September 2011

MODULE	DRUG INTERACTION	DUPLICATION OF THERAPY	DRUG-DISEASE PRECAUTIONS	DOSING & DURATION
Total # of messages	62,282	66,237	963,322	32,629
Limits applied	Established, Major, Males and Females, Age 36-50	Duplication of Atypical Antipsychotics, Males and Females, Age 0-10	Contraindicated, Pregnant, Females, Age 22-45	High Dose Only, NSAIDs, Males and Females, 22-25
Total # of messages after limits were applied	116	38	1,055	54
Total # of members reviewed	116	38	1,055	54

LETTERS

Category	Prescribers	Pharmacies	Total Letters
Drug Interaction	2	2	4
Duplication of Therapy	38	0	38
Drug-Disease Precautions	1	0	1
Dosing & Duration	24	0	24
Total Letters Sent	65	2	67

Retrospective Drug Utilization Review Report

Claims Reviewed for August 2011

Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
Limits which were applied	Established, Major, Males and Females, Age 19-35	Duplication of Tumor Necrosis Factors, Males and Females, Age 0-150	Contraindicated, Pregnancy, Females, Age 0-21	High Dose, NSAIDs, Males and Females, Age 22-25

Response Summary (Prescriber)
Letters Sent: 3
Response Forms Returned: 0

The response forms returned yielded the following results:

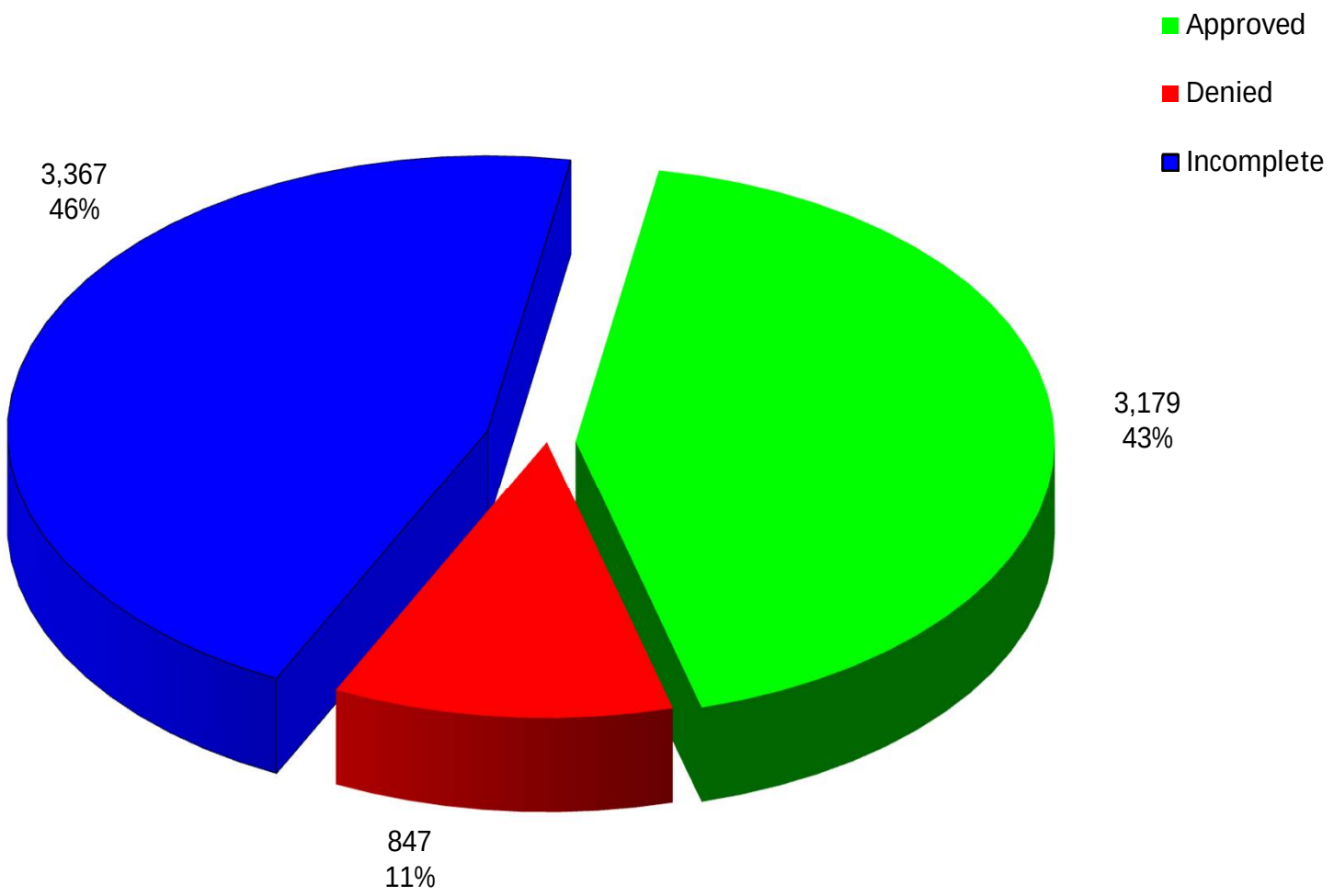
	Record Error—Not my patient.
	No longer my patient.
	Medication has been changed prior to date of review letter.
	I was unaware of this situation & will consider making appropriate changes in therapy.
	I am aware of this situation and will plan to continue monitoring therapy.
	Other

Response Summary (Pharmacy)
Letters Sent: 4
Response Forms Returned: 2

The response forms returned yielded the following results:

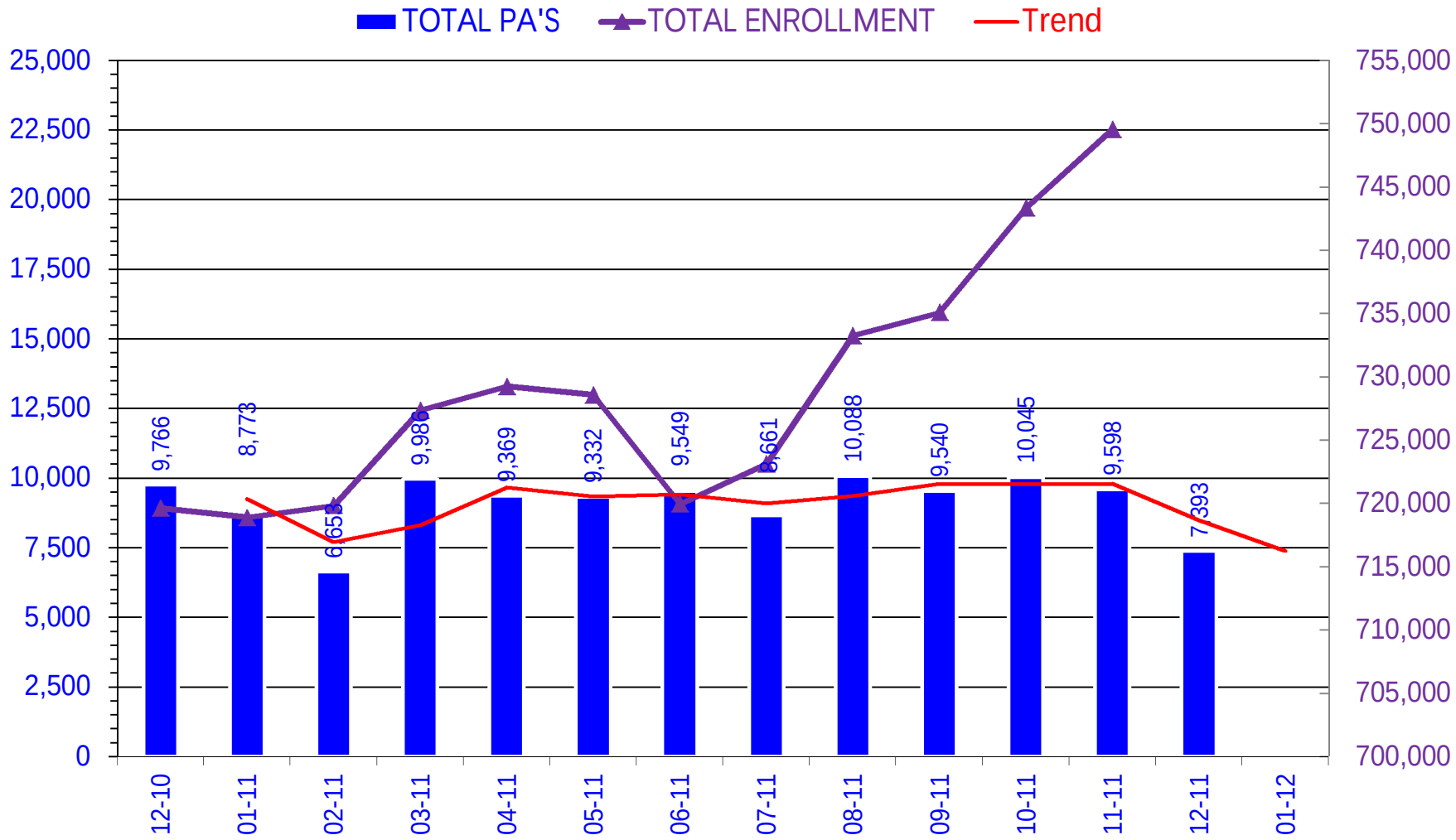
0 (0%)	*Record Error—Not my patient.*
1 (50%)	*No longer my patient.*
0 (0%)	*Medication has been changed prior to date of review letter.*
0 (0%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
0 (0%)	*I am aware of this situation and will plan to continue monitoring therapy.*
1 (50%)	*Other*

PRIOR AUTHORIZATION ACTIVITY REPORT: December 2011



PA totals include overrides

PRIOR AUTHORIZATION REPORT: December 2010 – December 2011



PA totals include overrides

Prior Authorization Activity

12/1/2011 Through 12/31/2011

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort	350	137	21	192	357
Amitiza	12	6	0	6	270
Anti-Ulcer	425	158	95	172	105
Antidepressant	310	99	25	186	347
Antihistamine	160	112	5	43	338
Antihypertensives	81	17	7	57	361
Antimigraine	108	26	25	57	344
Atypical Antipsychotics	651	354	36	261	350
Benign Prostatic Hypertrophy	7	0	0	7	0
Benzodiazepines	44	22	2	20	235
Bladder Control	59	8	18	33	362
Brovana (Arformoterol)	5	1	0	4	211
Byetta	18	7	1	10	362
Elidel/Protopic	38	17	1	20	106
ESA	98	74	1	23	108
Fibric Acid Derivatives	1	0	1	0	0
Fibromyalgia	119	33	21	65	361
Fortamet/Glumetza	13	3	0	10	362
Forteo	10	3	1	6	361
Glaucoma	12	3	0	9	360
Growth Hormones	60	42	6	12	171
HFA Rescue Inhalers	67	19	5	43	301
Insomnia	93	18	20	55	182
Insulin	2	1	0	1	183
Misc Analgesics	41	2	35	4	72
Multiple Sclerosis	7	2	1	4	363
Muscle Relaxant	123	22	67	34	90
Nasal Allergy	186	57	42	87	125
NSAIDS	176	35	21	120	318
Ocular Allergy	45	14	6	25	166
Ocular Antibiotics	46	9	3	34	10
Opioid Analgesic	342	166	17	159	264
Other	938	324	110	504	280
Otic Antibiotic	30	8	4	18	11
Pediculicides	154	80	14	60	16
Plavix	175	121	1	53	324
Singulair	786	379	44	363	242
Smoking Cessation	61	19	10	32	35
Statins	100	64	4	32	361
Stimulant	856	452	71	333	304
Suboxone/Subutex	154	111	5	38	72
Symlin	6	2	0	4	363
Synagis	190	110	32	48	91
Topical Antibiotics	8	1	1	6	361
Topical Antifungals	18	4	3	11	146
Topical Corticosteroids	145	8	60	77	232
Ultram ER and ODT	4	2	0	2	271
Xolair	9	1	2	6	362
Xopenex Nebs	22	8	1	13	327
Zetia (Ezetimibe)	20	10	2	8	361
Emergency PAs	8	8	0	0	
Total	**7,393**	**3,179**	**847**	**3,367**	

Overrides					
Brand	77	52	6	19	292
Dosage Change	573	529	12	32	10
High Dose	3	3	0	0	129
IHS-Brand	7	6	0	1	2
Lost/Broken Rx	102	98	3	1	14
NDC vs Age	8	8	0	0	274
Nursing Home Issue	113	108	2	3	14
Other	24	18	0	6	25
Quantity vs. Days Supply	830	538	71	221	283
Stolen	11	10	1	0	5
Overrides Total	**1,748**	**1,370**	**95**	**283**	
Total Regular PAs + Overrides	**9,141**	**4,549**	**942**	**3,650**	

Denial Reasons	
Unable to verify required trials.	2,897
Does not meet established criteria.	912
Lack required information to process request.	755
Drug Not Deemed Medically Necessary	2
Considered duplicate therapy. Member has a prior authorization for similar medication.	1

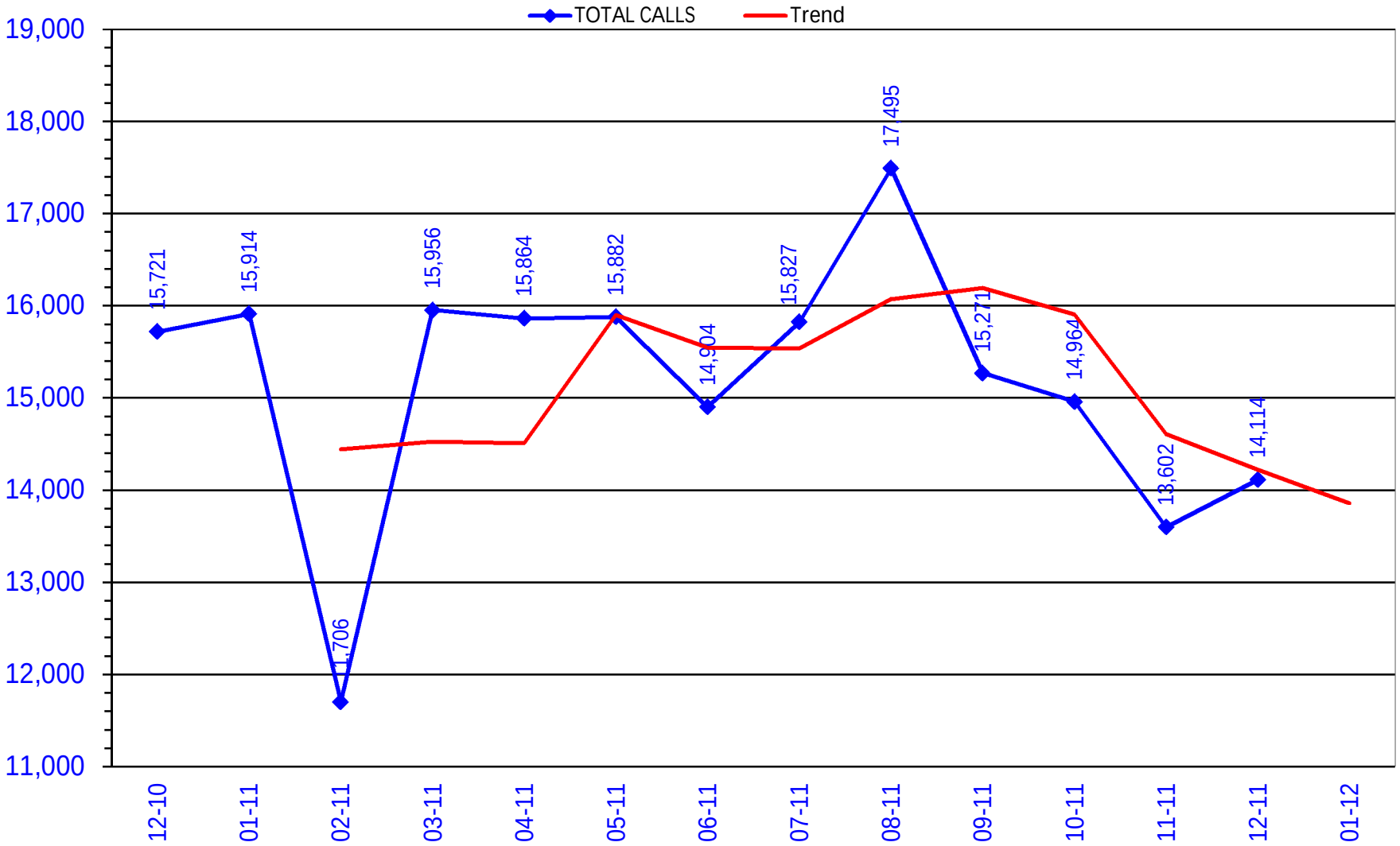
Duplicate Requests: 623

Letters: 1,961

No Process: 331

Changes to existing PAs: 520

CALL VOLUME MONTHLY REPORT:
December 2010 – December 2011



MONTHLY LOCK-IN REPORT

OKLAHOMA HEALTH CARE AUTHORITY

CALENDAR YEAR 2011

	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
Total in Database	4149	4232	4287	4291	4374	4433	4530	4607	4707	4712	4819	4852
Total Locked-In	294	299	297	296	299	305	305	296	295	306	295	300
Total Reviewed	164	152	127	170	152	190	174	207	129	245	119	147
	Results of Reviews											
Extended Lock-in	13	2	8	4	9	7	12	9	14	10	7	6
In Lock-In process	10	12	9	15	13	11	13	8	9	19	6	7
Warned	2	7	3	3	10	9	8	5	7	11	6	4
Completed Lock-In	8	8	6	8	13	6	2	15	14	1	11	5

Total in Database- The number of cases reviewed by a pharmacist since the College of Pharmacy took over the program from OHCA.

Total Locked-In- The total number of members that are locked into one pharmacy at the end of the month.

Total Reviewed- The total number of cases reviewed during the month specified.

Extended Lock-in- Members already locked into one pharmacy for two years with an extension for one more year due to continued abuse or increased potential for continued abuse.

In Lock-In Process- Members have been notified that they have been locked in and need to respond back with a pharmacy of their choice.

Warned- The total number of members that have been sent a warning letter due to the potential for abuse.

Completed Lock-in- The total number of members that were locked into one pharmacy during the month specified.

Appendix C

Vote to Prior Authorize Brilinta™ (ticagrelor)

Oklahoma Health Care Authority, January 2012

Product Summary

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

Recommendation

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

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

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

REFERENCES

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

Appendix D

Vote to Prior Authorize Xarelto® (rivaroxaban)

Oklahoma Health Care Authority, January 2012

Product Summary

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

Recommendation

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

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

REFERENCES

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

Appendix E

30 DAY NOTICE TO PRIOR AUTHORIZE SELECT PRENATAL VITAMINS

OKLAHOMA HEALTH CARE AUTHORITY, JANUARY 2012

INTRODUCTION

While a balanced diet is always the best way to ensure that proper nutrients are consumed during pregnancy, the addition of a multivitamin is recommended. The American College of Obstetricians and Gynecologists recommend extra iron and folic acid during pregnancy. [1] Along with these, the essential vitamins and minerals often listed include Vitamins A, D, E, C, B1, B2, B3, B6, Calcium, and Zinc. [2] Newer products on the market also include fish oils, Omega-3, or docosahexaenoic acid (DHA). While some researchers do not consider any nutrient other than folic acid to be proven to prevent structural birth defects[3], there have been small studies looking at Omega-3 fatty acids or DHA in maturation of the central visual pathways. [4, 5]

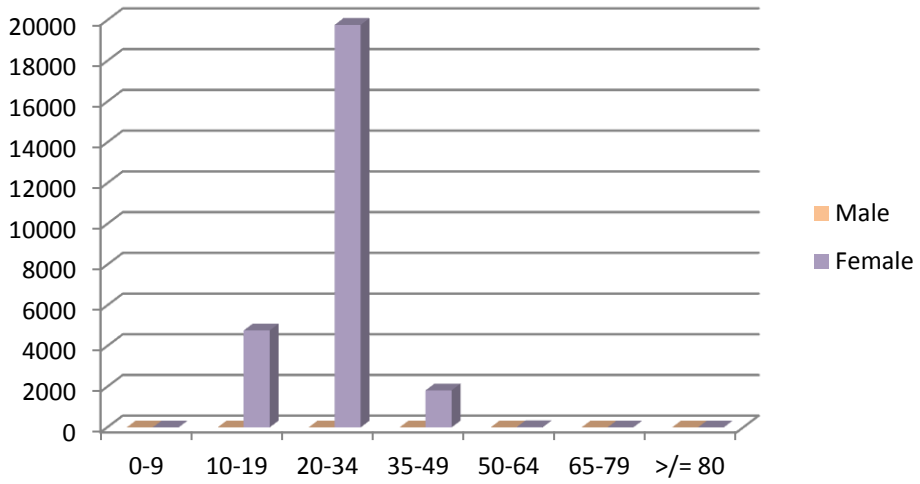
Although most vitamins and minerals are not required to be covered by state Medicaid programs, one exception is prenatal vitamins for pregnant females up to 50 years of age. However, with the new products and formulations which are being added to the market, some control over the basic use of these products is necessary.

UTILIZATION REVIEW FOR FISCAL YEAR 2011

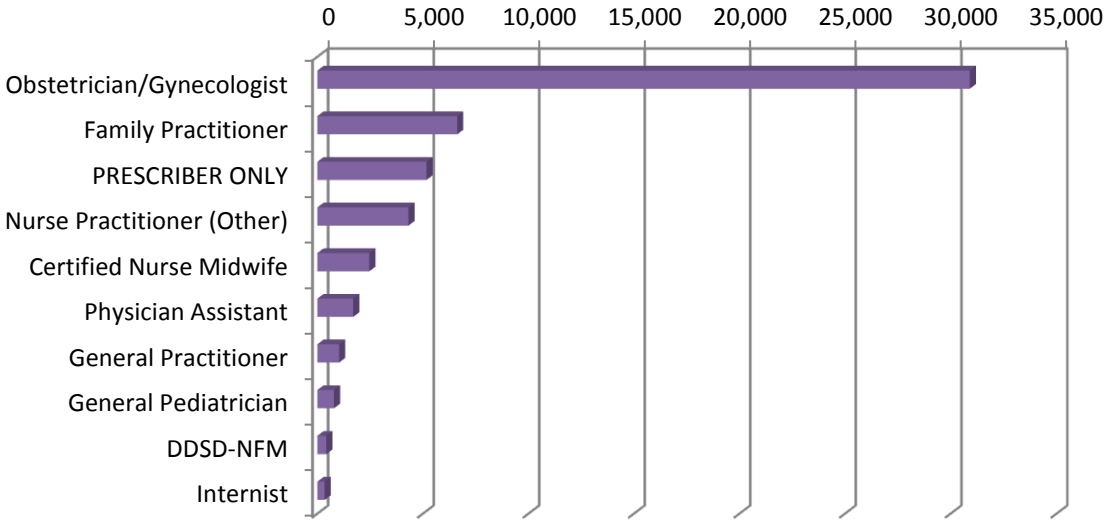
FISCAL YEAR COMPARISON – FY2010 TO FY2011

Fiscal Year	Total Members	Total Claims	Total Cost	Cost per Claim	Per-Diem Cost	Total Units	Total Days
2010	25,520	52,212	$2,712,930.40	$51.96	$1.09	2,713,775	2,487,679
2011	26,369	54,800	$2,828,600.33	$51.62	$1.10	2,765,285	2,560,845
Percent Change	**3.3%**	**5.0%**	**4.3%**	**-0.7%**	**0.9%**	**1.9%**	**2.9%**
Absolute Change	**849**	**2,588**	**$115,669.93**	**-$0.34**	**$0.01**	**51,510**	**73,166**

MEMBER DEMOGRAPHICS FY2011



PRESCRIBER SPECIALTY BY NUMBER OF CLAIMS



DISCUSSION

Currently the average cost per day for the prenatal vitamins is $1.10. Approximately 22% of the available product groups have a cost per day of less than $0.50. These products account for about 30% of the total utilization with 4 of the groups belonging to the top ten prescribed product groups for the category. It is estimated that if all utilization was for products priced at $0.50 daily it would result in a savings of approximately 50% of the current annual reimbursement to the pharmacies. The most commonly used ingredients not included in this group of products are DHA, Omega-3, and Fish Oil. Below is a table representing the key ingredients included in the products priced at $0.50 per day or lower along with one commonly prescribed brand name example for each product group.

Key Ingredients/Group	Example Brand
Iron 29 mg, Docusate Sodium, Folic Acid 1 mg	Prenatal 19
Iron 29 mg, Folic Acid 1 mg	Vinate II
No Calcium, Iron Fumarate 106.5 mg, Folic Acid 1 mg Capsule	Prenatal-U
Calcium, Iron 27 mg, Folic Acid 1 mg	Prenatal Plus
Iron (Carbonyl) 29 mg, Folic Acid 1 mg	Re-Nata 29 OB
Iron 28 mg, Folic Acid 1 mg	Trinate
Iron (Fumarate) 29 mg, Folic Acid 1 mg Chewable	Se-Natal 19
Iron (Fumarate) 27 mg, Folic Acid 1 mg, Selenium	Vinate-M
Iron (Carbonyl) 90 mg, Folic Acid 1 mg, Docusate Sodium 50 mg	Triadvance
Iron (Carbonyl and Gluconate) 27 mg, Folic Acid 1 mg, Docusate Sodium 50 mg	Vinacal
Calcium, Iron 60 mg, Folic Acid 1 mg	Trinatal Rx 1
Iron (Fumarate) 17 mg, Folic Acid 1 mg	Prenafirst

By raising the cost per day capitation to $0.75, four additional choices which contain either Omega-3 or DHA would be included. This would also raise the current utilization to 40%, but would decrease the percent of estimated savings to approximately 42%.

RECOMMENDATIONS

The College of Pharmacy recommends placing a prior authorization on any prenatal vitamin with a cost per day of greater than $0.75. Products with a cost greater than $0.75 per day will require prior authorization with the following criteria for approval: clinically significant reason why the member cannot use any available non-prior authorized product.

Due to the transient nature of the use of prenatal vitamins during pregnancy, current members will be allowed to stay on their product for the duration of their pregnancy as long they remain compliant.

Prior authorization requirements may be removed when the product's price is at or below the designated pricing cutoff.

REFERENCES

1. American College of Obstetricians and Gynecologists. "FAQ001: Nutrition During Pregnancy." August 2011. *American Congress of Obstetricians and Gynecologists.* Accessed: 29 December 2011. <http://www.acog.org/~/media/For%20Patients/faq001.ashx?dmc=1&ts=20111229T0958362541>.

2. American Pregnancy Association. *Essential Nutrients and Viatmins for Pregnancy*. June 2011. Accessed: 29 December 2011. <http://www.americanpregnancy.org/pregnancyhealth/nutrientsvitaminspregnancy.html>.

3. Czeizel AE, Banhidy F. Vitamin supply in pregnancy for prevention of congenital birth defects. *Curr Opin Clin Nutr Metab Care* 2011;14:291-296.

4. Jaques C, Levy E, Muckle G, et. al. Long-term effects of prenatal Omega-3 fatty acid intake on visual function in schoole-age children. *J Pediatr* 2011;158:73-80.

5. Malcom CA, McCulloch DL, Montgomery C, Shepherd A, Weaver LT. Maternal docosahexaenoic acid supplementation during pregnancy and visual evoked potential development in term infants: a double blind, prospective, randomised trial. *Arch Dis Child Fetal Neonatal Ed* 2003;88:F383-F390.

Appendix F

30 Day Notice to Prior Authorize Soliris® (eculizumab)

Oklahoma Health Care Authority, January 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.

Manufacturer	**Alexion Pharmaceuticals, Inc.**
FDA Status	**Prescription Only**
Classification	**Monoclonal Antibody**

Introduction

Soliris® (eculizumab) is an intravenous solution of monoclonal antibodies that specifically binds to the complement protein C5 inhibiting terminal complement mediated intravascular hemolysis and is indicated for:

1. The treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis.
2. The treatment of patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy.

Paroxysmal Nocturnal Hemoglobinuria[i]

Paroxysmal nocturnal hemoglobinuria is an acquired disorder that leads to the premature death and impaired production of blood cells. Paroxysmal nocturnal hemoglobinuria affects both sexes equally, and can occur at any age, although it is most often diagnosed in young adulthood.

People with paroxysmal nocturnal hemoglobinuria have sudden, recurring episodes of symptoms which may be triggered by stresses on the body, such as infections or physical exertion, manifested as dark-colored urine due to the presence of hemoglobin in the urine. In many, but not all cases, hemoglobinuria is most noticeable in the morning, upon passing urine that has accumulated in the bladder during the night.

The premature destruction of red blood cells results in a deficiency of these cells which can cause signs and symptoms such as fatigue, weakness, abnormally pale skin, shortness of breath, and an increased heart rate. People with paroxysmal nocturnal hemoglobinuria may also be prone to infections due to a deficiency of white blood cells. Abnormal platelets associated with paroxysmal nocturnal hemoglobinuria can also cause problems in the blood clotting process such as thrombosis, or less often, episodes of severe hemorrhage.

Paroxysmal nocturnal hemoglobinuria is a rare disorder, estimated to affect between 1 and 5 per million people. In some cases, people who have been treated for aplastic anemia may develop paroxysmal nocturnal hemoglobinuria. Paroxysmal nocturnal hemoglobinuria is believed to be caused by a gene mutation acquired in a person's lifetime, as it has not been shown to be inherited.

Treatment consists of symptomatic and supportive therapy to reduce mortality and morbidity.[ii] Soliris® (eculizumab) has been shown to increase 5 year survival rates from 66.8% to 95.5%. The rate of thrombotic complications prior to eculizumab was 5.6 per 100 patient years and 0.8 per 100 patient years after use of Soliris® (eculizumab).[iii]

Atypical Hemolytic-Uremic Syndrome[iv]

Atypical hemolytic-uremic syndrome is a disease that causes abnormal blood clots to form in small blood vessels in the kidneys leading to three major features related to abnormal clotting: hemolytic anemia, thrombocytopenia, and kidney failure. As a result of clot formation in small blood vessels, people with atypical hemolytic-uremic syndrome experience kidney damage and acute kidney failure that lead to end-stage renal disease (ESRD) in about half of all cases.

Atypical hemolytic-uremic syndrome should be distinguished from a more common condition called typical hemolytic-uremic syndrome. The two disorders have different causes and different signs and symptoms. Unlike the atypical form, the typical form is caused by infection with certain strains of *Escherichia coli* bacteria that produce toxic substances called Shiga-like toxins. The typical form is characterized by severe diarrhea and most often affects children younger than 10. The typical form is less likely than the atypical form to involve recurrent attacks of kidney damage that lead to ESRD.

The atypical form is probably about 10 times less common than the typical form, with the incidence estimated to be 1 in 500,000 people per year in the United States. Atypical hemolytic-uremic syndrome often results from a combination of environmental and genetic factors. Mutations in at least seven genes appear to increase the risk of developing the disorder. Although gene mutations increase the risk of atypical hemolytic-uremic syndrome, studies suggest that they are often not sufficient to cause the disease. In people with certain genetic changes, the signs and symptoms of the disorder may be triggered by factors including certain medications (such as anticancer drugs), chronic diseases, viral or bacterial infections, cancers, organ transplantation, or pregnancy. Some people with atypical hemolytic-uremic syndrome do not have any known genetic changes or environmental triggers for the disease. In these cases, the disorder is described as idiopathic.

Treatment[v] consists of supportive care. The following anticoagulation therapy may be considered for adults: antiplatelet or antioxidant agents, fibrinolytics; streptokinase, plasmapheresis and plasma exchange, infusions of plasma, prostacyclin, or gamma globulin; however, these therapies have not been proven to yield better results than supportive care. Other therapies that have been tried in adults in which evidence of efficacy is strongest include: prednisone, azathioprine, vincristine, and intravenous immunoglobulin (IVIg). Use of Soliris® (eculizumab) demonstrated improvement in platelet count from baseline, reduction of thrombotic microangiopathy events, with reports of improved or maintenance of kidney function.

Cost of Soliris® (eculizumab)

The estimated acquisition cost of Soliris® (eculizumab) is $5,820 per 300mg vial. Based on this pricing, the estimated cost of therapy for the first month is $46,560, and approximately $34,920 per month thereafter (900mg infused on the 5th week and every 14 days) for paroxysmal nocturnal hemoglobinuria. For atypical hemolytic-uremic syndrome, the cost is estimated to be $69,840 for the first month, and $46,560 thereafter (1200mg infused on the 5th week and every 14 days.)

Recommendations

The College of Pharmacy recommends medical prior authorization of Soliris® (eculizumab) with the following approval criteria:

1. Established diagnosis of paroxysmal nocturnal hemoglobinuria or atypical hemolytic uremic syndrome via ICD-9 coding in member's medical claims.

PRODUCT DETAILS OF SOLIRIS ® (ECULIZUMAB)[vi]

FDA-APPROVED IN MARCH 2007

INDICATIONS:

- Soliris® (eculizumab) Intravenous solution is indicated for the treatment of paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis, and treatment of patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy.

DOSAGE FORMS:

- Soliris® Intravenous Solution is a concentrated solution 10mg/mL that must be diluted to a final concentration of 5mg/mL prior to administration.

ADMINISTRATION:

Recommended dosage Regimen - PNH

- 600 mg weekly for the first 4 weeks, followed by
- 900 mg for the fifth dose 1 week later, then
- 900 mg every 2 weeks thereafter.

Recommended dosage Regimen - aHUS

- 900 mg weekly for the first 4 weeks, followed by
- 1200 mg for the fifth dose 1 week later, then
- 1200 mg every 2 weeks thereafter

PREPARATION FOR ADMINISTRATION:

- Eculizumab must be diluted to a final admixture concentration of 5 mg/mL.
- Withdraw the required amount of eculizumab from the vial into a sterile syringe. Transfer the recommended dose to an infusion bag. Dilute eculizumab to a final concentration of 5 mg/mL by adding the appropriate amount (equal volume of diluent to drug volume) of sodium chloride 0.9% injection, sodium chloride 0.45% injection, dextrose 5% in water, or Ringer's lactate to the infusion bag.
- The final admixed eculizumab 5 mg/mL infusion volume is 120 mL for 600 mg doses or 180 mL for 900 mg doses. Gently invert the infusion bag containing the diluted eculizumab solution to ensure thorough mixing of the product and diluent. Do not shake.
- Prior to administration, the admixture should be allowed to adjust to room temperature (18° to 25°C [64° to 77°F]). The admixture must not be heated in a microwave or with any heat source other than ambient air temperature.
- The eculizumab admixture should be inspected visually for particulate matter and discoloration prior to administration

STORAGE AND STABILITY:

- Eculizumab vials must be stored in the original carton until time of use under refrigerated conditions at 2° to 8°C (36° to 46°F) and protected from light. Admixed solutions of eculizumab are stable for 24 hours at 2° to 8°C (36° to 46°F) and at room temperature. Do not freeze. Discard any unused portion left in a vial because the product contains no preservatives.

CONTRAINDICATIONS:

- Unresolved serious Neisseria meningitidis infection; patients who are not currently vaccinated against N. meningitides.

SPECIAL POPULATIONS:

- **Pregnancy**:
    - Category C. PNH is a serious illness. Pregnant women with PNH and their fetuses have high rates of morbidity and mortality during pregnancy and the postpartum period. There are no adequate and well-controlled studies of eculizumab in pregnant women. Eculizumab, a recombinant immunoglobulin G (IgG) molecule (humanized anti-C5 antibody), is expected to cross the placenta. Animal studies using a mouse analogue of the eculizumab molecule (murine anti-C5 antibody) showed increased rates of developmental abnormalities and an increased rate of dead and moribund offspring at doses 2 to 8 times the human dose. Administer eculizumab during pregnancy only if the potential benefit justifies the potential risk to the fetus.
- **Labor and Delivery:** No information is available on the effects of eculizumab during labor and delivery.
- **Nursing Mothers:** It is not known whether eculizumab is secreted into human milk. IgG is excreted in human milk; therefore, it is expected that eculizumab will be present in human milk. However, published data suggest that breast milk antibodies do not enter the neonatal and infant circulation in substantial amounts. Exercise caution when administering eculizumab to a breast-feeding woman. Weigh the unknown risks to the infant from GI or limited systemic exposure to eculizumab against the known benefits of breast-feeding.
- **Pediatric Use:** Safety and effectiveness of Soliris® in pediatric patients have not been established.
- **Geriatric Use:** No apparent age-related differences have been observed, but further studies are needed to adequately assess safety.
- **Renal Impairment:** Studies have not been conducted to evaluate the pharmacokinetics of eculizumab in the presence of renal impairment.
- **Hepatic Functional Impairment:** Studies have not been conducted to evaluate the pharmacokinetics of eculizumab in the presence of hepatic impairment.

WARNINGS AND PRECAUTIONS:

Soliris is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) and prescribers must enroll in the program.

- **Serious meningococcal infections:**
    - The use of eculizumab increases a patient's susceptibility to serious meningococcal infections (septicemia and/or meningitis). All patients without a history of prior meningococcal vaccination must receive the meningococcal vaccine at least 2 weeks prior to receiving the first dose of eculizumab and be revaccinated according to current medical guidelines for vaccine use. Quadravalent, conjugated meningococcal vaccines are strongly recommended. Vaccination may not prevent meningococcal infections.
    - Monitor all patients for early signs and symptoms of meningococcal infections, and immediately evaluate if an infection is suspected. Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early. Strongly consider discontinuation of eculizumab during the treatment of serious meningococcal infections.
- **Other infections:** Eculizumab blocks terminal complement; therefore, patients may have increased susceptibility to infections, especially with encapsulated bacteria. Use caution when administering eculizumab to patients with any systemic infection.
- **Discontinuation of therapy:**
    - Because eculizumab therapy increases the number of PNH cells, patients who discontinue treatment with eculizumab may be at increased risk for serious hemolysis. Serious hemolysis is identified by serum lactate dehydrogenase (LDH)

levels greater than the pretreatment level, along with any of the following: more than 25% absolute decrease in PNH clone size (in the absence of dilution due to transfusion) in 1 week or less, a hemoglobin level of less than 5 g/dL or a decrease of more than 4 g/dL in 1 week or less, angina, change in mental status, a 50% increase in serum creatinine level, or thrombosis.
    - If serious hemolysis occurs after eculizumab discontinuation, consider the following procedures/treatments: blood transfusion (packed RBCs) or exchange transfusion if the PNH RBCs are greater than 50% of the total RBCs by flow cytometry, anticoagulation, corticosteroids, or reinstitution of eculizumab.
- **Thrombosis prevention and management:** The effect of withdrawal of anticoagulant therapy during eculizumab treatment has not been established. Therefore, treatment with eculizumab should not alter anticoagulant management.
- **Infusion reactions:**
    - As with all protein products, administration of eculizumab may result in infusion reactions, including anaphylaxis or other hypersensitivity reactions.
    - No reports demonstrate patients with PNH experienced an infusion reaction that required discontinuation of eculizumab.
    - Interrupt eculizumab administration in all patients experiencing severe infusion reactions and administer appropriate medical therapy.
- **Immunogenicity:**
    - As with all proteins, there is a potential for immunogenicity. Low titers of antibodies to eculizumab were detected in 2% of all patients with PNH treated with eculizumab. No apparent correlation of antibody development to clinical response was observed.
    - The immunogenicity data reflect the percentage of patients whose test results were considered positive for antibodies to eculizumab in an enzyme-linked immunosorbent assay and are highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody positivity in the assay may be influenced by several factors, including sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to eculizumab with the incidence of antibodies to other products may be misleading.
- **Carcinogenesis:** Long-term have not been conducted to evaluate the carcinogenic potential of eculizumab.
- **Mutagenesis:** Long-term have not been conducted to evaluate the genotoxic potential of eculizumab.
- **Fertility impairment:** Effects of eculizumab on fertility have not been studied.

ADVERSE REACTIONS: (≥10% and at least 2 times the rate of placebo)

- back pain
- fatigue

DRUG INTERACTIONS:

- None well documented.

PATIENT COUNSELING INFORMATION:

- Prior to treatment, ensure that patients fully understand the risks and benefits of eculizumab, particularly the risk of meningococcal infection.
- Ensure that patients receive the Medication Guide.
- Inform patients that they are required to receive a meningococcal vaccination at least 2 weeks prior to receiving the first dose of eculizumab if they have not previously been vaccinated. They are required to be revaccinated according to current medical guidelines for

meningococcal vaccine use while on eculizumab therapy. Inform patients that vaccination may not prevent meningococcal infection.

- Educate patients about any of the signs and symptoms of meningococcal infection, and strongly advise them to seek immediate medical attention if the following signs or symptoms occur: moderate to severe headache with nausea or vomiting, moderate to severe headache and a fever, moderate to severe headache with a stiff neck or stiff back, fever of 103°F (39.4°C) or higher, fever and a rash, confusion, severe muscle aches with flu-like symptoms, and eyes sensitive to light.
- Inform patients that they should be provided with the Patient Safety Card that they should carry with them at all times. This card describes symptoms that, if experienced, should prompt the patient to immediately seek medical evaluation.
- Inform patients that there is a potential for serious hemolysis when eculizumab is discontinued and that they will be monitored by their health care provider for at least 8 weeks following eculizumab discontinuation.

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[i] http://ghr.nlm.nih.gov/condition/paroxysmal-nocturnal-hemoglobinuria

[ii] http://emedicine.medscape.com/article/207468-treatment

[iii] Kelly RJ, Hill A, Arnold LM, et al. Long-term treatment with eculizumab in paroxysmal nocturnal hemoglobinuria: sustained efficacy and improved survival. *Blood*. Jun 23 2011;117(25):6786-92

[iv] http://ghr.nlm.nih.gov/condition/atypical-hemolytic-uremic-syndrome

[v] http://emedicine.medscape.com/article/1183555-treatment

[vi] Drug Facts and Comparisons. Wolters Kluwer Health Inc. Available Online at: http://online.factsandcomparisons.com/MonoDisp.aspx?monoID=fandc-hcp14978&quick=678864%7c5&search=678864%7c5&isstemmed=True#firstMatch. Last revised August 2010

Appendix G

30 Day Notice to Prior Authorize Onfi™ (Clobazam)

Oklahoma Health Care Authority
January 2012

Manufacturer	Catalent Pharmaceuticals for Lundbeck, Inc.
Classification	Benzodiazepine Anti-epileptic
Status	Prescription Only, C-IV

Summary

Onfi™ (clobazam) is a benzodiazpine anti-epileptic medication indicated for adjunctive treatment of seizures associated with Lennox-Gastaut syndrome (LGS) in patients 2 years of age or older. The exact mechanism of action for clobazam, a 1,5-benzodiazepine, is not fully understood but is thought to involve potentiation of GABA neurotransmission resulting from binding at the benzodiazepine site of the GABA receptor.

The effectiveness of Onfi™ (clobazam) for the adjunctive treatment of seizures associated with Lennox-Gastaut syndrome was established in two multicenter controlled studies. The first study was a randomized, double-blind, placebo-controlled study consisting of a 4-week baseline period followed by a 3-week titration period and 12- week maintenance period involving 238 patients. The primary efficacy measure was the percent reduction in the weekly frequency of drop seizures (atonic, tonic, or myoclonic), also known as drop attacks, from the 4-week baseline period to 12-week maintenance period between the placebo, low, medium, and high dose groups. All dose groups of Onfi™ (clobazam) were statistically superior to the placebo group in mean percent reduction of seizure rates. This effect appeared to be dose dependent with a mean percent reduction of 41.2% in the low dose group and up to 68.3% in the high dose group. The second study was a randomized, double-blind comparison study of high (20mg-40mg per day) vs. low dose (5mg-10mg per day) of Onfi™ (clobazam), consisting of a 4-week baseline period followed by a 3-week titration period and 4-week maintenance period in 68 patients. The primary efficacy measure was the percent reduction in the weekly frequency of drop seizures from the 4-week baseline period to the 4-week maintenance period. A statistically significantly greater reduction in seizure frequency was observed in the high-dose group compared to the low-dose group (median percent reduction of 93% vs 29%). In both trials Onfi™ (clobazam) was added to the patient's existing anti-epileptic therapy.

As a benzodiazepine, Onfi™ (clobazam) has warnings and precautions similar to other benzodiazepines. The estimated acquisition costs of Onfi™ (clobazam) tabs are $3.30 per 5mg tab, $6.60 per 10mg tab, and $13.20 per 20mg tab. At BID dosing, Onfi™ (clobazam) therapy can range from $200 to $800 per 30 days.

Recommendations

The College of Pharmacy recommends prior authorization of Onfi™ (clobazam) with the following approval criteria:

1. Diagnosis of Lennox-Gastaut syndrome; **and**
2. Failure of or concomitant use of at least one anti-epileptic medication.

PRODUCT DETAILS OF ONFI™ (CLOBAZAM)[1]

INDICATIONS: Onfi™ is indicated for adjunctive treatment of seizures associated with Lennox-Gastaut syndrome (LGS) in patients 2 years of age or older.

DOSAGE FORMS: 5mg, 10mg, and 20mg Tablets.

ADMINISTRATION:

- Patients ≤30 kg body weight: initiate therapy at 5 mg daily and titrate as tolerated up to 20 mg daily.
- Patients >30 kg body weight: initiate therapy at 10 mg daily and titrate as tolerated up to 40 mg daily.
- Doses above 5 mg/day should be administered in two divided doses.
- ONFI tablets can be administered whole, or crushed and mixed in applesauce.
- Reduce dose, or discontinue drug, gradually.
- Dosage adjustment needed in the following groups:
    - Geriatric patients – start with 5mg and titrated to 20mg per day, or 40mg if necessary based on clinical response.
    - Known CYP2C19 poor metabolizers – start with 5mg and titrated to 20mg per day, or 40mg if necessary based on clinical response.
    - Mild or moderate hepatic impairment – start with 5mg and titrated to 20mg per day, or 40mg if necessary based on clinical response.

CONTRAINDICATIONS: None listed.

SPECIAL POPULATIONS:

- **Pregnancy Category C.**
- **Pediatric Use:** Safety and effectiveness in patients <2 years of age have not been established.

WARNINGS & PRECAUTIONS:

- **Somnolence or Sedation**: Monitor for central nervous system (CNS) depression. Risk may be increased with concomitant use of other CNS depressants.
- **Withdrawal**: Symptoms may occur with rapid dose reduction or discontinuation. Discontinue Onfi™ gradually.
- **Physical and psychological dependence**: Patients with a history of substance abuse should be monitored for signs of habituation and dependence.
- **Suicidal behavior and ideation**: Monitor for suicidal thoughts or behaviors.

ADVERSE REACTIONS: (Adverse reactions that occurred in at least 5% of patients)

- somnolence or sedation
- drooling
- constipation
- cough
- urinary tract infection
- aggression
- insomnia
- dysarthria
- fatigue

DRUG INTERACTIONS:

- Lower doses of some drugs metabolized by CYP2D6 may be required when used concomitantly with Onfi™.

- Onfi™ is a weak CYP3A4 inducer. Some hormonal contraceptives are metabolized by CYP3A4, their effectiveness may be diminished when given with Onfi™. Additional nonhormonal forms of contraception are recommended when using Onfi™.
- Dosage adjustment of Onfi™ may be necessary when coadministered with strong or moderate CYP2C19 inhibitors such as fluconazole, fluvoxamine, ticlopidine, or omeprazole.
- Alcohol increases the blood levels of clobazam by approximately 50%.

PATIENT INFORMATION:

Somnolence or Sedation

Advise patients or caregivers to check with their healthcare provider before Onfi™ is taken with other CNS depressants such as other benzodiazepines, opioids, tricyclic antidepressants, sedating antihistamines, or alcohol. If applicable, caution patients about operating hazardous machinery, including automobiles, until they are reasonably certain that ONFI does not affect them adversely (e.g., impair judgment, thinking or motor skills).

Increasing or Decreasing the ONFI Dose

Inform patients or caregivers to consult their healthcare provider before increasing the Onfi™ dose or abruptly discontinuing Onfi™. Advise patients or caregivers that abrupt withdrawal of anti-epileptic medications may increase their risk of seizure.

Interactions with Hormonal Contraceptives

Counsel women to use non-hormonal methods of contraception when Onfi™ is used with hormonal contraceptives, and to continue these alternative methods for 28 days after discontinuing Onfi™ to ensure contraceptive reliability.

Suicidal Thinking and Behavior

Counsel patients, their caregivers, and their families that AEDs, including ONFI, may increase the risk of suicidal thoughts and behavior and advise them of the need to be alert for the emergence or worsening of symptoms of depression, any unusual changes in mood or behavior, or the emergence of suicidal thoughts, behavior, or thoughts of self-harm. Patients should report behaviors of concern immediately to healthcare providers.

Use in Pregnancy

Instruct patients to notify their healthcare provider if they become pregnant or intend to become pregnant during therapy. Encourage patients to enroll in the NAAED Pregnancy Registry if they become pregnant. This registry is collecting information about the safety of antiepileptic drugs during pregnancy. To enroll, patients can call the toll free number 1-888-233- 2334. Information on the registry can also be found at the website http://www.aedpregnancyregistry.org

Use in Nursing

Instruct patients to notify their physician if they are breast feeding or intend to breastfeed during therapy.

[1] Onfi Product Information. Catalent Pharmaceuticals for Lundbeck Inc. Accessed online at: http://www.lundbeck.com/upload/us/files/pdf/Products/Onfi_PI_US_EN.pdf. Last revised October 2011.

Appendix H

FISCAL YEAR 2011 ANNUAL REVIEW OF MISCELLANEOUS RIBAVIRIN PRODUCTS

OKLAHOMA HEALTH CARE AUTHORITY
JANUARY 2012

CURRENT PRIOR AUTHORIZATION CRITERIA

Prior authorization of ribavirin tablets (higher strengths only), suspension and dose packs is based on clinical supporting information regarding the inability of member to swallow, medical reasons why member cannot take lower strength tablet, or for use in children 3 to 10 years of age (suspension only).

UTILIZATION OF RIBAVIRIN PRODUCTS

Fiscal Year Comparison

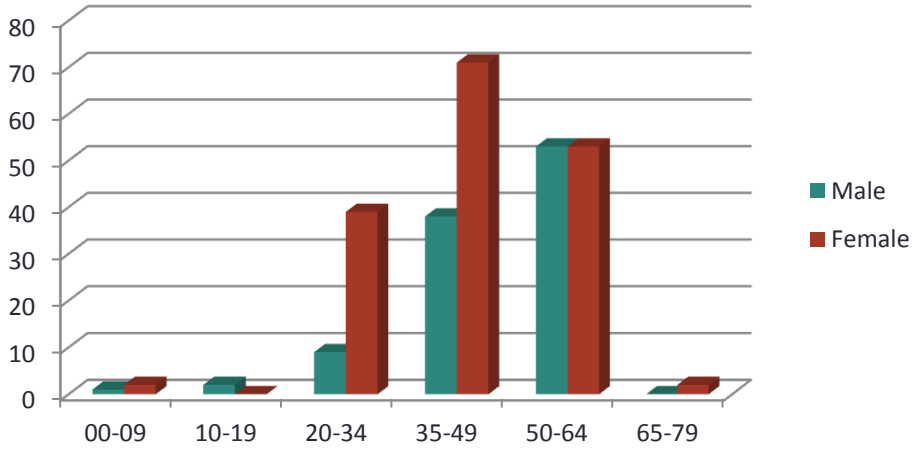
Fiscal Year	Members	Claims	Paid	Paid/Claim	Perdiem	Units	Days
2010	282	1,181	$548,808.64	464.70	16.23	153,205	33,821
2011	270	1,088	$183,164.02	168.35	5.82	166,801	31,457
% Change	**-4.30%**	**-7.90%**	**-66.60%**	**-63.80%**	**-64.10%**	**8.90%**	**-7.00%**
Change	**-12**	**-93**	**-$365,644.62**	**-296.35**	**-10.41**	**13,596**	**-2,364**

Utilization Details

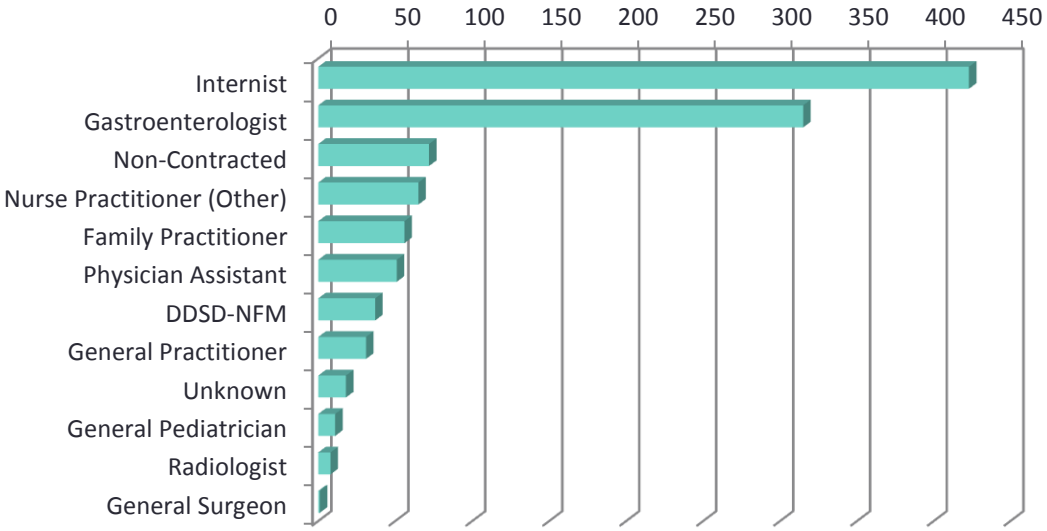
BRAND NAME	CLAIMS	MEMBERS	COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ DAY	% COST
Ribasphere Cap 200mg	456	104	$80,987.20	5.28	4.38	$6.20	44.22%
Ribavirin Cap 200mg	323	91	$58,302.01	5.34	3.55	$6.16	31.83%
Ribavirin tab 200mg	242	67	$28,964.15	4.99	3.61	$4.12	15.81%
Ribasphere tab 200mg	57	19	$6,921.72	5.23	3	$4.34	3.78%
Rebetol soln 40MG/ML	10	3	$7,988.94	12.4	3.33	$25.52	4.36%
	1,088	**270***	**$183,164.02**	**5.3**	**4.03**	**$5.82**	**100%**

*Unduplicated members

Demographics of Members during FY 2011

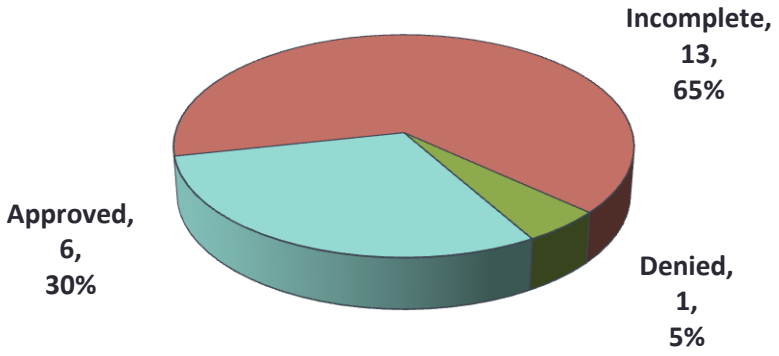


Top Prescribers by Number of Claims for FY 2011



PRIOR AUTHORIZATION OF RIBAVIRIN PRODUCTS

There were a total of 20 petitions submitted for this category during fiscal year 2011. The following chart shows the status of the submitted petitions.



MARKET NEWS AND UPDATE

Anticipated Patent Expirations

- **Rebetol® (ribavirin capsule & solution)** – anticipated to expire 2016.[1]
- **Copegus® (ribavirin tablet)** – exclusivity anticipated to expire 2014.[2]

In June 2010, the FDA issued warnings regarding pancytopenia and bone marrow suppression after administration of concomitant pegylated interferon/ribavirin and azathioprine. The myelotoxicity resolved upon withdrawal of these drugs and did not reoccur with either treatment alone.

In December 2010, the FDA issued a warning/precaution for chronic hepatitis C patients with cirrhosis who may be at risk of hepatic decompensation and death when treated with alpha interferons, including Pegasys®. Those patients co-infected with HIV who were receiving highly active antiretroviral therapy (HAART) and interferon alfa-2a with or without ribavirin appeared to be at increased risk for developing hepatic decompensation compared to patients not receiving HAART. Therefore Copegus® is contraindicated in patients co-infected with Hepatitis C and HIV.

RECOMMENDATIONS

The College of Pharmacy recommends no changes at this time.

[1] http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm

[2] http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm

Appendix I

Annual Review of Nasal Allergy Medications-Fiscal Year 2011

Oklahoma HealthCare Authority
January 2012

Current Prior Authorization Criteria

Criteria for approval:

1. The following criteria are required for approval of a Tier 2 product:
    a. Documented adverse effect or contraindication to the preferred products.
    b. Failure with all Tier 1 medications defined as no beneficial response after at least three weeks use of each during which time the drug has been titrated to the recommended dose.
2. The following criteria are required for approval of a Tier 3 product:
    a. All Tier 2 criteria must be met.
    b. Failure with all available Tier 2 products defined as no beneficial response after at least three weeks use of each during which time the drug has been titrated to the recommended dose.
3. Approvals will be for the duration of three months, except for members with chronic diseases such as asthma or COPD, in which case authorizations will be for the duration of one year.

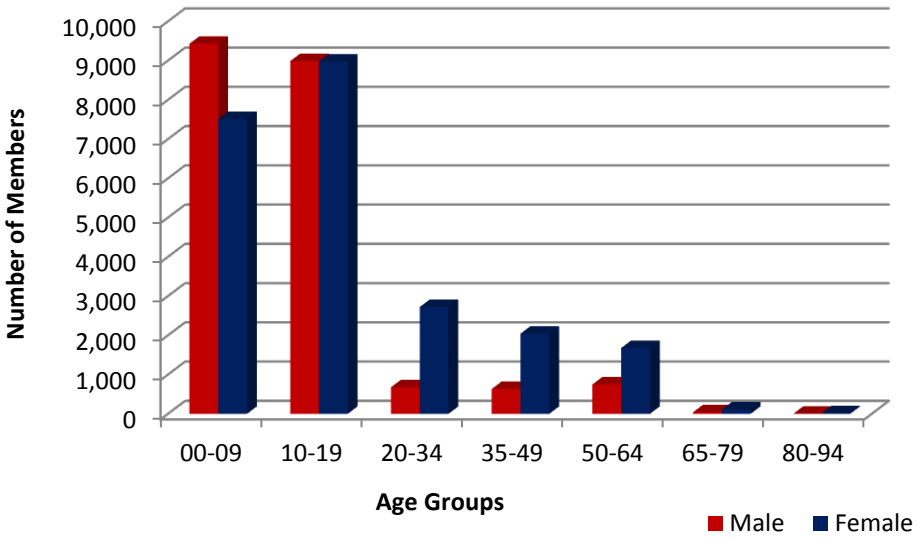
Nasal Allergy Products		
Tier 1	**Tier 2**	**Tier 3**
Fluticasone (Flonase®)	Mometasone (Nasonex®)	Ciclesonide (Omnaris™)
Flunisolide (Nasalide®, Nasarel™)	Beclomethasone (Beconase®AQ)	Budesonide (Rhinocort®AQ)
	Triamcinolone (Nasacort®AQ)	Fluticasone (Veramyst™)
	Olapatadine (Patanase®)	Azelastine (Astepro®)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

Utilization of Nasal Allergy Medications

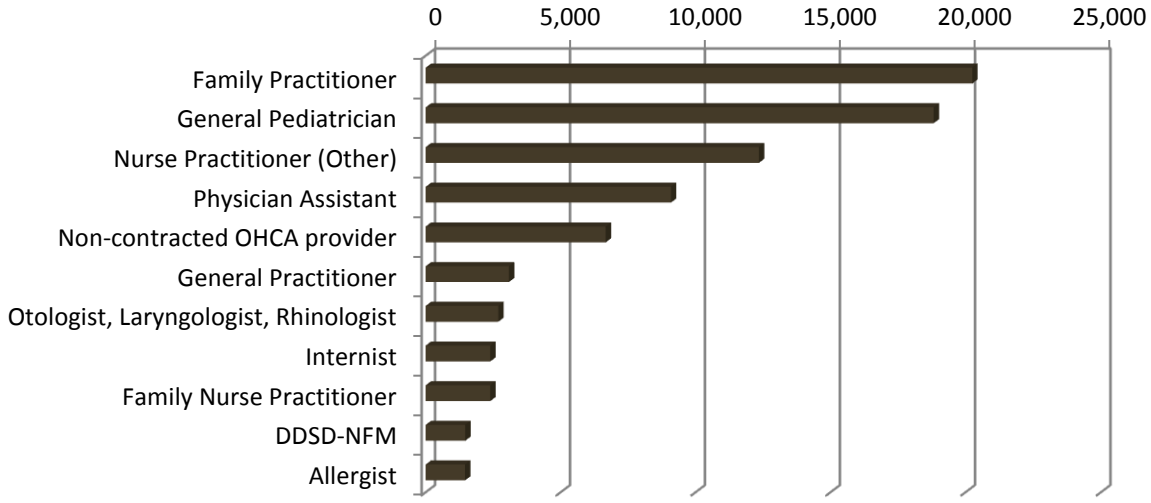
Comparison of Fiscal Years

Fiscal Year	Members	Claims	Cost	Cost/Claim	Perdiem	Units	Days
2010	41,040	72,282	$3,076,180.96	$42.56	$1.28	1,101,964	2,407,377
2011	43,587	84,945	$2,785,778.04	$32.80	$0.98	1,375,332	2,854,082
% Change	**6.20%**	**17.50%**	**-9.40%**	**-22.90%**	**-23.40%**	**24.80%**	**18.60%**
Change	**2,547**	**12,663**	**-$290,402.92**	**-$9.76**	**-$0.30**	**273,368**	**446,705**

Demographics of Members Utilizing Nasal Allergy Medications: FY 2011



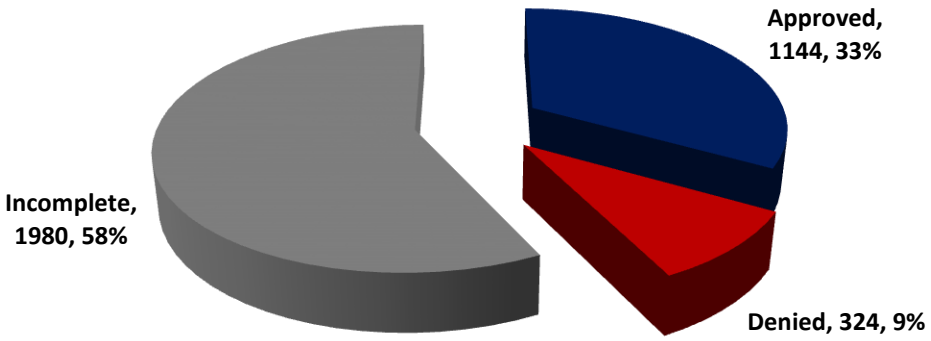
Top Prescribers of Nasal Allergy Medications by Number of Claims: FY 2011



Prior Authorization of Nasal Allergy Medications

There were a total of 3,448 petitions submitted for this PBPA category during fiscal year 2011. Please note that for this PBPA category the Point-of-Sale system will automatically search for Tier 1 medications in the member's claim history within a certain timeframe and if detected, the member can automatically get the Tier 2 medication without submitting a prior authorization form. The following chart shows the status of the submitted petitions:

Status of Petitions for Nasal Allergy Medications: FY 2011



Market News and Updates

New Generic Approvals:

- **Triamcinolone acetonide nasal spray (Nasacort® AQ)**
  - Entered the market 02/2011.
  - Cost is about $90 for a 30 day supply. In contrast, the cost of fluticasone nasal spray is about $20 for 30 days.

In the pipeline:

- Possible combination products such as fluticasone/azelastine.

Conclusion and Recommendations

The College of Pharmacy recommends moving triamcinolone acetonide nasal spray to Tier 1 when the price of the triamcinolone acetonide nasal spray is comparable to other Tier 1 medications.

Utilization Details of Nasal Allergy Medications: Fiscal Year 2011

BRAND NAME	CLAIMS	UNITS	DAYS	MEMBERS	COST	CLAIMS/ MEMBER	PER DIEM	% COST
FLUTICASONE SPR 50MCG	79,145	1,265,767	2,668,604	41,971	$2,344,870.63	1.89	$0.88	84.17%
FLUNISOLIDE SPR 0.025%	1,919	48,150	59,985	1,099	$62,971.23	1.75	$1.05	2.26%
VERAMYST SPR 27.5MCG	1,619	16,184	52,660	429	$158,941.45	3.77	$3.02	5.71%
NASACORT AQ AER 55MCG/AC	1,129	18,932	36,279	270	$123,678.51	4.18	$3.41	4.44%
NASONEX SPR 50MCG/AC	360	6,120	12,212	234	$39,100.63	1.54	$3.20	1.40%
FLUNISOLIDE SPR 29MCG	245	6,125	7,569	168	$5,392.64	1.46	$0.71	0.19%
PATANASE SPR 0.6%	185	5,560	5,732	62	$20,792.38	2.98	$3.63	0.75%
AZELASTINE SPR 0.1%	137	4,110	4,170	41	$12,686.71	3.34	$3.04	0.46%
ASTEPRO SPR 0.15%	62	1,860	2,240	23	$6,022.01	2.7	$2.69	0.22%
FLONASE SPR 0.05%	51	816	1,530	18	$999.79	2.83	$0.65	0.04%
RHINOCORT SUS AQUA	34	292	1,230	26	$3,542.44	1.31	$2.88	0.13%
BECONASE AQ SUS 0.042%	24	600	760	9	$3,393.16	2.67	$4.46	0.12%
ASTELIN NASA SPR 137MCG	20	600	600	11	$2,030.53	1.82	$3.38	0.07%
OMNARIS SPR	8	100	240	3	$576.22	2.67	$2.40	0.02%
TRIAMCINOLON SPR 55MCG/AC	7	116	271	7	$779.71	1	$2.88	0.03%
TOTALS:	**84,945**	**1,375,332**	**2,854,082**	**43,587***	**$2,785,778.04**	**1.95**	**$0.98**	**100.00%**

**Total unduplicated number of members*

Appendix J

U.S. Department of Health & Human Services

U.S. Food & Drug Administration

Drugs

FDA Drug Safety Communication: Safety review of post-market reports of serious bleeding events with the anticoagulant Pradaxa (dabigatran etexilate mesylate)

Safety Announcement

[12-7-2011] The U.S. Food and Drug Administration (FDA) is evaluating post-marketing reports of serious bleeding events in patients taking Pradaxa (dabigatran etexilate mesylate). Pradaxa is a blood thinning (anticoagulant) medication used to reduce the risk of stroke in patients with non-valvular atrial fibrillation (AF), the most common type of heart rhythm abnormality.

At this time, FDA continues to believe that Pradaxa provides an important health benefit when used as directed and recommends that healthcare professionals who prescribe Pradaxa follow the recommendations in the approved drug label (See Additional Information for Healthcare Professionals).

Patients with AF should not stop taking Pradaxa without talking to their healthcare professional. Stopping use of blood thinning medications can increase their risk of stroke. Strokes can lead to permanent disability and death.

Bleeding that may lead to serious or even fatal outcomes is a well-recognized complication of all anticoagulant therapies. The Pradaxa drug label contains a warning about significant and sometimes fatal bleeds. In a large clinical trial (18,000 patients) comparing Pradaxa and warfarin, major bleeding events occurred at similar rates with the two drugs.

Facts about Pradaxa (dabigatran etexilate mesylate)

- A blood thinner (anticoagulant) known as a direct thrombin inhibitor.
- Approved to reduce the risk of stroke and blood clots (systemic embolism) in patients with non-valvular atrial fibrillation.
- Available as 75 mg and 150 mg oral capsules.
- From approval in October 2010 through August 2011, a total of approximately 1.1 million Pradaxa prescriptions were dispensed and approximately 371,000 patients received Pradaxa prescriptions from U.S. outpatient retail pharmacies.[1]

FDA is working to determine whether the reports of bleeding in patients taking Pradaxa are occurring more commonly than would be expected, based on observations in the large clinical trial that supported the approval of Pradaxa. (See Data Summary). FDA is working closely with the manufacturer of Pradaxa (Boehringer Ingelheim) to evaluate the post-market reports of bleeding.

FDA will communicate any new information on the risk of bleeding and Pradaxa when it becomes available.

Additional Information for Patients

- Pradaxa is an anticoagulant medicine that reduces the risk of blood clots forming in your body and causing a stroke. Having a stroke can cause permanent disability and death.
- Do not stop taking Pradaxa without talking to your healthcare professional. Stopping use of your blood thinner suddenly can put you at risk of a stroke.
- Be aware that while taking Pradaxa you may bruise more easily and it may take longer for any bleeding to stop.
- Call your healthcare professional and seek immediate care if you develop any signs or symptoms of bleeding such a
    - unusual bleeding from the gums
    - nose bleeding that happens often
    - menstrual or vaginal bleeding that is heavier than normal
    - bleeding that is severe or you cannot control
    - pink or brown urine
    - red or black stools (looks like tar)
    - bruises that happen without a known cause or that get larger
    - coughing up blood or blood clots
    - vomiting blood or vomit that looks like coffee grounds.
- Discuss any questions or concerns about Pradaxa with your healthcare professional.
- Report any side effects you experience to your healthcare professional and the FDA MedWatch program using the information in the "Contact Us" box at the bottom of the page.

Additional Information for Healthcare Professionals

- If you prescribe Pradaxa, carefully follow the approved indication and other recommendations, such as dosage and administration, in the professional drug label.
- Make sure your patients know the signs and symptoms of bleeding and when to seek care.
- Pradaxa is eliminated by the kidneys, therefore:
  - Renal function should be assessed prior to treatment with Pradaxa to determine the appropriate dose.
  - Renal function should be reassessed during treatment with Pradaxa if clinically indicated (fluctuating renal function, diuretic use, hypovolemia), and the dose should be adjusted following recommendations in the label.
- There is no need for dosage adjustment in patients with mild to moderate renal impairment (creatinine clearance [CrCl] > 30 mL/min). These patients should be given a dose of Pradaxa 150 mg orally twice daily.
- For patients with severe renal impairment, follow the recommended doses:
  - For patients with CrCl 15-30 mL/min, the recommended dose is 75 mg orally twice daily.
  - Dosing recommendations for patients with a CrCl <15 mL/min or on dialysis cannot be provided.
- Report adverse events involving Pradaxa to the FDA MedWatch program, using the information in the "Contact Us" box at the bottom of the page.

Data Summary

Bleeding that may lead to serious or even fatal outcomes is a well-recognized complication of all anticoagulant therapies. In a large clinical trial (18,000 patients) comparing Pradaxa (dabigatran etexilate mesylate) and warfarin, major bleeding events occurred at similar rates with the two drugs. At present, the FDA is evaluating the post-marketing reports of serious bleeding in patients taking Pradaxa submitted to the Adverse Events Reporting System (AERS) database. While serious, even fatal events have been reported, the FDA is analyzing the events to determine whether the reports of bleeding in patients taking Pradaxa are occurring more commonly than would be expected, based on observations in the large clinical trial that supported the approval of Pradaxa.

Complicating this analysis, many factors can influence whether or not adverse effects are reported, particularly the length of time a drug has been marketed, whether or not the adverse effect is described in the drug label, and the amount of publicity about an event or safety concern.

For patients with non-valvular AF, the main alternative to Pradaxa is warfarin. Because warfarin has been marketed for over 50 years and is well-known to cause bleeding, patients and healthcare professionals are not likely to report bleeding in association with warfarin. Thus, a simple comparison between Pradaxa and warfarin with respect to the numbers of post-marketing reports of bleeding is of limited value.

FDA is working with the manufacturer, Boehringer Ingelheim, to analyze the post-market reports for evidence of inappropriate dosing, use of interacting drugs, or other clinical factors that might lead to a bleeding event.

FDA is also using its Mini-Sentinel active surveillance system to compare new users of Pradaxa and warfarin with respect to the likelihood of being hospitalized for bleeding.

At this time, FDA believes the benefits of Pradaxa continue to exceed the potential risks when the drug is used appropriately following the approved drug label. FDA recommends that healthcare professionals continue to prescribe Pradaxa following the recommendations in the drug label.

References
1. Source: SDI, Vector One: National (VONA) and Total Patient Tracker (TPT). October 2010 to August 2011. Extracted October 2011.

Related Information

- Information on Pradaxa (dabigatran etexilate mesylate)
- FDA Drug Safety Podcast for Healthcare Professionals: Safety review of post-market reports of serious bleeding events with the anticoagulant Pradaxa (dabigatran etexilate mesylate)
  12/8/2011

Contact FDA

1-800-332-1088
1-800-FDA-0178 Fax
Report a Serious Problem
MedWatch Online
Regular Mail: Use postage-paid FDA Form 3500
Mail to: MedWatch 5600 Fishers Lane
Rockville, MD 20857

U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
Ph. 1-888-INFO-FDA (1-888-463-6332)

U.S. Department of Health & Human Services

U.S. Food & Drug Administration

Safety

Liquid Acetaminophen marketed for infants: Drug Safety Communication - Potential for Dosing Errors

[Posted 12/22/2011]

AUDIENCE: Pediatrics, Consumers, Pharmacy

ISSUE: The FDA is informing the public that an additional concentration of liquid acetaminophen marketed for "infants "(160 mg/5 mL) is now available. This change in the concentration will affect the amount of liquid given to an infant, and should be especially noted if someone is accustomed to using the 80 mg /0.8 mL or 80 mg/mL concentrations of liquid acetaminophen.

BACKGROUND: Over-the-Counter (OTC) Liquid acetaminophen is used to temporarily reduce fever and relieve minor aches and pains due to the common cold, flu, headache, minor sore throat, and toothache. Acetaminophen is marketed under brand names such as Tylenol, Little Fevers, Triaminic, Infant/Pain Reliever, Pedia Care, Triaminic Infants 'Syrup Fever Reducer Pain Reliever and other store brands (e.g., Rite Aid, CVS, Walgreens brand, etc.).

This change in the concentration will affect the amount of liquid given to an infant, and should be especially noted if someone is accustomed to using the 80 mg /0.8 mL or 80 mg/mL concentrations of liquid acetaminophen. In addition to this change in concentration, this product may also be packaged with an oral syringe instead of a dropper.

RECOMMENDATION: Read the Drug Facts label on the package to identify the concentration of the liquid acetaminophen (in mg/mL), dosage, and directions for use.

Use the dosing device provided with the product in order to correctly measure the amount of liquid acetaminophen to be given. Healthcare professionals should provide directions to patients that specify the concentration and dose of liquid acetaminophen that should be given to a child.

Healthcare professionals and patients are encouraged to report adverse events or side effects related to the use of these products to the FDA's MedWatch Safety Information and Adverse Event Reporting Program:

- Complete and submit the report Online: www.fda.gov/MedWatch/report.htm
- Download form or call 1-800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178

[12/22/2011 - Drug Safety Communication - FDA]
[12/22/2011 - Consumer Update - FDA]
[12/22/2011 - Podcast - FDA]
[12/22/2011 - Questions and Answers - FDA]

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Safety

Gilenya (fingolimod): Drug Safety Communication - Safety Review of a Reported Death After the First Dose

[Posted 12/20/2011]

AUDIENCE: Neurology, Patients

ISSUE: The FDA has received a report of a patient with multiple sclerosis (MS) who died within 24 hours of taking the first dose of Gilenya (fingolimod). At this time, FDA cannot conclude whether the drug resulted in the patient's death. FDA is continuing to evaluate the case and will communicate any new information that results from this investigation.

BACKGROUND: Gilenya (fingolimod) is an oral medication for the treatment of relapsing forms of Multiple Sclerosis (MS) in adults. Gilenya is used to reduce the frequency of flare-ups (clinical exacerbations) and delay physical disability.

RECOMMENDATION: At this time, FDA continues to believe that Gilenya provides an important health benefit when used as directed and recommends that healthcare professionals who prescribe Gilenya follow the recommendations in the approved drug label. Patients with MS should not stop taking Gilenya without talking to their healthcare professional.

FDA will communicate any new information on Gilenya and this case when it becomes available.

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[12/20/2011 - Drug Safety Communication - FDA]

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Safety

Zocor (simvastatin): Label Change - New Restrictions, Contraindications, and Dose Limitations

Simvastatin sold under the brand-name Zocor, as a single-ingredient generic product, and sold in combination with ezetimibe as Vytorin and in combination with niacin as Simcor

[UPDATED 12/15/2011] FDA notified the public that it has revised the dose limitation for simvastatin from 10 mg to 20 mg when it is co-administered with the cardiac drug amiodarone. The simvastatin drug labels (Zocor and generics, Vytorin) have been updated to reflect this correction.

[Posted 06/08/2011]

AUDIENCE: Family Practice, Cardiology, Pharmacy

ISSUE: FDA notified healthcare professionals that it is recommending limiting the use of the highest approved dose of the cholesterol-lowering medication simvastatin (80 mg) because of increased risk of muscle damage. Patients taking simvastatin 80 mg daily have an increased risk of myopathy compared to patients taking lower doses of this drug or other drugs in the same class. This risk appears to be higher during the first year of treatment, is often the result of interactions with certain medicines, and is frequently associated with a genetic predisposition toward simvastatin-related myopathy. The most serious form of myopathy, called rhabdomyolysis, can damage the kidneys and lead to kidney failure which can be fatal. FDA is requiring changes to the simvastatin label to add new contraindications (should not be used with certain medications) and dose limitations for using simvastatin with certain medicines.

BACKGROUND: The new changes to the drug labels for simvastatin-containing medicines are based on FDA's review of the Study of the Effectiveness of Additional Reductions in Cholesterol and Homocysteine (SEARCH) trial and other data described in the Agency's March 2010 Ongoing safety review of high-dose Zocor (simvastatin) and increased risk of muscle injury. Simvastatin 80 mg should be used only in patients who have been taking this dose for 12 months or more without evidence of muscle injury (myopathy).

RECOMMENDATION: Simvastatin 80 mg should not be started in new patients, including patients already taking lower doses of the drug.

Healthcare professionals and patients are encouraged to report adverse events, side effects, or product quality problems related to the use of these products to the FDA's MedWatch Safety Information and Adverse Event Reporting Program:

- Complete and submit the report Online: www.fda.gov/MedWatch/report.htm
- Download form or call 1-800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178

[12/15/2011 - Drug Safety Communication - FDA
[06/08/2011 - Drug Safety Communication - FDA]
[06/08/2011 - News Release - FDA]
[06/08/2011 - Consumer Update - FDA

Previous MedWatch Alert

[03/19/2010]

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Stimulant Medications used in Children with Attention-Deficit/Hyperactivity Disorder - Communication about an Ongoing Safety Review

Products involved include: Focalin, Focalin XR (dexmethylphenidate HCl); Dexedrine, Dexedrine Spansules, Dextroamphetamine ER, Dextrostat (dextroamphetamine sulfate); Vyvanse (lisdexamfetamine dimesylate); Desoxyn (methamphetamine); Concerta, Daytrana, Metadate CD, Metadate ER, Methylin, Methylin ER, Ritalin, Ritalin-LA, Ritalin-SR (methylphenidate); Adderall, Adderall XR (mixed salts amphetamine); Cylert (pemoline) and generics.

[UPDATED 12/12/2011] A large, recently-completed study, that included one study that evaluated heart attacks and sudden deaths in a sample of adults, and a second study that assessed strokes in these adults, has not shown an increased risk of serious adverse cardiovascular events in adults treated with ADHD medications. Patients should continue to use their medicine for the treatment of ADHD as prescribed by their healthcare professional.

Stimulant products and atomoxetine should generally not be used in patients with serious heart problems, or for whom an increase in blood pressure or heart rate would be problematic. Patients treated with ADHD medications should be periodically monitored for changes in heart rate or blood pressure.

[UPDATED 11/01/2011] FDA notified the public that a large, recently-completed study in children and young adults treated with medication for Attention-Deficit/Hyperactivity Disorder (ADHD) has not shown an association between use of certain ADHD medications and adverse cardiovascular events. FDA continues to recommend that healthcare professionals prescribe these medications according to the professional prescribing label. See the Data Summary of the FDA Drug Safety Communication for more information.

Audience: Pediatricians, Neuropsychiatric healthcare professionals

[Posted 06/15/2009] FDA notified healthcare professionals that it is providing its perspective on study data published in the American Journal of Psychiatry on the potential risks of stimulant medications used to treat Attention-Deficit/Hyperactivity Disorder (ADHD) in children. This study, funded by the FDA and the National Institute of Mental Health (NIMH), compared the use of stimulant medications in 564 healthy children from across the United States who died suddenly to the use of stimulant medications in 564 children who died as passengers in a motor vehicle accident.The study authors concluded that there may be an association between the use of stimulant medications and sudden death in healthy children. Given the limitations of this study ś methodology, the FDA is unable to conclude that these data affect the overall risk and benefit profile of stimulant medications used to treat ADHD in children. FDA believes that this study should not serve as a basis for parents to stop a child ś stimulant medication. Parents should discuss concerns about the use of these medicines with the prescribing healthcare professional. Any child who develops cardiovascular symptoms (such as chest pain, shortness of breath or fainting) during stimulant medication treatment should immediately be seen by a doctor.

FDA is continuing its review of the strengths and limitations of this and other epidemiological studies that evaluate the risks of stimulant medications used to treat ADHD in children. FDA and the Agency for Healthcare Research and Quality are sponsoring a large epidemiological study that will provide further information about the potential risks associated with stimulant medication use in children. The data collection for this study will be complete later in 2009.

[11/01/2011 - Drug Safety Communication: Safety Review Update of Medications Used to Treat Attention-Deficit/Hyperactivity Disorder (ADHD) - FDA]

[06/15/2009 - Communication About An Ongoing Safety Review - FDA]
[06/15/2009 - News Release - FDA]
[06/15/2009 - Stimulant Medications Prescribing Information, Medication Guides - FDA]

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