Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
July 9, 2014
4 p.m.

Oklahoma Health Care Authority
4345 N. Lincoln Blvd.
Oklahoma City, OK 73105

THE UNIVERSITY OF OKLAHOMA COLLEGE OF PHARMACY

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

MEMORANDUM

TO: Drug Utilization Review Board Members

FROM: Bethany Holderread, Pharm.D.

SUBJECT: Packet Contents for Board Meeting – July 9, 2014

DATE: July 1, 2014

NOTE: The DUR Board will meet at 4:00 p.m. The meeting will be held at 4345 N Lincoln Blvd.

Enclosed are the following items related to the July meeting. Material is arranged in order of the Agenda.

Call to Order

Public Comment Forum

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

Update of Medication Coverage Authorization Unit/Opioid RetroDUR – See Appendix B

Action Item – Vote to Prior Authorize Esomeprazole Strontium and Aciphex® Sprinkle™ (Rabeprazole) – See Appendix C

Action Item – Vote to Prior Authorize Liptruzet™ (Ezetimibe/Atorvastatin) and Omtryg™ (Omega-3-Acid Ethyl Esters A) – See Appendix D

Action Item – Vote to Prior Authorize Zecuity® (Sumatriptan Iontophoretic Transdermal System) – See Appendix E

Action Item – Annual Review of Relistor® (Methylnaltrexone), Linzess® (Linaclotide), and Amitiza® (Lubiprostone) – See Appendix F

Annual Review of Anticoagulants and Platelet Aggregation Inhibitors and 30-Day Notice to Prior Authorize Zontivity™ (Vorapaxar) – See Appendix G

Annual Review of Opioid Analgesics and 30-Day Notice to Prior Authorize Zohydro™ ER (Hydrocodone Bitartrate) and Xartemis™ XR (Oxycodone/Acetaminophen) – See Appendix H

Action Item – Annual Review of Xolair® (Omalizumab) – See Appendix I

FDA and DEA Updates – See Appendix J

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board

(DUR Board)

Meeting – July 9, 2014 @ 4:00 p.m.

Oklahoma Health Care Authority
4345 N. Lincoln Blvd.
Oklahoma City, Oklahoma 73105

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. June 11, 2014 DUR Minutes – Vote

B. June 11, 2014 DUR Recommendations Memorandum

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

4. Update of Medication Coverage Authorization Unit/Opioid RetroDUR – See Appendix B

A. Medication Coverage Activity for June 2014

B. Pharmacy Help Desk Activity for June 2014

C. Opioid Prescriptions in Pregnant Women

D. Concomitant Benzodiazepine and Opioid Utilization

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

5. Action Item – Vote to Prior Authorize Esomeprazole Strontium and Aciphex® Sprinkle™ (Rabeprazole) – See Appendix C

A. COP Recommendations

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

6. Action Item – Vote to Prior Authorize Liptruzet™ (Ezetimibe/Atorvastatin) and Omtryg™ (Omega-3-Acid Ethyl Esters A) – See Appendix D

A. COP Recommendations

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

7. Action Item – Vote to Prior Authorize Zecuity® (Sumatriptan Iontophoretic Transdermal System) – See Appendix E

A. COP Recommendations

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

8. Action Item – Annual Review of Relistor® (Methylnaltrexone), Linzess® (Linaclotide), and Amitiza® (Lubiprostone) – See Appendix F

A. Current Authorization Criteria

B. Utilization of Relistor®, Linzess®, and Amitiza®
C. Prior Authorization
D. Market News and Updates
E. COP Recommendations
F. Utilization Details

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

9. Annual Review of Anticoagulants and Platelet Aggregation Inhibitors and 30-Day Notice to Prior Authorize Zontivity™ (Vorapaxar) – See Appendix G

A. Current Authorization Criteria
B. Utilization of Anticoagulants and Platelet Aggregation Inhibitors
C. Prior Authorization
D. Market News and Updates
E. Summary
F. COP Recommendations
G. Utilization Details
H. Product Details

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

10. Annual Review of Opioid Analgesics and 30-Day Notice to Prior Authorize Zohydro™ ER (Hydrocodone Bitartrate) and Xartemis™ XR (Oxycodone/Acetaminophen) – See Appendix H

A. Current Authorization Criteria
B. Utilization of Opioid Analgesics
C. Prior Authorization
D. Utilization Trend
E. Market News and Updates
F. Summary
G. COP Recommendations
H. Utilization Details

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

11. Action Item – Annual Review of Xolair® (Omalizumab) – See Appendix I

A. Introduction
B. Current Prior Authorization
C. Utilization of Xolair®
D. Prior Authorization
E. Summary
F. COP Recommendations

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

12. FDA and DEA Updates – See Appendix J

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

13. Future Business

A. Annual Reviews
B. New Product Reviews

Items to be presented by Dr. Muchmore, Chairman:

14. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF JUNE 11, 2014

BOARD MEMBERS:	PRESENT	ABSENT
Mark Feightner, Pharm.D.		x
Anetta Harrell, Pharm.D.	x	
John Muchmore, M.D., Ph.D.; Chairman	x	
James Osborne, Pharm. D	x	
Paul Louis Preslar, D.O., MBA	x	
James Rhymer, D.Ph.	x	
Bruna Varalli-Claypool, MHS, PA-C		x
Eric Winegardener, D.Ph.	x	

COLLEGE OF PHARMACY STAFF:	PRESENT	ABSENT
Terry Cothran, D.Ph.; Pharmacy Director	x	
Michyla Adams, Pharm.D.; Clinical Pharmacist	x	
Karen Egesdal, D.Ph.; SMAC-ProDUR Coordinator/OHCA Liaison	x	
Bethany Holderread, Pharm. D.; Clinical Coordinator	x	
Shellie Keast, Ph.D.; Assistant Professor	x	
Carol Moore, Pharm.D.; Clinical Pharmacist		x
Brandy Nawaz, Pharm.D.; Clinical Pharmacist	x	
Leslie Robinson, D.Ph.; PA Coordinator		x
Jennifer Sipols, Pharm.D.; Clinical Pharmacist		x
Ashley Teel, Pharm.D.; Clinical Pharmacist	x	
Melissa Anderson, Pharm.D.; Clinical Pharmacist	x	
Graduate Students: David George; Pharm. D.		x
Tammy Lambert; Pharm .D.	x	
Timothy Pham, Pharm. D.	x	
Visiting Pharmacy Student(s): N/A		

	PRESENT	ABSENT
Marlene Asmussen, R.N.; Population Care Management Director		x
Nico Gomez, Chief Executive Officer		x
Sylvia Lopez, M.D., FAAP; Chief Medical Officer	x	
Ed Long, Chief Communications Officer	x	
Kelli Brodersen, Marketing Coordinator	x	
Nancy Nesser, Pharm.D., J.D.; Pharmacy Director	x	
Rebecca Pasternik-Ikard, Deputy State Medicaid Director		x
Lynn Rambo-Jones, J.D.; Deputy General Counsel III	x	
Jill Ratterman, D.Ph.; Pharmacy Specialist	x	
Garth Splinter, M.D., M.B.A.; Medicaid Director	x	
Kerri Wade, Pharmacy Operations Manager		x

OTHERS PRESENT:		
Bruce Christian	Jim Chapman, Abbvie	David Williams, Forest
Melvin Nwamadi, Abbott	Kathleen Karnik, Janssen	Terry Green, Ok Transplant
Patrick Harvey, Walgreens	Russ Wilson, Johnson & Johnson	Bob Gustafson, Lundbeck
Brent Hildebrand, Gilead	Jim Dunlap, Pharma	Audrey Rattan, Otsuka
Jesse, BMS	Charlene Kaiser, Amgen	Jim Fowler, Astra Zeneca
Anthony DeLeon, BMS	Hayley Endicott, Gilead	Clint Degner, Novartis
Michele Puyear, Gilead	Kent Peterson, Merck	Melvin Nwamadi, Abbott

PRESENT FOR PUBLIC COMMENT:	
Michele Puyear	Gilead
Kathleen Karnik	Janssen

AGENDA ITEM NO. 1: **CALL TO ORDER**

1A: ROLL CALL

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 2: **INTRODUCTION OF NEW BOARD MEMBER**

Dr. Cothran introduced new board member.

ACTION: NONE REQUIRED

AGENDA ITEM NO. 3: **PUBLIC COMMENT FORUM**

MICHELE PUYEAR **AGENDA ITEM NO. 7**

KATHLEEN KARNIK **AGENDA ITEM NO. 7**

ACTION: NONE REQUIRED

AGENDA ITEM NO. 4: **APPROVAL OF DUR BOARD MINUTES**

4A: MAY 14, 2014 DUR MINUTES-VOTE

4B: MAY 14, 2014 DUR RECOMMENDATIONS MEMORANDUM

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 5: **UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/ FDA SAFETY ALERTS**

5A: MEDICATION COVERAGE ACTIVITY FOR MAY 2014

5B: PHARMACY HELP DESK ACTIVITY FOR MAY 2014

5C: FDA SAFETY ALERTS

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 6:</u> **UTILIZATION BREAKDOWN OF HYDROCODONE CONTAINING MEDICATIONS**

6A: UTILIZATION OF HYDROCODONE

6B: UTILIZATION DETAILS

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 7:</u> **VOTE TO PRIOR AUTHORIZE SOVALDI™ (SOFOSBUVIR), OLYSIO™ (SIMEPREVIR), VICTRELIS® (BOCEPREVIR), AND INCIVEK® (TELAPREVIR)**

7A: COP RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Holderread

Dr. Muchmore endorsed changes and consent draft forms which includes consent to treat, pharmacy agreement and Olysio™ and Sovaldi™ PA form. Dr. Muchmore approved Olysio™ as indicated by FDA approval. Dr. Muchmore recommends "*Hep A or B must have been started; member must not be pregnant, those who are continuing treatment on Victrelis®, be grandfathered."*

Dr. Harrell recommends "*Member not willing to comply with parameters of contract will be denied."*

Dr. Preslar recommends *"Three days of non-compliance"*

Dr. Winegardener moved to approve; seconded by Dr. Preslar

ACTION: MOTION CARRIED

<u>AGENDA ITEM NO. 8:</u> **VOTE TO PRIOR AUTHORIZE TROKENDI XR™ (TOPIRAMATE ER), APTIOM® (ESLICARBAZEPINE ACETATE), QUDEXY™ XR (TOPIRAMATE ER), AND GENERIC DIVALPROEX ER**

8A: COP RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Adams

Dr. Harrell moved to approve; seconded by Dr. Rhymer.

ACTION: MOTION CARRIED

<u>AGENDA ITEM NO. 9:</u> **ANNUAL REVIEW OF TRIPTAN ANTI-MIGRAINE MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ZECUITY® (SUMATRIPTAN IONTOPHORETIC TRANSDERMAL SYSTEM)**

9A: CURRENT AUTHORIZATION CRITERIA

9B: UTILIZATION OF TRIPTAN ANTI-MIGRAINE MEDICATIONS

9C: PRIOR AUTHORIZATION

9D MARKET NEWS AND UPDATES

9E: SUMMARY

9F: COP RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Adams

ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 10:</u> **ANNUAL REVIEW OF ANTI-ULCER MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ESOMEPRAZOLE STRONTIUM AND ACIPHEX® SPRINKLE™ (RABEPRAZOLE)**

10A: CURRENT AUTHORIZATION CRITERIA

10B: UTILIZATION OF ANTI-ULCER MEDICATIONS

10C: PRIOR AUTHORIZATION

10D: MARKET NEWS AND UPDATES

10E: SUMMARY

10F: COP RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Teel

ACTION: NONE REQUIRED

AGENDA ITEM NO. 11: **ANNUAL REVIEW OF ANTIHYPERLIPIDEMICS AND 30-DAY NOTICE TO PRIOR AUTHORIZE LIPTRUZET™ (EZETIMIBE/ATORVASTATIN) AND OMTRYG™ (OMEGA-3-ACID ETHYL ESTERS A)**

11A: CURRENT AUTHORIZATION CRITERIA
11B: UTILIZATION OF ANTIHYPERLIPIDEMIC MEDICATIONS
11C: PRIOR AUTHORIZATION
11D: MARKET NEWS AND UPDATES
11E: SUMMARY
11F: DISCUSSION
11G: COP RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nawaz

ACTION: NONE REQUIRED

AGENDA ITEM NO. 12: **FDA AND DEA UPDATES**

Materials included in agenda packet; presented by Dr. Cothran

ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: **FUTURE BUSINESS**

13A: ANNUAL REVIEWS
13B: NEW PRODUCT REVIEWS

Materials included in agenda packet; submitted by Dr. Cothran

ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: **ADJOURNMENT**

The meeting was adjourned at 5:09 pm.

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

Memorandum

Date: June 12, 2014

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

From: Bethany Holderread, Pharm.D.
Clinical Pharmacist
Pharmacy Management Consultants

Subject: DUR Board Recommendations From Meeting of June 11, 2014

Recommendation 1: Vote to Prior Authorize Sovaldi™ (Sofosbuvir), Olysio™ (Simeprevir), Victrelis® (Boceprevir), and Incivek® (Telaprevir)

MOTION CARRIED by unanimous approval.

The coverage of hepatitis C treatments will be updated as new medications, new indications, and clinical guidelines become available.

The College of Pharmacy recommends the prior authorization of Sovaldi™ (sofosbuvir), Olysio™ (simeprevir), Victrelis® (boceprevir), and Incivek® (telaprevir) with the following criteria:

Sovaldi™ (Sofosbuvir) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) with a METAVIR fibrosis score of F2 or greater; and
3. Sovaldi™ must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated by a gastroenterologist, infectious disease specialist, or transplant specialist within the last three months; and

4. Sovaldi™ must be used as a component of a combination regimen; and
5. Member must be eligible for ribavirin (RBV) therapy. Approvals will not be granted for regimens without RBV; and
6. Hepatitis C Virus (HCV) genotype testing must be confirmed and indicated on prior authorization request; and
7. The following regimens and requirements based on genotype will apply:
    a. Genotype 1:
        i. Triple therapy: Sovaldi™ + Pegylated Interferon (PEG-IFN) + RBV x 12 weeks
        ii. Members who are PEG-IFN ineligible may be approved for total treatment duration of 24 weeks with a patient-specific, clinically significant reason why member cannot use PEG-IFN.
    b. Genotype 2:
        i. Dual therapy: Sovaldi™ + RBV x 12 weeks
    c. Genotype 3:
        i. Dual therapy: Sovaldi™ + RBV x 24 weeks
    d. Genotype 4:
        i. Triple therapy: Sovaldi™ + PEG-IFN + RBV x 12 weeks
    e. Hepatocellular Carcinoma:
        i. Dual therapy: Sovaldi™ + RBV x 48 weeks or until time of liver transplant (whichever occurs first)
        ii. Approvals will only be granted for HCV infected members (regardless of genotype) with hepatocellular carcinoma meeting the MILAN criteria (MILAN criteria defined as presence of a tumor 5cm or less in diameter in patients with single hepatocellular carcinomas and not more than three tumor nodules, each 3cm or less in diameter in patients with multiple tumors and no extrahepatic manifestations of the cancer or evidence of vascular invasion of tumor).
    f. New regimens will apply as approved by the FDA
8. Member must sign the intent to treat contract; and
9. Member must have no illicit IV drug use or alcohol abuse in the last six months and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
10. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
11. Member must not have decompensated hepatic disease (Child Turcotte Pugh (CTP) class B or C); and
12. Female members must not be pregnant and must have a pregnancy test immediately prior to therapy initiation. Female partners of male patients should also be checked for pregnancy for informational purposes. Male and female members must be willing to use two forms of non-hormonal birth control while on therapy and for six months after therapy completion; and

13. Member must not be taking the following medications: rifampin, rifabutin, rifapentine, carbamazepine, phenytoin, oxcarbazepine, tipranavir/ritonavir, didanosine or St. John's wort; and
14. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight management, severe concurrent medical diseases, such as but not limited to, retinal disease or autoimmune thyroid disease.
15. Members must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy.

Olysio™ (Simeprevir) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) (genotype 1) with a METAVIR fibrosis score of F2 or greater; and
3. HCV genotype testing must be confirmed and indicated on prior authorization request; and
4. Members with genotype 1a must be screened for the NS3 Q80K polymorphism prior to initiation of therapy. Approvals will not be granted for members with this polymorphism; and
5. Olysio™ must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated by a gastroenterologist, infectious disease specialist, or transplant specialist within the last three months; and
6. As indicated by the FDA, Olysio™ must be used as a component of a combination regimen.
   a. Olysio™ will be approved for combination therapy only.
   b. Triple therapy: Olysio™ + RBV + PEG-IFN x 12 weeks
   c. After completion of Olysio™ therapy member must continue on RBV and PEG-IFN therapy for:
      i. an additional 12 weeks for treatment naïve patients and prior relapsers including those with cirrhosis
      ii. an additional 36 weeks for prior non-responder patients (including partial and null-responders), including those with cirrhosis
   d. New regimens will apply as approved by the FDA
7. Member must not have previously failed treatment with a hepatitis C protease inhibitor (non-responder or relapsed); and
8. Member must not have decompensated hepatic disease (Child Turcotte Pugh (CTP) class B or C); and
9. Member must sign the intent to treat contract; and
10. Member must have no illicit IV drug use or alcohol abuse in the last six months and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and

11. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
12. Female members must not be pregnant and must have a pregnancy test immediately prior to therapy initiation. Female partners of male patients should also be checked for pregnancy for informational purposes. Male and female members must be willing to use two forms of non-hormonal birth control while on therapy and for six months after therapy completion; and
13. Member must not be taking the following medications: efavirenz, delavirdine, etravirine, nevirapine, ritanovir and any HIV protease inhibitor (boosted or not by ritanovir), rifampin, rifabutin, rifapentine, erythromycin, clarithromycin, telithromycin, carbamazepine, oxcarbazepine, phenobarbital, phenytoin, itraconazole, ketoconazole, posaconazole, fluconazole, voriconazole, dexamethasone, cisapride, didanosine, milk thistle, or St. John's wort; and
14. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity weight management, severe concurrent medical diseases such as but not limited to retinal disease or autoimmune thyroid disease.
15. Members must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy.

Victrelis® (Boceprevir) and Incivek® (Telaprevir) Approval Criteria:

1. Use of Victrelis® or Incivek® requires a patient-specific, clinically significant reason why the member cannot use Olysio™ (simeprevir).
2. Those members currently receiving Victrelis® or Incivek® for the diagnosis of hepatitis C will be grandfathered for therapy completion.

Recommendation 2: Vote to Prior Authorize Trokendi XR™ (Topiramate ER), Aptiom® (Eslicarbazepine Acetate), Qudexy™ XR (Topiramate ER), and Generic Divalproex ER

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Trokendi XR™ (topiramate extended-release), Aptiom® (eslicarbazepine acetate), Qudexy™ XR (topiramate extended-release), and generic divalproex extended-release with the following criteria:

1. **Trokendi XR™ (Topiramate Extended-Release) Approval Criteria:**
    a. An FDA approved diagnosis of partial onset or primary generalized tonic-clonic seizures or as adjunctive therapy in seizures associated with Lennox-Gastaut syndrome; and

   b. A patient-specific, clinically significant reason why member cannot use the short-acting formulation, Topamax® (topiramate).
   c. A quantity limit of 30 per 30 days will apply on the lower strength capsules (25mg, 50mg, and 100mg) and 60 per 30 days on the higher strength capsules (200mg).
2. **Aptiom® (Eslicarbazepine Acetate) Approval Criteria:**
   a. An FDA approved diagnosis of partial-onset seizures as adjunctive therapy; and
   b. Member must be on current antiepileptic drug therapy (Aptiom® is only indicated for adjunctive treatment); and
   c. Member must not currently be taking oxcarbazepine (concurrent use is contraindicated); and
   d. A patient-specific, clinically significant reason why member cannot use oxcarbazepine.
   e. A quantity limit of 30 per 30 days will apply on the lower strength tablets (200mg and 400mg) and 60 per 30 days on the higher strength tablets (600mg and 800mg).
3. **Qudexy™ XR (Topiramate Extended-Release) Approval Criteria:**
   a. An FDA approved diagnosis of partial onset or primary generalized tonic-clonic seizures or as adjunctive therapy in seizures associated with Lennox-Gastaut syndrome; and
   b. A patient-specific, clinically significant reason why member cannot use the short-acting formulation, Topamax® (topiramate).
   c. A quantity limit of 30 per 30 days will apply on the lower strength capsules (25mg, 50mg, and 100mg) and 60 per 30 days on the higher strength capsules (150mg and 200mg).
4. **Divalproex Extended-Release Approval Criteria:**
   a. Generic divalproex ER will require a patient-specific, clinically significant reason why member cannot use brand name Depakote® ER.
   b. Brand name Depakote® ER will be the preferred product and will not require prior authorization.

Recommendation 3: Annual Review of Triptan Anti-Migraine Medications and 30-day Notice to Prior Authorize Zecuity® (Sumatriptan Iontophoretic Transdermal System)

NO ACTION REQUIRED.

Recommendation 4: Annual Review of Anti-Ulcer Medications and 30-Day Notice to Prior Authorize Esomeprazole Strontium and Aciphex® Sprinkle™ (Rabeprazole)

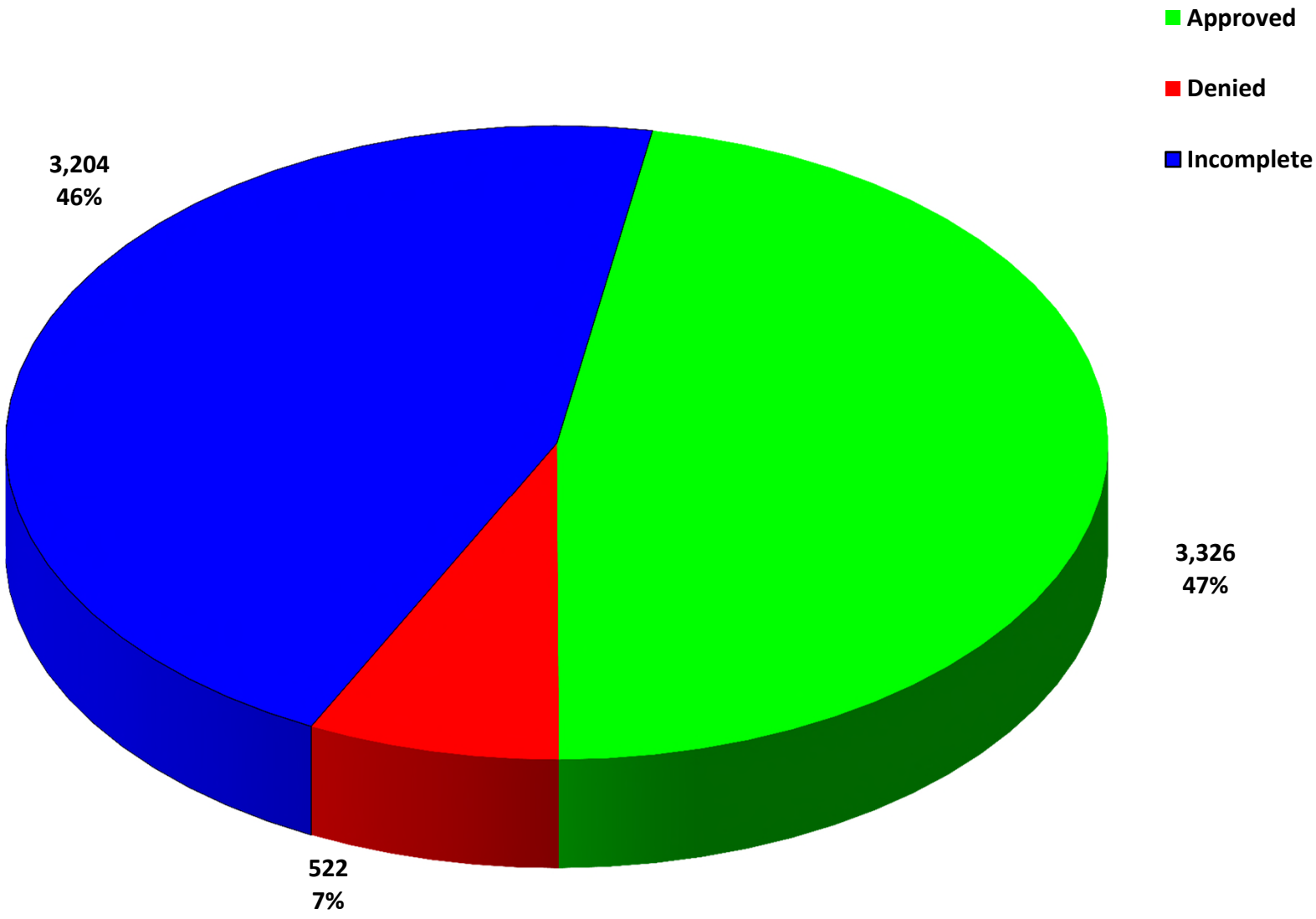
NO ACTION REQUIRED.

Recommendation 5: Annual Review of Antihyperlipidemics and 30-Day Notice to Prior Authorize Liptruzet™ (Ezetimibe/Atorvastatin) and Omtryg™ (Omega-3-Acid Ethyl Esters A)

NO ACTION REQUIRED.

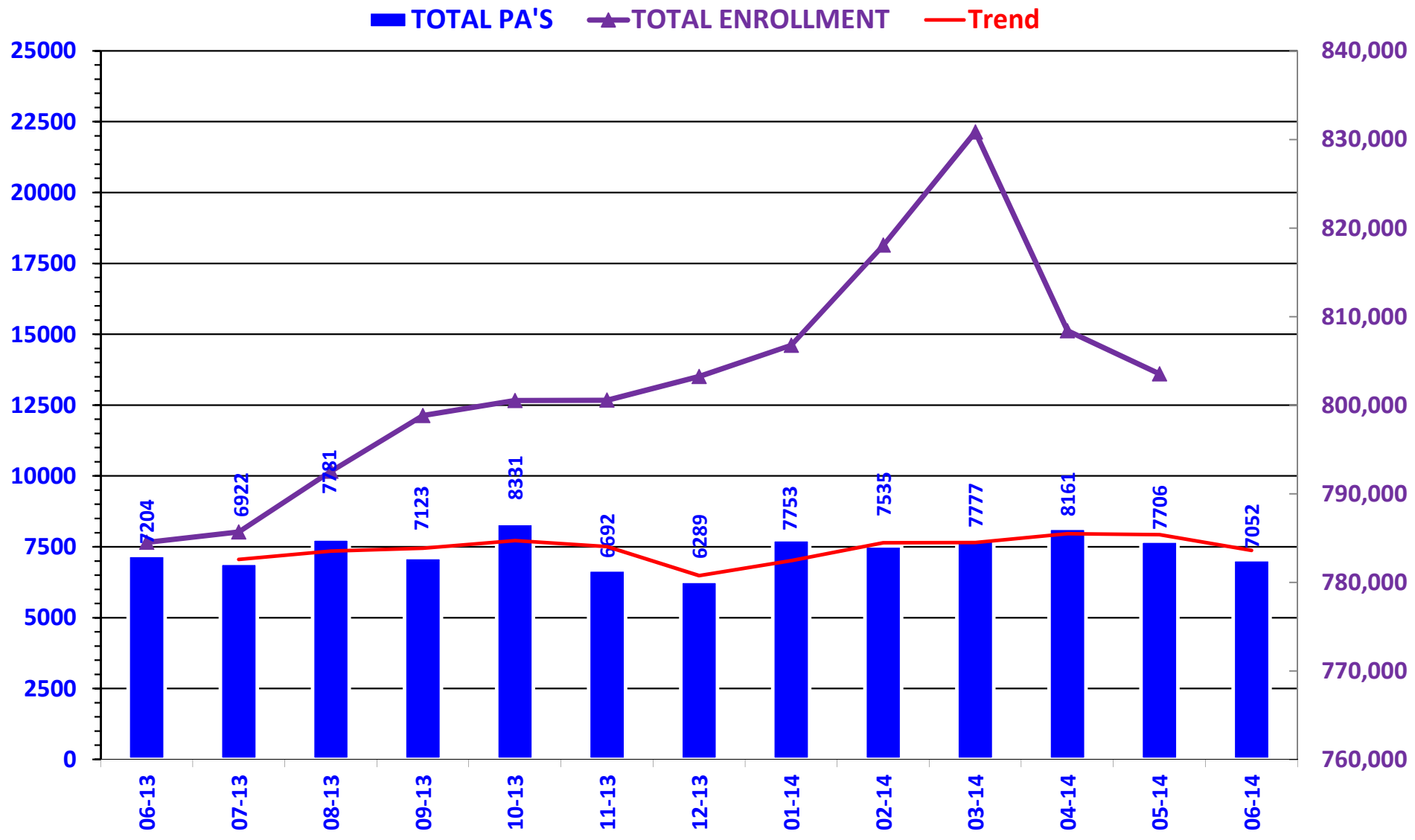
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: JUNE



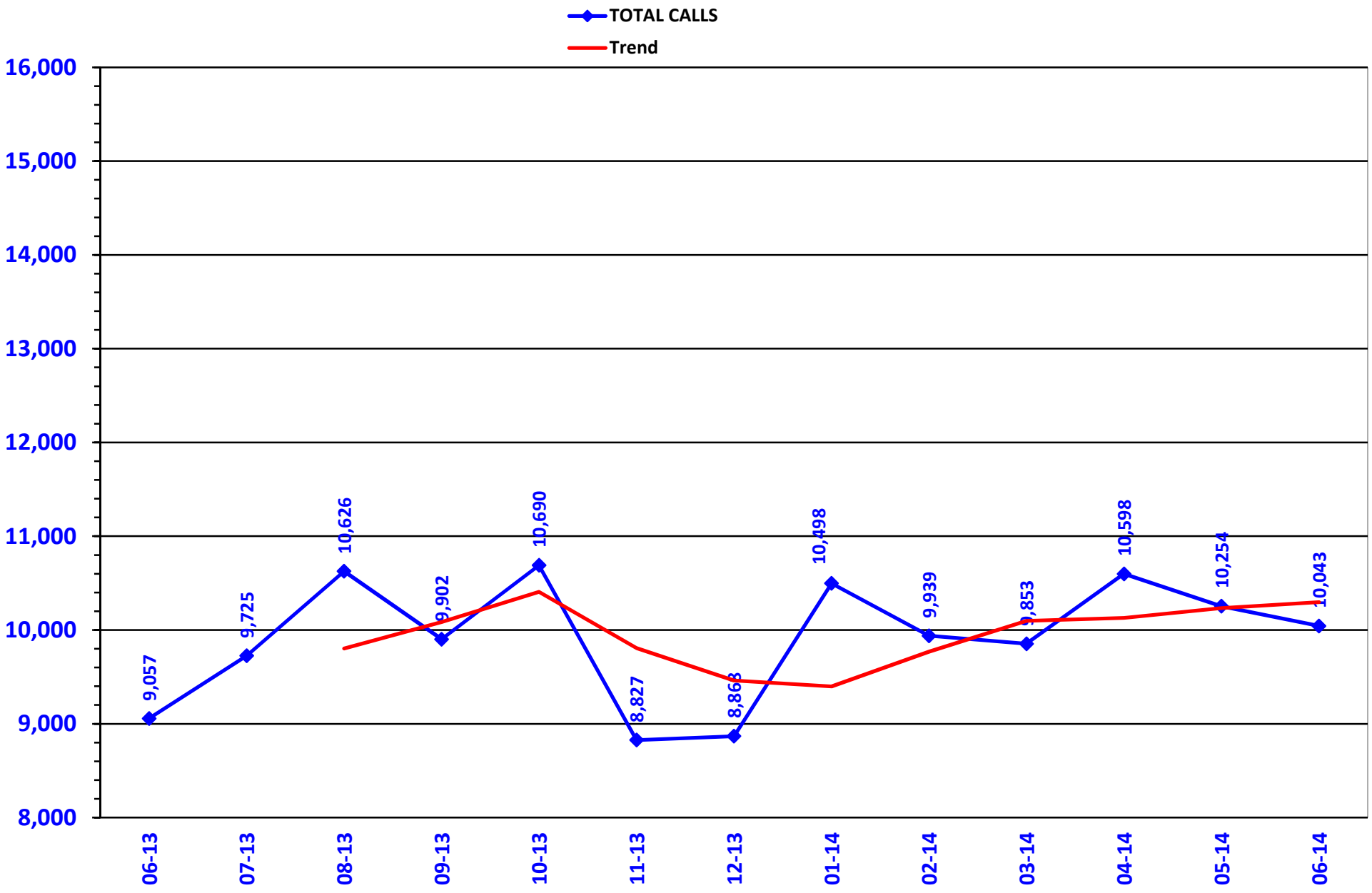
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: JUNE 2013- JUNE 2014



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
JUNE 2013 – JUNE 2014



Prior Authorization Activity
6/1/2014 Through 6/30/2014

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	298	139	3	156	347
Analgesic - NonNarcotic	12	1	1	10	178
Analgesic, Narcotic	494	252	25	217	180
Angiotensin Receptor Antagonist	29	6	1	22	358
Antiasthma	179	70	9	100	319
Antibiotic	42	13	2	27	218
Anticoagulant	111	70	4	37	252
Anticonvulsant	95	35	2	58	311
Antidepressant	241	53	17	171	331
Antidiabetic	128	56	2	70	352
Antifungal	14	4	3	7	36
Antihistamine	171	132	7	32	355
Antihyperlipidemic	13	3	0	10	359
Antimigraine	64	26	8	30	310
Antiplatelet	15	8	0	7	359
Antiulcers	183	48	32	103	183
Anxiolytic	84	50	7	27	215
Atypical Antipsychotics	332	171	9	152	342
Biologics	73	33	2	38	351
Bladder Control	69	9	10	50	241
Botox	21	15	4	2	336
Cardiovascular	34	19	0	15	244
Dermatological	108	14	49	45	107
Endocrine & Metabolic Drugs	53	34	2	17	126
Erythropoietin Stimulating Agents	43	24	0	19	115
Fibromyalgia	164	33	27	104	359
Gastrointestinal Agents	117	29	10	78	129
Growth Hormones	55	41	0	14	160
Hepatitis C	14	11	1	2	55
HFA Rescue Inhalers	60	15	8	37	295
Insomnia	44	4	4	36	178
Multiple Sclerosis	40	29	0	11	210
Muscle Relaxant	87	23	25	39	55
Nasal Allergy	102	9	21	72	203
Neurological Agents	63	44	2	17	237
Nsaids	187	22	18	147	278
Ocular Allergy	68	16	5	47	169
Ophthalmic Anti-infectives	31	3	3	25	6
Osteoporosis	23	9	2	12	358
Other*	165	27	23	115	223
Otic Antibiotic	40	3	1	36	6
Pediculicide	86	45	5	36	21
Prenatal Vitamins	14	0	0	14	0
Statins	67	22	3	42	344
Stimulant	739	322	17	400	342
Suboxone/Subutex	184	143	7	34	79
Testosterone	63	21	3	39	348
Topical Antibiotic	11	2	1	8	17
Topical Antifungal	58	2	7	49	11
Topical Corticosteroids	83	1	6	76	87
Vitamin	56	11	27	18	343
Pharmacotherapy	77	69	0	8	218
Emergency PAs	1	1	0	0	
Total	**5,605**	**2,242**	**425**	**2,938**	

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

Overrides					
Brand	42	25	4	13	244
Cumulative Early Refill	10	10	0	0	180
Dosage Change	393	361	5	27	9
High Dose	2	2	0	0	14
IHS-Brand	1	1	0	0	32
Ingredient Duplication	71	56	6	9	6
Lost/Broken Rx	70	68	1	1	7
NDC vs Age	14	14	0	0	181
Nursing Home Issue	164	132	25	7	7
Other*	29	22	3	4	5
Quantity vs. Days Supply	579	355	40	184	244
STBS/STBSM	18	16	0	2	58
Stolen	11	7	2	2	17
Temporary Unlock	16	11	4	1	17
Third Brand Request	35	12	7	16	21
Wrong D.S. on Previous Rx	2	2	0	0	4
Overrides Total	**1,447**	**1,084**	**97**	**266**	
Total Regular PAs + Overrides	**7,052**	**3,326**	**522**	**3,204**	

Denial Reasons	
Unable to verify required trials.	2,666
Does not meet established criteria.	520
Lack required information to process request.	503
Medication not covered as pharmacy benefit.	1

Other PA Activity	
Duplicate Requests	465
Letters	3,442
No Process	9
Changes to existing PAs	0
Helpdesk Initiated Prior Authorizations	854
PAs Missing Information	95

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

Opioid RetroDUR

Opioid Prescriptions in Pregnant Women

Oklahoma Health Care Authority
July 2014

Introduction[1,2,3,4]

A recent study published in the *Journal of Obstetrics & Gynecology* evaluated the use of prescription opioids in a large national cohort of Medicaid-insured pregnant women. The authors initiated the evaluation study over concerns of evidence that opioid analgesic use after the first trimester may be associated with neural tube defects. Authors cited additional alarm relating to the well-established risk of neonatal withdrawal syndrome after prolonged opioid exposure late in pregnancy.

The study population consisted of approximately 1.1 million women from 46 U.S. states and Washington, DC. Overall study results found approximately one in five Medicaid-enrolled pregnant women filled at least one prescription for an opioid at any time during their pregnancy between 2000 and 2007.

The majority of pregnant women receiving an opioid prescription had a diagnosis of abdominal pain (48.4%), lower back pain (33.0%), headache syndromes (13.3%), joint pain (11.2%), or migraine (7.9%) at some point during their pregnancy.

Among women filling any opioid prescription, the median cumulative days of opioid availability during pregnancy was 5 (3–13) days overall. The median number of prescriptions filled during pregnancy was one. The proportion of pregnant women potentially exposed to opioids chronically—defined as cumulative days of opioid availability greater than 30 during pregnancy—was 2.5%.

Codeine and hydrocodone accounted for the majority of the opioid prescriptions. Overall, 11.1% women filled prescriptions for codeine, 10.0% for hydrocodone, 2.9% for propoxyphene, and 2.2% for oxycodone at any time during pregnancy.

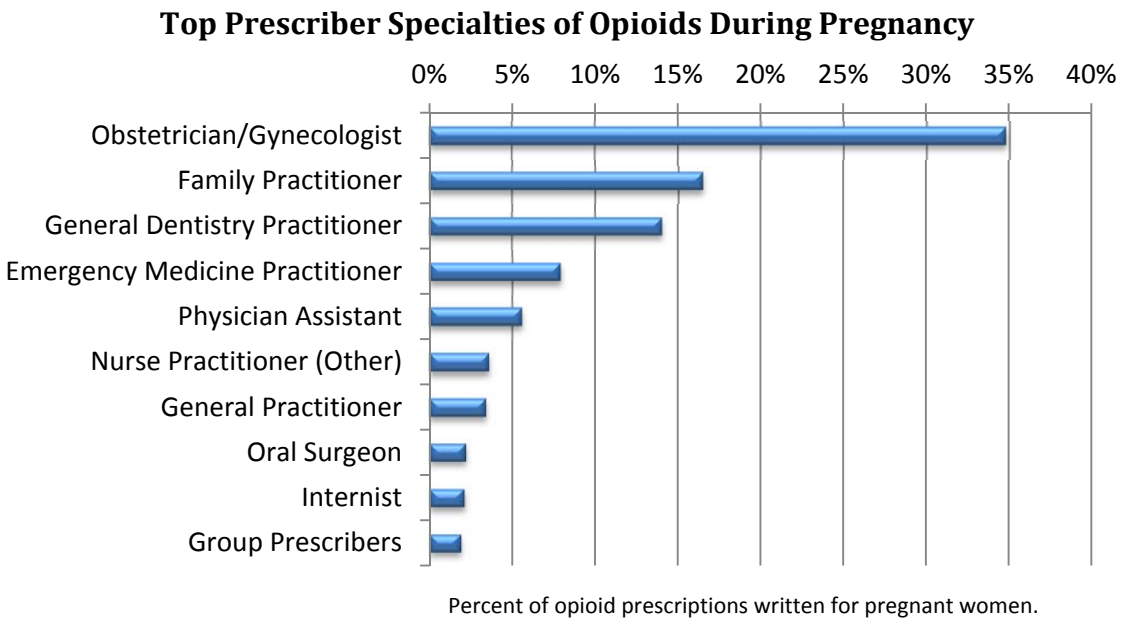
The proportion of women who filled an opioid prescription at any time during pregnancy gradually increased from 18.5% in 2000 to 22.8% in 2007 marking an increase of 23.1%. This time trend of increasing opioid prescription fills was also seen during each trimester separately.

SoonerCare Claims Review

Approximately 42,291 pregnant SoonerCare members were reviewed for opioid utilization during pregnancy. Members were eligible for inclusion in the review if they had more than two paid pharmacy claims for an opioid medication while listed as pregnant. The review was conducted over 12 a month period. Pregnancy was determined by pregnancy specific eligibility aid categories.

Pregnant Members with >2 Opioid Claims	Total Number of Opioid Claims for Pregnant Members with >2 Opioid Claims
3,969	18,606

Approximately 9.38% of pregnant members had more than two paid pharmacy claims for an opioid medication.



Despite attempting to limit the inclusion of opioid claims written post-delivery a portion of the claims included may have been for after delivery. If the parameters were modified to exclude opioid prescriptions written by a prescriber with an obstetrician/gynecologist specialty approximately 3,537 pregnant members were found to have more than 2 opioid claims for a total of 12,139 claims. Approximately 8.36% of pregnant members had more than two paid pharmacy claims for an opioid medication not written by a prescriber with an obstetrician/gynecologist specialty.

Opioid Utilization Details

The following table includes the most common opioid medication used during pregnancy by SoonerCare members.

Most Common Opioid Medications Used in Pregnancy	
Drug Name	**Percent of All Opioid Medication Usage During Pregnancy**
HYDROCODONE/APAP PRODUCTS	62.56%
OXYCODONE/APAP PRODUCTS	19.96%
CODEINE/APAP PRODUCTS	6.19%
TRAMADOL PRODUCTS	5.36%
BUPRENORPHINE PRODUCTS	1.57%

Discussion[2]

In light of the recent studies suggesting the teratogenic potential of these medications, and the known risks of neonatal withdrawal after in utero exposure, this is a significant public health concern. Current proposals to limit inappropriate opioid use by SoonerCare members during pregnancy include a computer edit that would prevent an opioid claim to pay while a woman is pregnant without a prior authorization approval. Prior to implementing this prior authorization restriction a ProDUR edit that is override-able at the pharmacy will be implemented to monitor opioid claims processed during pregnancy.

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[1] Saint Louis, Catherine. "Surge in Narcotic Prescriptions for Pregnant Women." *New York Times* April 2013. Web. May 7 2014.

[2] Desai RJ, Hernandez-Diaz S, Bateman BT, Huybrechts KF. Increase in Prescription Opioid Use During Pregnancy Among Medicaid-Enrolled Women. *Obstet Gynecol* 2014; 123:99-1002.

[3] Broussard CS, Rasmussen SA, Reefhuis J, et al. Maternal Treatment with Opioid Analgesics and Risk for Birth Defects. *Am J Obstet Gynecol* 2011; 204:314.e1-11.

[4] Center for Disease Control. Opioid Pain Killers Linked to Increased Risk of Some Birth Defects. Available online at: http://www.cdc.gov/media/releases/2011/p0302_opioidbirthdefects.html. Last revised: 03/2011. Last accessed: 06/2014.

Concomitant Benzodiazepine and Opioid Utilization

Oklahoma Health Care Authority
July 2014

Introduction[1,2,3]

A recent scientific poster presented at the American Academy of Pain Medicine's 30th annual meeting highlighted the increasing trend in benzodiazepine prescriptions, and their frequent combined use with opioid analgesics. Concomitant use of benzodiazepine and opioid medications can have additive effects and doses that are well tolerated when taken alone have greater risk for the depressing central nervous system when combined. Data have shown that drug combinations of benzodiazepines and opioids contribute to at least 30% of opioid-related deaths.

The authors cited further concerns associated with benzodiazepine medications including emergency department visits, falls in the elderly, and the development of physical and psychological dependence.

Of 3.1 billion primary care visits between 2002 and 2009, represented by the National Ambulatory Medical Center Survey (NAMCS) from the Centers for Disease Control and Prevention, 12.6% involved prescriptions for benzodiazepines or opioids, and prescriptions of benzodiazepines grew by 12.5% a year.

After controlling for patient demographics, including race, ethnicity, age, gender, and insurance type, patient visits involving opioid prescriptions were 4.2 times more likely to also have simultaneous prescriptions of a benzodiazepine. The study also found joint prescriptions of both benzodiazepines and opioids increased by 12% a year.

The researchers also evaluated data on 733 emergency department visits in the same time period and found 32.4% of patients had benzodiazepine or opioid prescriptions. After adjusting for the same factors as primary care visits, the data showed an increase in prescription of opioids in the emergency department at a rate of 3.4% per year and an increase of 3.7% per year for benzodiazepines. Prescriptions of benzodiazepines in combination with opioids increased by twice as much at a rate of 6.4% per year.

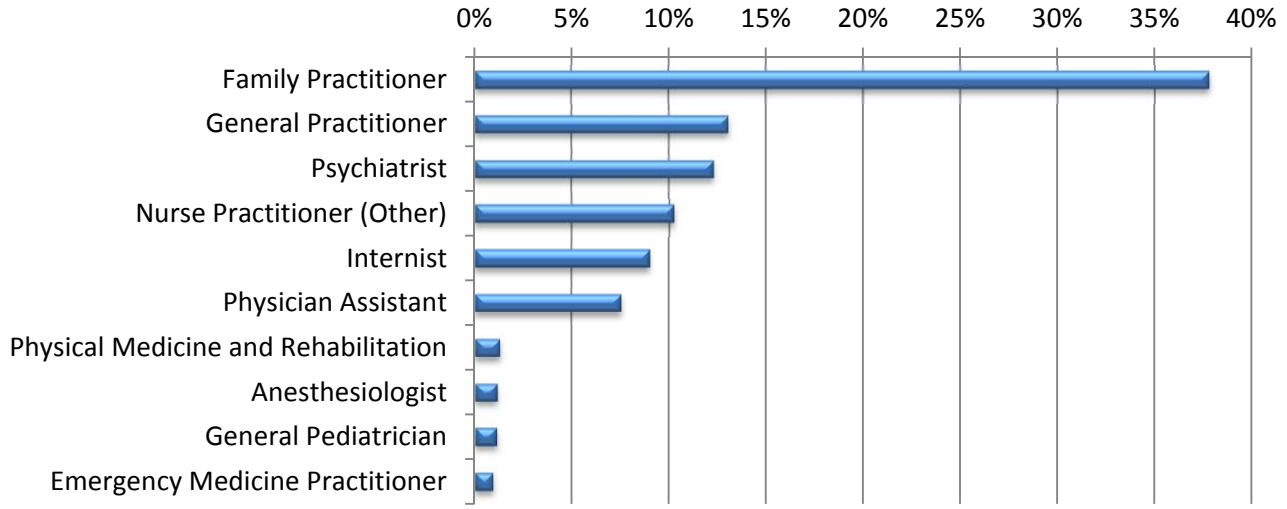
Concomitant Benzodiazepine and Opioid Utilization

Members were reviewed for paid pharmacy claims for at least one benzodiazepine and at least one opioid medication in the 12 months prior to the report date. A total of 34,715 distinct members with benzodiazepine claims were reviewed for concomitant opioid medication use. Concomitant use was determined by paid claims for a benzodiazepine <u>and</u> an opioid medication concurrently for greater than 90 consecutive days. A total of 223,303 benzodiazepine claims and 736,978 opioid medication claims were reviewed for concomitant use.

Members on Concomitant Therapy for > 90 Days
5,235 Total Members
71.29% Female and 28.71% Male
Age (mean ± SD): 45.71 ± 11.5

Approximately 15.08% of members utilizing benzodiazepines were also on an opioid medication for more than 90 days of therapy and approximately 5.74% of members utilizing benzodiazepines were also on an opioid medication for 365 days or more.

Top Prescriber Specialties of Benzodiazepines For Members on Concomitant Opioid Medications



Percent of benzodiazepine claims for members who had concomitant opioid usage.

Concomitant Utilization Details

The following table includes the most common benzodiazepines used concomitantly with at least one opioid medication.

Most Common Benzodiazepines Used Concomitantly	
Drug Name	**Percent of All Benzodiazepine Claims with an Opioid Medication**
ALPRAZOLAM TAB 1MG	28.88%
ALPRAZOLAM TAB 2MG	14.06%
CLONAZEPAM TAB 1MG	12.05%
DIAZEPAM TAB 10MG	10.88%
ALPRAZOLAM TAB 0.5MG	9.76%

The following table includes the most common opioid medications used concomitantly with at least one benzodiazepine.

Most Common Opioid Medications Used Concomitantly	
Drug Name	**Percent of All Opioid Medication Claims with a Benzodiazepine**
HYDROCO/APAP TAB 10-325MG	23.53%
HYDROCO/APAP TAB 10-500MG	14.95%
TRAMADOL TAB 50MG	8.00%
HYDROCO/APAP TAB 7.5-325MG	7.77%
HYDROCO/APAP TAB 7.5/500MG	6.19%

Discussion[3,4]

Prescription drug abuse is a fast growing issue in Oklahoma. Of the nearly 3,200 unintentional poisoning deaths in Oklahoma from 2007-2011, 81% involved at least one prescription drug. In 2010, Oklahoma had the fourth highest unintentional poisoning death rate in the nation (17.9 deaths per 100,000 population).

The pattern for drug overdose deaths has changed considerably over the past 40 years. Prior to the late 1990's, heroin, cocaine, and methamphetamines were most commonly associated with unintentional poisoning deaths. Prescription painkillers or opioid medications are now the most common class of drugs involved in overdose deaths in Oklahoma (involved in 87% of prescription drug-related deaths, with 417 opioid-involved deaths in 2011). **The most common prescription drugs involved in overdose deaths are hydrocodone, oxycodone, and alprazolam**. In Oklahoma, more overdose deaths involved hydrocodone than methamphetamines, heroin, and cocaine combined.

Action Items (3) related to the use of both opioids and benzodiazepines may be warranted.

1. Review by age and concurrent diagnoses, consider step down therapy
2. Enhanced Oversight – Referral to the Lock-in Program
3. Prescriber Education

Further review of the diazepam and alprazolam category may be warranted. Members should be evaluated for concurrent inappropriate diagnoses particularly abuse-related diagnoses. Some consideration may be given to limiting the dose of benzodiazepines for members over 55 years of age and older. Safer pharmacologic alternatives should be considered, including a **step down** option to a shorter half-life anxiolytic such as lorazepam.

Patients that are utilizing opioid medications and benzodiazepines concurrently may need to be reviewed for possible referral to the current **Lock-in** program. Members of particular concern are in the age category 35-54 years. This age group is found to be at the highest risk for unintentional prescription overdose deaths. Males age 35-54 years comprise the majority of drug overdose deaths.

A prescriber educational initiative may also be considered. Studies have found patients who are using benzodiazepines and opioid medications concurrently are frequently receiving those prescriptions from different prescribers. The medications have often been started at different episodes of care and prescribers are not always aware of the concomitant usage. A letter to those prescribers with members using both therapies with encouragement to use the Oklahoma Prescription Monitoring Program (PMP) may be an appropriate intervention.

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[1] Kao, Ming-Chih (March 2014). *Trends in Benzodiazepine Prescription and Co-Prescription with Opioids in the United States, 2002-2009*. Poster presented at the American Academy of Pain Medicine's 30th Annual Meeting, Phoenix, AZ.

[2] American Academy of Pain Medicine. Prescriptions for Benzodiazepines Rising and Risky When Combined with Opioids, Stanford Researchers Warn. Available online at: http://www.painmed.org/2014press/files/prescriptions-for-benzodiazepines-rising-and-risky-when-combined-with-opioids.pdf. Last revised 03/2014. Last accessed 06/2014.

[3] Melville, Nancy A. Benzodiazepine, Opioid Prescribing Rises in Primary Care. Available online at: http://www.medscape.com/viewarticle/821836. Last revised: 03/2014. Last accessed 06/2014.

[4] Oklahoma Department of Mental Health and Substance Abuse Services. A State Plan: Reducing Prescription Drug Abuse in Oklahoma. Available online at: http://www.ok.gov/odmhsas/documents/Rx%20Abuse%20Prevention%20Plan.pdf. Last revised 11/2013. Last accessed 06/2014.

Appendix C

Vote to Prior Authorize Esomeprazole Strontium and Aciphex® Sprinkle™ (Rabeprazole)

Oklahoma Health Care Authority
July 2014

Recommendations

The College of Pharmacy recommends the addition of Aciphex® Sprinkle™ and Esomeprazole Strontium to Tier-3 of the Anti-Ulcer Product Based Prior Authorization category. The existing criteria for this category will apply.

Anti-Ulcer Medications		
Tier-1	**Tier-2**	**Tier-3**
omeprazole (Prilosec®)	dexlansoprazole (Dexilant®)	esomeprazole magnesium (Nexium® Capsules, Packets, and I.V.)
pantoprazole (Protonix® Tablets)	lansoprazole (Prevacid® and ODT)	esomeprazole strontium
	rabeprazole sodium (Aciphex® Tablets)	omeprazole (Prilosec® Suspension and Powder)
		pantoprazole (Protonix® Suspension & I.V.)
		rabeprazole sodium (Aciphex® Sprinkle™)

Anti-Ulcer Medications Tier-2 Approval Criteria:

1. A 14-day trial of all available Tier-1 medications titrated up to the recommended dose that has resulted in inadequate relief of symptoms or intolerable adverse effects; or
2. Contraindication to all available Tier-1 medications; or
3. An indication not covered by lower tiered medications.

Anti-Ulcer Medications Tier-3 Approval Criteria:

1. A 14-day trial of all available Tier-1 and Tier-2 medications that has resulted in inadequate relief of symptoms or intolerable adverse effects; or
2. Contraindication to all available Tier-1 and Tier-2 medications; or
3. An indication not covered by lower tiered medications.
4. Special formulations including ODTs, Sprinkle Capsules, Granules, Suspension, and Solution for I.V. require special reason for use.

Proton-Pump Inhibitors for Pediatric Members Approval Criteria:

1. A recent 14-day trial of an H_2 receptor antagonist that has resulted in inadequate relief of symptoms or intolerable adverse effects; or
2. Recurrent or severe disease such as:
    a. GI bleed
    b. Zollinger-Ellison Syndrome or similar disease

Appendix D

Vote to Prior Authorize Liptruzet™ (Ezetimibe/Atorvastatin) and Omtryg™ (Omega-3-Acid Ethyl Esters A)

Oklahoma Health Care Authority
July 2014

Recommendations

The College of Pharmacy recommends the placement of Liptruzet™ (ezetimibe/atorvastatin) into the Special PA category of the Statin and Zetia® Product Based Prior Authorization category. The existing criteria for this category will apply.

Statin Medications and Zetia® (Ezetimibe) Tier-2 Approval Criteria:

1. A trial with atorvastatin, consisting of at least 8 weeks of continuous therapy, titrated to 40mg, which did not yield adequate LDL reduction. The minimum starting dose of the Tier-2 medication may only be at the moderate to high LDL lowering doses (20mg rosuvastatin or higher); or
2. Documented adverse effect or contraindication to all available lower tiered products; and
3. A clinical exception will apply for Crestor® (rosuvastatin) 40mg for high risk members hospitalized for recent acute myocardial infarction or acute coronary syndrome.

Special PA Approval Criteria:

1. A patient-specific, clinically significant reason why lower tiered medications with similar or higher LDL reduction cannot be used; and
2. Simcor® (simvastatin/niacin) and Advicor® (lovastatin/niacin) will also require a patient-specific, clinically significant reason why the member cannot use the individual products separately; and
3. Clinical exceptions for Zetia® (ezetimibe) include the following:
   i. Documented active liver disease; or
   ii. Documented unexplained, persistent elevations of serum transaminases; or
   iii. Documented statin related myopathy.

Statin Medications and Zetia® (Ezetimibe)		
Tier-1	**Tier-2**	**Special PA**
atorvastatin (Lipitor®)	rosuvastatin (Crestor®)*	ezetimibe (Zetia®)
lovastatin (Mevacor®)		ezetimibe/atorvastatin (Liptruzet™)
pravastatin (Pravachol®)		fluvastatin (Lescol®, Lescol® XL)
simvastatin (Zocor®)		lovastatin (Altoprev®)
		lovastatin/niacin (Advicor®)
		pitavastatin (Livalo®)
		simvastatin/ezetimibe (Vytorin®)
		simvastatin/niacin (Simcor®)

* Crestor® 5 mg and Crestor® 10 mg require special reason for use.

Additionally the College of Pharmacy recommends the prior authorization of Omtryg™ (omega-3-acid ethyl esters A) with the following criteria:

Omtryg™ (Omega-3-Acid Ethyl Esters A) Approval Criteria:

1. Laboratory documentation of severe hypertriglyceridemia (fasting triglycerides ≥500mg/dL), and controlled diabetes (fasting glucose <150mg/dL at the time of triglycerides measurement and HgA_1C <7.5%); and
2. Previous failure with both nicotinic acid and fibric acid medications.

% LDL Reduction	*Lovastatin (Mevacor®)*	*Pravastatin (Pravachol®)*	*Simvastatin (Zocor®)*	*Atorvastatin (Lipitor®)*	*Rosuvastatin (Crestor®)*	*Pitavastatin (Livalo®)*	*Fluvastatin (Lescol®)*
25-32 %	20mg	20mg	10mg			1 mg	40mg
31-39 %	40mg	40mg	20mg	10mg		2 mg	80mg*
37-45 %		80mg	40mg	20mg	5mg	4 mg	
48-52 %			80mg	40mg	10mg		
55-60 %				80mg	20mg		
60-63 %					40mg		

*Lescol® 40 mg bid and Lescol® XL 80 mg both fall into 31-39% LDL Reduction category.

Appendix E

Vote to Prior Authorize Zecuity® (Sumatriptan Iontophoretic Transdermal System) and Update the Triptan Anti-Migraine Medications Prior Authorization Category

Oklahoma Health Care Authority
July 2014

Recommendations

The College of Pharmacy recommends the addition of Zecuity® to Tier-3 of the Triptan Anti-Migraine Medications Product Based Prior Authorization category. The existing criteria for this category will apply. Additionally, use of Zecuity® will require a patient-specific, clinically significant reason why member cannot use all available generic formulations of sumatriptan (tablets, nasal spray, and injection). A quantity limit of four Zecuity® TDS per month will apply, based on the prescribing information and recommended dosing. Furthermore, the College of Pharmacy recommends the following changes to the Triptan Anti-Migraine Medications Product Based Prior Authorization category:

1. Move products to lower tiers when appropriate and cost effective.
2. Change the quantity limit on zolmitriptan 2.5mg tablets and ODTs to 6 tablets per 30 days to be consistent with the other existing quantity limits.
3. Use of any non-oral formulation in a higher tier will require a patient-specific, clinically significant reason why member cannot use the oral tablet formulation.

Triptan Anti-Migraine Medications		
Tier-1	**Tier-2**	**Tier-3**
rizatriptan (Maxalt®, Maxalt MLT®) sumatriptan tablets (Imitrex®)	naratriptan (Amerge®) zolmitriptan tablets & ODTs (Zomig®, Zomig-ZMT®)	almotriptan (Axert®) eletriptan (Relpax®) frovatriptan (Frova®) sumatriptan injection (Imitrex®) sumatriptan nasal spray (Imitrex®) sumatriptan (Sumavel® DosePro®) sumatriptan (Zecuity® TDS) sumatriptan/Naproxen (Treximet®) zolmitriptan nasal spray (Zomig®)

Triptan Anti-Migraine Medication Tier-2 Approval Criteria:

1. A trial of all available Tier-1 products with inadequate response; or
2. Documented adverse effect to all available Tier-1 products; or
3. Previous success with a Tier-2 product within the last 60 days

Triptan Anti-Migraine Medication Tier-3 Approval Criteria:

1. A trial of all available Tier-2 products with inadequate response; or
2. Documented adverse effect to all available Tier-2 products; or
3. Previous success with a Tier-3 product within the last 60 days
4. Use of any non-oral formulation will require a patient-specific, clinically significant reason why member cannot use the oral tablet formulation
5. Additionally, Zecuity® will require a patient-specific, clinically significant reason why member cannot use all available generic formulations of sumatriptan (tablets, nasal spray, and injection)

Appendix F

Calendar Year 2013 Annual Review of Relistor® (Methylnaltrexone), Linzess® (Linaclotide), and Amitiza® (Lubiprostone)

Oklahoma Health Care Authority
July 2014

Current Prior Authorization Criteria

Relistor® (Methylnaltrexone) Approval Criteria:

1. An FDA approved indication for the treatment of Opioid-Induced Constipation (OIC) in patients with severe terminal disease who are receiving only palliative care (life expectancy less than six months); and
2. Current use of opioid medications; and
3. Documented treatment attempts with a minimum of three alternate products, excluding bulk forming laxatives; and
4. Mechanical gastrointestinal obstruction has been ruled out.
5. The 12mg single-use vials, syringes or kits will be the preferred products. Criteria for consideration of 8mg single-use syringes:
    a. Weight range of 38kg -62kg; and/or
    b. Caregiver unable to draw up dose from vial.
6. A quantity limit of 30 units per month will apply.

Linzess® (Linaclotide) Approval Criteria:

1. An FDA approved diagnosis of Chronic Idiopathic Constipation (CIC) or Irritable Bowel Syndrome characterized by constipation (IBS-C) in members 18 years of age or older; and
2. Documentation that constipation-causing therapies for other disease states have been discontinued (excluding opioid pain medications for cancer patients); and
3. Documented and updated colon screening for members >50 years of age; and
4. Documentation of hydration attempts and trials of at least three different types of products that failed to relieve constipation. Trials must be within the past 90 days. Products may be OTC or prescription (does not include fiber or stool softeners).
5. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment.
6. A quantity limit of 30 units for a 30 day supply will apply.

Amitiza® (Lubiprostone) Approval Criteria:

1. An FDA approved diagnosis of Chronic Idiopathic Constipation (CIC) in members 18 years of age or older, or Irritable Bowel Syndrome characterized by constipation (IBS-C) in female members 18 years of age or older; and
2. Documentation that constipation-causing therapies for other disease states have been discontinued (excluding opioid pain medications for cancer patients); and
3. Documented and updated colon screening for members >50 years of age; and
4. Documentation of hydration attempts and trials of at least three different types of products that failed to relieve constipation. Trials must be within the past 90 days. Products may be OTC or prescription (does not include fiber or stool softeners).
5. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment.
6. A quantity limit of 60 units for a 30 day supply will apply.

Utilization of Relistor®, Linzess®, and Amitiza®

Comparison of Calendar Years: Relistor®

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2012	28	80	$65,098.68	$813.73	$31.56	953	2,063
2013	11	21	$12,620.00	$600.95	$27.32	179	462
% Change	**-60.70%**	**-73.80%**	**-80.60%**	**-26.10%**	**-13.40%**	**-81.20%**	**-77.60%**
Change	**-17**	**-59**	**-$52,478.68**	**-$212.78**	**-$4.24**	**-774**	**-1,601**

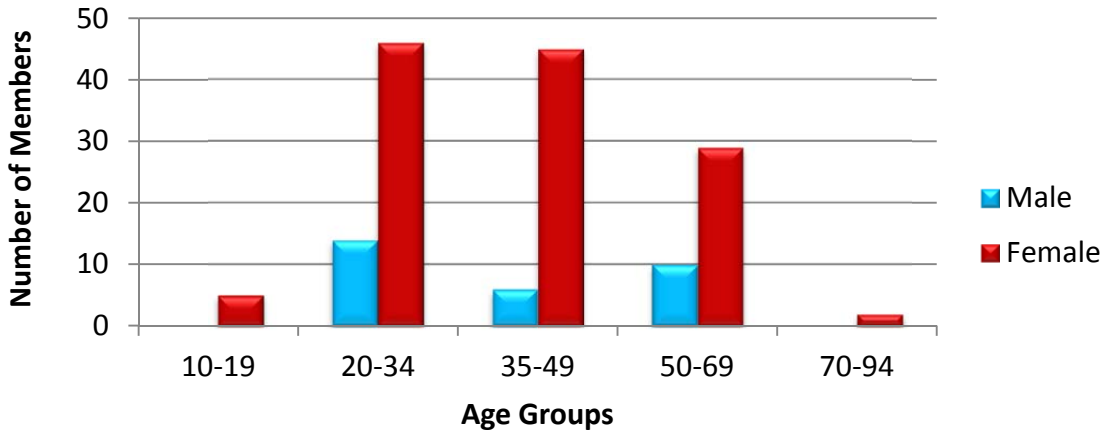
*Total number of unduplicated members.

Comparison of Calendar Years: Linzess® and Amitiza®

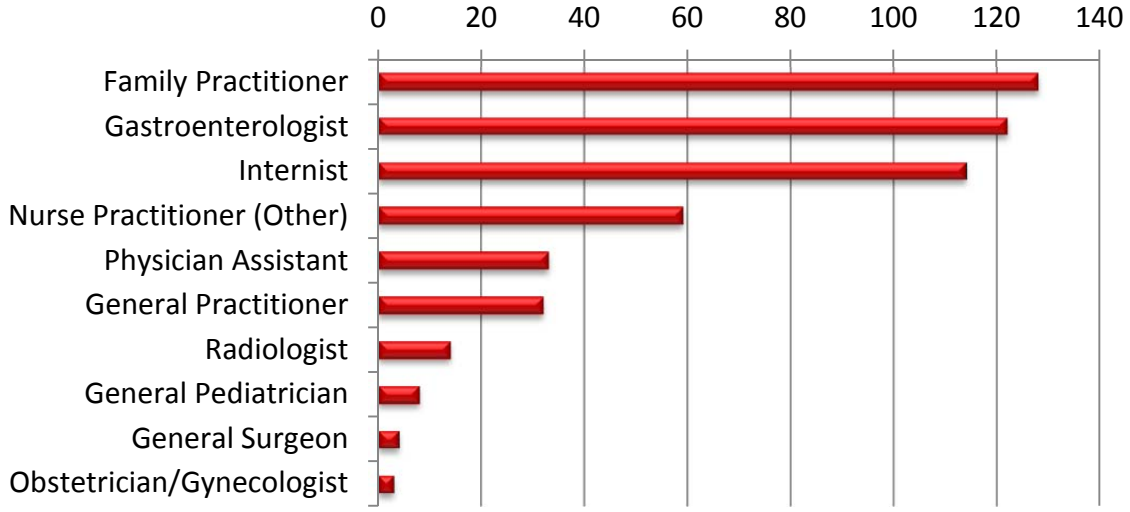
Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2012	84	309	$72,890.61	$235.89	$7.55	17,746	9,653
2013	149	501	$119,808.16	$239.14	$7.76	23,687	15,447
% Change	**77.40%**	**62.10%**	**64.40%**	**1.40%**	**2.80%**	**33.50%**	**60.00%**
Change	**65**	**192**	**$46,917.55**	**$3.25**	**$0.21**	**5,941**	**5,794**

*Total number of unduplicated members.

Demographics of Members Utilizing Relistor®, Linzess®, and Amitiza®



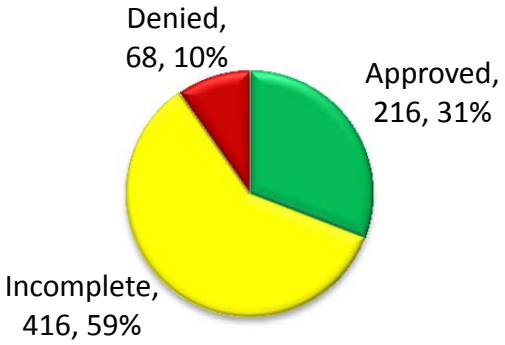
Top Prescriber Specialties of Relistor®, Linzess®, and Amitiza® By Number of Claims



Prior Authorization of Relistor®, Linzess®, and Amitiza®

There was a total of 700 petitions submitted for Relistor®, Linzess®, and Amitiza® during calendar year 2013. The following chart shows the status of the submitted petitions.

Status of Petitions



Market News and Updates[1,2,3,4,5]

Anticipated Patent Expirations:

- Linzess® (linaclotide)- 01/2024
- Amitiza® (lubiprostone)- 10/2027
- Relistor® (methylnaltrexone)- 12/2030

New Indications and Medications in the Pipeline:

In April 2013, the FDA approved Amitiza® (lubiprostone) for the indication of Opioid-Induced Constipation (OIC) in adults with chronic non-cancer pain. This is in addition to its indications for Chronic Idiopathic Constipation (CIC) in adults and Irritable Bowel Syndrome with Constipation (IBS-C) in women ages 18 years and older. This is the first and only oral medication for the treatment of OIC in adult patients with chronic, non-cancer pain. However, the effectiveness of Amitiza® in the treatment of OIC in patients taking diphenylheptane opioids (e.g. methadone) has not been established.

A new medication to treat OIC, Movantik™ (naloxegol), has completed phase 3 clinical trials, and a New Drug Application (NDA) has been submitted to the FDA. Naloxegol is a peripherally-acting mu-opioid receptor antagonist (PAMORA), which selectively blocks mu-opioid receptors in the gastrointestinal tract, preventing constipation, while staying out of the central nervous system, so pain relief is unaffected. If approved, naloxegol would be the first once-daily, oral PAMORA for the treatment of OIC in patients with chronic non-cancer pain.

Recommendations

The College of Pharmacy recommends continuing the existing criteria for Relistor® and Linzess®. Additionally, the College of Pharmacy recommends adding the following criteria for Amitiza® for the new indication of Opioid-Induced Constipation (OIC) in adults with chronic non-cancer pain:

Amitiza® (Lubiprostone) Approval Criteria – Opioid-Induced Constipation (OIC):

1. An FDA approved diagnosis of Opioid-Induced Constipation (OIC) in members 18 years of age or older with chronic, non-cancer pain who are currently on chronic opioid therapy, except methadone; and
2. Documentation of the underlying cause of chronic pain, or reason why member is on chronic opioid therapy; and
3. Documented and updated colon screening for members >50 years of age; and
4. Documentation of hydration attempts and trials of at least three different types of products that failed to relieve constipation. Trials must be within the past 90 days. Products may be OTC or prescription (does not include fiber or stool softeners).
5. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment.
6. A quantity limit of 60 units for a 30 day supply will apply.

Utilization Details of Relistor®, Linzess®, and Amitiza®

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
METHYLNALTREXONE PRODUCTS						
RELISTOR INJ 12/0.6ML	11	9	$8,820.85	$28.64	$801.90	69.90%
RELISTOR KIT 12/0.6ML	10	2	$3,799.15	$24.67	$379.92	30.10%
TOTAL	**21**	**11***	**$12,620.00**	**$27.32**	**$600.95**	**100.00%**

*Total number of unduplicated members.

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
LUBIPROSTONE PRODUCTS						
AMITIZA CAP 24MCG	238	58	$60,924.05	$8.12	$255.98	50.85%
AMITIZA CAP 8MCG	103	36	$23,884.76	$7.64	$231.89	19.94%
SUBTOTAL	**341**	**93***	**$84,808.81**	**$7.98**	**$248.71**	**70.79%**
LINACLOTIDE PRODUCTS						
LINZESS CAP 290MCG	91	36	$19,455.74	$7.15	$213.80	16.24%
LINZESS CAP 145MCG	69	28	$15,543.61	$7.40	$225.27	12.97%
SUBTOTAL	**160**	**61***	**$34,999.35**	**$7.26**	**$218.75**	**29.21%**
TOTAL	**501**	**149***	**$119,808.16**	**$7.76**	**$239.14**	**100.00%**

*Total number of unduplicated members.

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[1] FDA: Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised 6/13/14. Last accessed 6/16/14.

[2] Drugs@FDA: FDA Approved Drug Products. Available online at: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.DrugDetails. Last revised 6/17/14. Last accessed 6/16/14.

[3] Amitiza® Package Insert: Medlibrary.org. Available online at: http://medlibrary.org/lib/rx/meds/amitiza-2/. Last revised 4/25/13. Last accessed 6/18/14.

[4] AstraZeneca Press Release: Results from Phase III Studies of Naloxegol for Treatment of Opioid-Induced Constipation Presented at Digestive Disease Week 2013. Available online at: http://www.astrazeneca-us.com/media/press-releases/Article/20130521-results-from-phase-iii-studies-of-naloxegol-for. Last revised 5/21/13. Last accessed 6/18/14.

[5] US News: Health: New Drug May Treat Constipation Caused by Strong Painkillers. Available online at: http://health.usnews.com/health-news/articles/2014/06/09/new-drug-may-treat-constipation-caused-by-strong-painkillers. Last revised 6/9/14. Last accessed 6/18/14.

Appendix G

Fiscal Year 2013 Annual Review of Anticoagulants and Platelet Aggregation Inhibitors and 30-Day Notice to Prior Authorize Zontivity™ (Vorapaxar)

Oklahoma Health Care Authority
July 2014

Current Prior Authorization Criteria

Effient® (Prasugrel) Approval Criteria:

1. The first 90 days of therapy do not require prior authorization.
2. Approved diagnostic criteria: unstable angina/non-ST-segment elevated myocardial infarction (UA/non-STEMI) and ST-segment elevated myocardial infarction (STEMI) patients who are to be managed with percutaneous coronary intervention (PCI), primary or delayed (stent placement)
3. Approvals will be for the duration of one year.
4. Effient® (prasugrel) will not be approved for members with the following situations:
    a. Coronary Artery Bypass Graft surgery (CABG)
    b. Members with a history of transient ischemic attack (TIA) or stroke
5. Members greater than 75 years of age will generally not be approved without supporting information.
6. After the end of 15 months, prescribers should provide supporting information for the continuation of this product.

Plavix® 300mg (Clopidogrel) Approval Criteria:

1. An FDA approved diagnosis of non-ST-segment elevated acute coronary syndrome or ST-segment elevated acute myocardial infarction.
2. Approvals will be for one dose only of 300mg.

Brilinta® (Ticagrelor) Approval Criteria:

1. The first 90 days of therapy do not require prior authorization.
2. Approved diagnostic criteria: acute coronary syndrome (ACS) (unstable angina, non-ST elevation myocardial infarction, or ST elevation myocardial infarction) with or without percutaneous coronary intervention (PCI).
3. Approvals will be for the duration of one year.

Pradaxa® (Dabigatran) Approval Criteria:

1. An FDA approved diagnosus of non-valvular atrial fibrillation. (Special consideration will be given for a diagnosis of deep vein thrombosis (DVT) when warfarin is not a viable option.)

Xarelto® (Rivaroxaban) Approval Criteria:

1. Approved diagnostic criteria: non-valvular atrial fibrillation, deep vein thrombosis (DVT), pulmonary embolism (PE), or to reduce the risk of recurrent DVT and PE.
2. Xarelto 15mg and 20mg:
    a. A diagnosis of non-valvular atrial fibrillation, DVT, PE, or prophylaxis of recurrent DVT or PE will be required.
3. Xarelto 10mg:
    a. One prescription for up to 35 days of therapy is allowed without prior authorization every 6 months to allow for DVT prophylaxis use.

Eliquis® (Apixaban) Approval Criteria:

1. An FDA approved diagnosis of non-valvular atrial fibrillation.

Utilization of Anticoagulants and Platelet Aggregation Inhibitors

Comparison of Fiscal Years: Anticoagulants

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2012	2,260	11,643	$271,545.81	$23.32	$0.69	474,488	395,716
2013	2,346	11,959	$392,705.16	$32.84	$0.98	480,877	401,189
% Change	**3.80%**	**2.70%**	**44.60%**	**40.80%**	**42.00%**	**1.30%**	**1.40%**
Change	**86**	**316**	**$121,159.35**	**$9.52**	**$0.29**	**6,389**	**5,473**

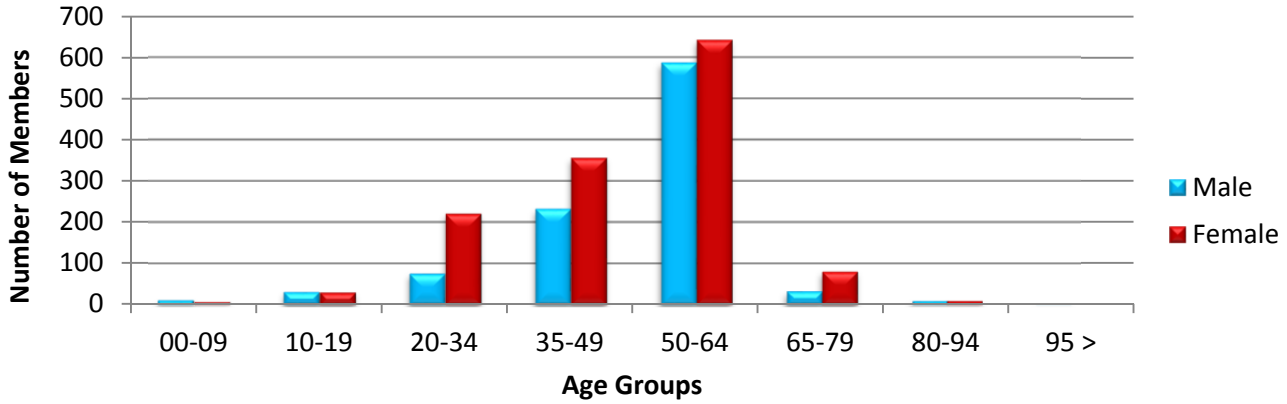
*Total number of unduplicated members.

Comparison of Fiscal Years: Platelet Aggregation Inhibitors

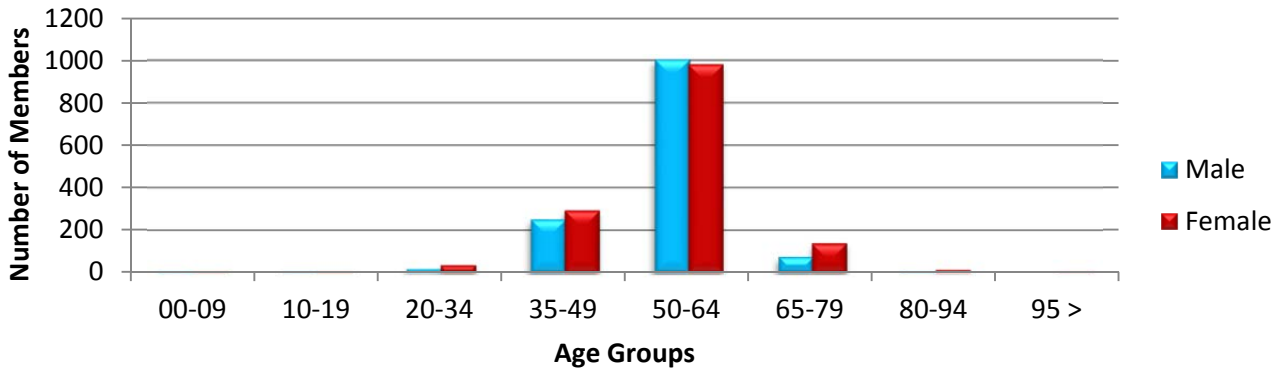
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2012	2,707	12,251	$2,755,234.95	$224.90	$6.01	459,741	458,683
2013	2,863	13,274	$401,499.71	$30.25	$0.77	525,391	522,440
% Change	**5.80%**	**8.40%**	**-85.40%**	**-86.50%**	**-87.20%**	**14.30%**	**13.90%**
Change	**156**	**1,023**	**-$2,353,735.24**	**-$194.65**	**-$5.24**	**65,650**	**63,757**

*Total number of unduplicated members.

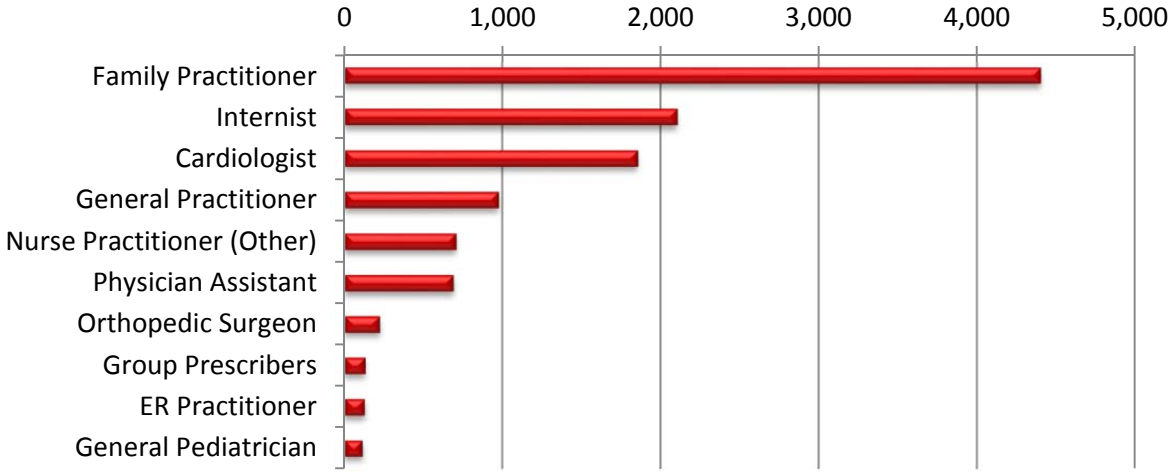
Demographics of Members Utilizing Anticoagulants



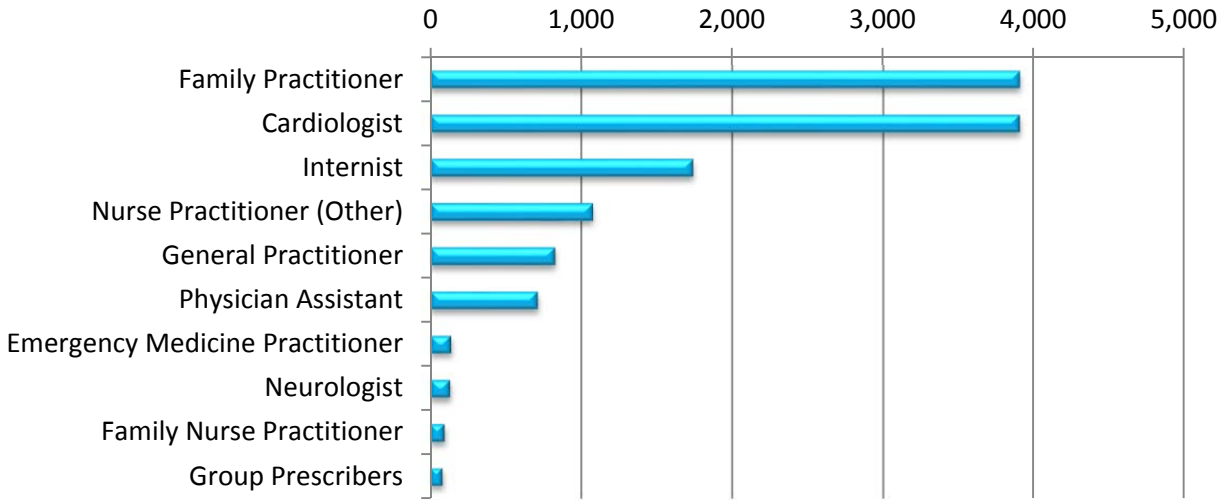
Demographics of Members Utilizing Platelet Aggregation Inhibitors



Top Prescriber Specialties of Anticoagulants by Number of Claims



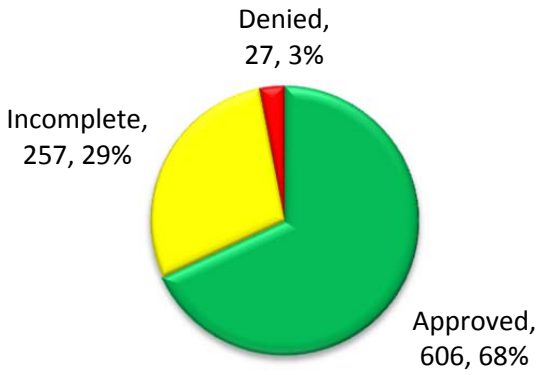
Top Prescriber Specialties of Platelet Aggregation Inhibitors by Number of Claims



Prior Authorization of Anticoagulants and Platelet Aggregation Inhibitors

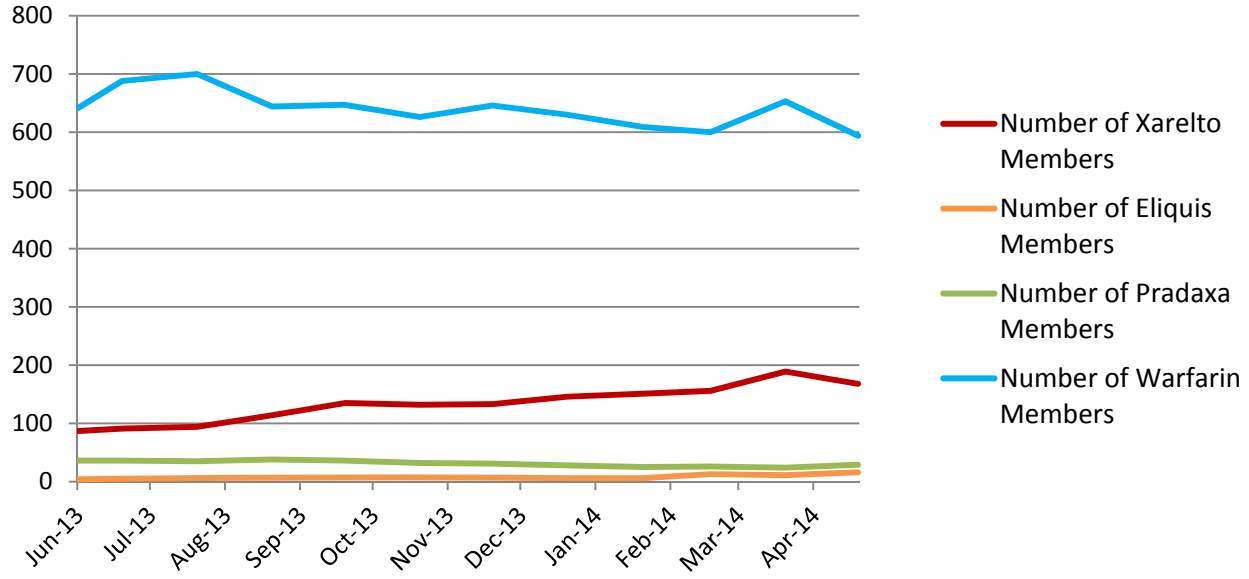
There was a total of 890 petitions submitted for anticoagulants and platelet aggregation inhibitors during fiscal year 2013. The following chart shows the status of the submitted petitions.

Status of Petitions



Oral Anticoagulation Utilization Trend

Number of Members per Month: June 2013-May 2014



Market News and Updates[1, 2, 3, 4, 5]

Anticipated Patent Expirations:

- Xarelto® (rivaroxaban)- 02/2021
- Effient® (prasugrel)- 07/2021
- Brilinta® (ticagrelor)- 07/2021
- Eliquis® (apixaban)- 02/2023
- Pradaxa® (dabigatran)- 08/2027

FDA Updates:

- **March 2014:** The FDA approved Eliquis® (apixaban) for the additional indications of prophylaxis of DVT and PE in adults who have undergone hip or knee replacement surgery.

- **March 2014:** The FDA approved Pradaxa® (dabigatran) for the additional indications of the treatment of DVT and PE in patients who have been treated with a parenteral anticoagulant for 5 to 10 days, and to reduce the risk of recurrent DVT and PE in patients who have been previously treated.

- **May 2014:** The FDA approved Zontivity™ (vorapaxar) for the reduction of thrombotic cardiovascular events in patients with a history of MI or peripheral arterial disease (PAD).

Zontivity™ (Vorapaxar) Medication Summary[5, 6]

- **FDA Approved:** May 2014

- **Indication:** Zontivity™ (vorapaxar) is indicated for the reduction of thrombotic cardiovascular events in patients with a history of myocardial infarction (MI) or with peripheral arterial disease (PAD).

- **Dosing:** 2.08mg orally once daily, with or without food, in combination with clopidogrel and/or aspirin.

- **Mechanism of Action:** Zontivity™ inhibits platelet aggregation by reversibly antagonizing the protease-activated receptor-1 (PAR-1) expressed on platelets. However, its long half-life makes it effectively irreversible.

- **Efficacy:** The efficacy of Zontivity™ for the reduction of thrombotic cardiovascular events in patients with a history of MI or with PAD is supported by the TRA 2°P – TIMI 50 study. This study was a multicenter, randomized, double-blind, placebo-controlled study, which included 26,449 patients with a history of MI within the prior two weeks to twelve months, ischemic stroke, or documented PAD and receiving aspirin and/or clopidogrel. Patients were followed for up to four years, with a median follow-up of 2.5 years. There was a 17 percent relative risk reduction for the composite primary efficacy endpoint of CV death, MI, stroke and urgent coronary revascularization. The composite primary efficacy endpoint occurred in 10.1% in the group taking Zontivity™ compared with 11.8% in the placebo group (Hazard Ratio [HR]: 0.83, $p<0.001$). These results demonstrated the significant benefit of Zontivity™ when used with aspirin and/or clopidogrel versus patients using aspirin and/or clopidogrel alone.

- **Utilization:** There has been no utilization of Zontivity™ since it was FDA approved in May 2014. It is anticipated to be available in July 2014.

- **Cost:**

Dosage Form	EAC Per Tablet or Capsule	EAC for 30 days of Therapy
Zontivity™ (vorapaxar) Tablet	$9.41	$282.30

EAC= estimated acquisition cost

Recommendations

The College of Pharmacy recommends the prior authorization of Zontivity™ (vorapaxar) with the following criteria:

Zontivity™ (Vorapaxar) Approval Criteria:

1. An FDA approved diagnosis of one of the following: history of myocardial infarction (MI) or peripheral arterial disease (PAD); and
2. Zontivity™ must be used in combination with aspirin and/or clopidogrel (not monotherapy); and
3. Zontivity™ will not be approved for members with the following situations: history of transient ischemic attack (TIA), stroke, or intracranial hemorrhage (ICH), or active pathological bleeding; and
4. A quantity limit of 30 tablets per 30 days will apply.

The College of Pharmacy also recommends updating the prior authorization criteria for the following medications to reflect new FDA approved indications:

Pradaxa® (Dabigatran) Approval Criteria:

1. An FDA approved diagnosis of one of the following:
    a. Non-valvular atrial fibrillation; or
    b. Treatment of deep vein thrombosis (DVT) or pulmonary embolism (PE) after treatment with parenteral anticoagulant for 5 to 10 days; or
    c. To reduce the risk of recurrent DVT or PE in patients who have been previously treated

Eliquis® (Apixaban) Approval Criteria:

1. An FDA approved diagnosis of one of the following:
    a. Non-valvular atrial fibrillation; or
    b. Pulmonary embolism (PE) or deep vein thrombosis (DVT) prophylaxis in patients who have had hip or knee replacement surgery

Utilization Details of Anticoagulants

Product Utilized	Total Claims	Total Members	Total Cost	Units/ Day	Claims/ Member	Cost/ Claim	%Cost
Warfarin Products							
WARFARIN TAB 1MG	900	273	$9,575.66	1.5	3.3	$10.64	2.44%
JANTOVEN TAB 1MG	50	13	$387.34	0.68	3.85	$7.75	0.10%
COUMADIN TAB 1MG	29	7	$1,800.03	1.73	4.14	$62.07	0.46%
WARFARIN TAB 2MG	693	226	$6,538.10	1.21	3.07	$9.43	1.66%
JANTOVEN TAB 2MG	42	14	$347.64	0.92	3	$8.28	0.09%
COUMADIN TAB 2MG	22	10	$249.91	1.35	2.2	$11.36	0.06%
WARFARIN TAB 2.5MG	624	241	$5,788.25	1.14	2.59	$9.28	1.47%
JANTOVEN TAB 2.5MG	27	13	$255.90	0.98	2.08	$9.48	0.07%
COUMADIN TAB 2.5MG	14	3	$98.87	1	4.67	$7.06	0.03%
WARFARIN TAB 3MG	869	245	$8,270.66	1.14	3.55	$9.52	2.11%
JANTOVEN TAB 3MG	47	12	$362.31	0.68	3.92	$7.71	0.09%
COUMADIN TAB 3MG	29	7	$719.25	0.98	4.14	$24.80	0.18%
WARFARIN TAB 4MG	831	272	$8,398.27	1.22	3.06	$10.11	2.14%
JANTOVEN TAB 4MG	23	11	$252.08	1.17	2.09	$10.96	0.06%
COUMADIN TAB 4MG	23	6	$697.35	1	3.83	$30.32	0.18%
WARFARIN TAB 5MG	3,777	1,080	$36,347.66	1.23	3.5	$9.62	9.26%
JANTOVEN TAB 5MG	64	33	$567.37	1.01	1.94	$8.87	0.14%
COUMADIN TAB 5MG	92	19	$2,144.29	1.15	4.84	$23.31	0.55%
WARFARIN TAB 6MG	732	210	$7,361.16	1.01	3.49	$10.06	1.87%
COUMADIN TAB 6MG	26	8	$673.07	1	3.25	$25.89	0.17%
WARFARIN TAB 7.5MG	763	273	$7,407.40	0.98	2.79	$9.71	1.89%
JANTOVEN TAB 7.5MG	2	2	$19.36	1	1	$9.68	0.00%
COUMADIN TAB 7.5MG	19	6	$161.20	1.14	3.17	$8.48	0.04%
WARFARIN TAB 10MG	1,024	306	$9,317.21	1.04	3.35	$9.10	2.37%
JANTOVEN TAB 10MG	2	2	$18.38	1	1	$9.19	0.00%
COUMADIN TAB 10MG	22	2	$1,844.30	1.42	11	$83.83	0.47%
Subtotal	**10,746**	**2,006***	**$109,603.02**	**1.17**	**5.36**	**$10.20**	**27.90%**
Dabigatran Products							
PRADAXA CAP 75MG	25	6	$6,076.27	2	4.17	$243.05	1.55%
PRADAXA CAP 150MG	466	93	$115,826.11	1.95	5.01	$248.55	29.49%
Subtotal	**491**	**96***	**$121,902.38**	**1.95**	**1.95**	**$248.27**	**31.04%**
Rivaroxaban Products							
XARELTO TAB 10MG	255	190	$46,441.96	1.13	1.34	$182.13	11.83%
XARELTO TAB 15MG	97	38	$24,468.63	1.17	2.55	$252.25	6.23%
XARELTO TAB 20MG	360	112	$87,646.57	1	3.21	$243.46	22.32%
Subtotal	**712**	**317***	**$158,557.16**	**1.06**	**2.25**	**$222.69**	**40.38%**
Apixaban Products							
ELIQUIS TAB 5MG	10	6	$2,642.60	2	1.67	$264.26	0.67%
Subtotal	**10**	**6***	**$2,642.60**	**2**	**1.67**	**$264.26**	**0.67%**
Total	**11,959**	**2,346***	**$392,705.16**	**1.2**	**5.1**	**$32.84**	**100%**

*Total number of unduplicated members.

Utilization Details of Platelet Aggregation Inhibitors

Product Utilized	Total Claims	Total Members	Total Cost	Units/ Day	Claims/ Member	Cost/ Claim	% Cost
Clopidogrel Products							
CLOPIDOGREL TAB	12,216	2,652	$137,804.78	1	4.61	$11.28	34.32%
PLAVIX TAB 75MG	65	21	$9157.51	1	3.1	$140.88	2.28%
Subtotal	**12,281**	**2673**	**$146,962.29**	**1**	**4.62**	**$76.08**	**36.6%**
Prasugrel Products							
EFFIENT TAB 10MG	915	246	$236,356.51	1	3.75	$258.31	58.87%
EFFIENT TAB 5MG	10	5	$2,184.17	1	2	$218.42	0.54%
Subtotal	**925**	**251**	**$238,540.68**	**1**	**2.88**	**$238.37**	**59.41%**
Ticagrelor Products							
BRILINTA TAB 90MG	68	20	$15,996.74	2	3.4	$235.25	3.98%
Subtotal	**68**	**20**	**$15,996.74**	**2**	**3.4**	**$235.25**	**3.98%**
Total	**13,274**	**2,863***	**$401,499.71**	**1.3**	**3.63**	**$183.23**	**100%**

*Total number of unduplicated members

PRODUCT DETAILS OF ZONTIVITY™ (VORAPAXAR)[5,6]

INDICATIONS AND USE:

- Zontivity™ (vorapaxar) is indicated for the reduction of thrombotic cardiovascular events in patients with a history of myocardial infarction (MI) or with peripheral arterial disease (PAD).

DOSAGE FORMS:

- Zontivity™ is available as a 2.08mg tablet.

ADMISTRATION:

- The dose is one tablet by mouth once daily, with or without food.
- Take with aspirin and/or clopidogrel according to their indications of standard care, Zontivity™ should not be taken as monotherapy.

CONTRAINDICATIONS:

- The use of Zontivity™ is contraindicated in patients with a history of stroke, transient ischemic attack (TIA), or intracranial hemorrhage (ICH).
- Discontinue Zontivity™ in patients who experience a stroke, TIA, or ICH
- Zontivity™ is contraindicated in patients with active pathological bleeding such as ICH or peptic ulcer.

SPECIAL POPULATIONS:

- **Pregnancy:** Category B. There are no adequate and well-controlled studies of Zontivity™ use in pregnant women. Zontivity™ should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the fetus.
- **Breast feeding:** It is unknown whether vorapaxar or its metabolites are excreted in human milk, but because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from Zontivity™, discontinue nursing or discontinue Zontivity™.
- **Pediatric Patients:** The safety and effectiveness of Zontivity™ in pediatric patients have not been established.
- **Geriatric Patients:** The relative risk of bleeding was similar across age groups. No overall differences in safety or effectiveness were observed between these patients and younger patients. Zontivity™ increases the risk of bleeding in proportion to a patient's underlying risk. Because older patients are generally at a higher risk of bleeding, consider patient age before initiating Zontivity™.
- **Renal Impairment:** No dose adjustment is required in patients with renal impairment.
- **Hepatic Impairment:** No dose adjustment is required in patients with mild and moderate hepatic impairment. Zontivity™ is not recommended in patients with severe hepatic impairment.

WARNINGS AND PRECAUTIONS:

- Zontivity™ increases the risk of bleeding in proportion to the patient's underlying bleeding risk. Consider the underlying risk of bleeding before initiating Zontivity™.
- Withholding Zontivity™ for a brief period will not be useful in managing an acute bleeding event because of its long half-life, as significant inhibition of platelet aggregation remains four weeks after discontinuation. There is no known treatment to reverse the antiplatelet effect of Zontivity™.

ADVERSE REACTIONS:

- Most common adverse reaction reported was bleeding.

DRUG INTERACTIONS:

- Avoid concomitant use of warfarin or other anticoagulants with Zontivity™.
- Avoid concomitant use of strong CYP3A inhibitors or inducers with Zontivity™.

PATIENT COUNSELING INFORMATION:

1. Zontivity™ should be taken exactly as prescribed.
2. Patient may bleed and bruise more easily. Patient should report any unanticipated, prolonged or excessive bleeding, or blood in their stool or urine.
3. Patients should always inform their doctors and dentists that they are taking Zontivity™ before any surgery or dental procedure.
4. Patients should talk to their doctor about all prescription medications, over-the-counter medications, or dietary supplements they are taking or plan to take so that the doctor knows about other treatments that may affect their bleeding risk.

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[1] FDA: Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://orange-book.findthebest.com/. Last accessed 6/16/2014.

[2] FDA: Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised 6/13/14. Last accessed 6/16/14.

[3] Boehringer Ingelheim Press Release: FDA approves Pradaxa® for treatment and reduction in risk of recurrent deep vein thrombosis (DVT) and pulmonary embolism (PE). Available online at: http://www.boehringer-ingelheim.com/news/news_releases/press_releases/2014/08_april_2014_dabigatranetexilate.html Last revised 4/8/2014. Last accessed 6/20/14.

[4] Bristol-Myers Squibb Press Release: U.S. FDA Approves Eliquis® (apixaban) To Reduce The Risk Of Blood Clots Following Hip Or Knee Replacement Surgery. Available online at: http://news.bms.com/press-release/us-fda-approves-eliquis-apixaban-reduce-risk-blood-clots-following-hip-or-knee-replace Last revised3/14/2014. Last accessed 6/20/14.

[5] Merck News Release: FDA Approves Zontivity™ (vorapaxar), First-in-Class PAR-1 Antagonist, for the Reduction of Thrombotic Cardiovascular Events in Patients with History of Heart Attack or with Peripheral Arterial Disease. Available online at: http://www.mercknewsroom.com/news-release/corporate-news/fda-approves-zontivity-vorapaxar-first-class-par-1-antagonist-reduction- Last revised 5/12/2014. Last accessed 6/20/2014.

[6] Zontivity™ Prescribing Information. Available online at: http://www.merck.com/product/usa/pi_circulars/z/zontivity/zontivity_pi.pdf. Last revised 5/2014. Last accessed 6/19/2014.

Appendix H

Fiscal Year 2013 Annual Review of Opioid Analgesics and 30-Day Notice to Prior Authorize Zohydro™ ER (Hydrocodone Bitartrate) and Xartemis™ XR (Oxycodone/Acetaminophen)

Oklahoma Health Care Authority
July 2014

Current Prior Authorization Criteria

Opioid Analgesics			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
codeine hydrocodone/APAP (Lortab®, Norco®) hydrocodone/IBU (Vicoprofen®, Ibudone®, Reprexain™) hydromorphone (Dilaudid®) methadone(Dolophine®) morphine IR (MSIR®) oxycodone/APAP (Percocet®) oxycodone/ASA (Percodan®) oxycodone IR (Oxy IR®) tramadol/APAP (Ultracet®) tramadol (Ultram®)	**Long-Acting:** fentanyl patches (Duragesic®) morphine ER tablets (MS Contin®) **Short-Acting:** tapentadol IR (Nucynta®) oxymorphone IR (Opana®)	**Long-Acting:** morphine sulfate ER (Avinza®) morphine sulfate ER (Kadian®) morphine/naltrexone (Embeda®) oxycodone ER (OxyContin®) oxymorphone (Opana® ER)* tramadol ER (Ultram ER®, Ryzolt®) hydromorphone ER (Exalgo®) buprenorphine patch (Butrans®) tapentadol ER (Nucynta® ER) **Short-Acting:** hydrocodone/APAP (Xodol®, Zamicet®, Hycet®, Zolvit®, Liquicet®) hydrocodone/APAP/caffeine (Trezix™) oxycodone/APAP (Primlev™, Xolox®) tramadol ODT (Rybix®) oxycodone (Oxecta®)	**Oncology Only:** fentanyl (Actiq®) fentanyl (Fentora®) fentanyl (Onsolis® buccal film) fentanyl (Abstral®,Lazanda®) fentanyl (Subsys™) SL spray

*Brand name Opana® ER preferred. Generic oxymorphone extended release tablets require special authorization. The generic formulation is not abuse-deterrent.

- Tier-1 products are covered with no prior authorization necessary.
- Members with an oncology-related diagnosis are exempt from the prior authorization process, and do not require pain contracts, although quantity and dosage limits still apply.
- Only one long-acting and one-short acting agent can be used concurrently.
- Quantity limits apply based on recommended daily dosing. All acetaminophen combination products have quantity limits based on a maximum of 3,250mg of acetaminophen per day.
- An age restriction applies on oral liquid narcotic analgesic products for all members older than 12 years of age and oral solid dosage forms for all members younger than 10 years of age.

Opioid Analgesics Tier-2 Approval Criteria:

1. A documented 30-day trial with at least two Tier-1 medications within the last 90 days; or
2. A clinically appropriate pain diagnosis requiring time-released medication

Opioid Analgesics Tier-3 Approval Criteria:

1. A documented 30-day trial with at least two long-acting Tier-2 medications within the last 90 days for approval of a long-acting Tier-3 medication; or
2. A documented 30-day trial with at least two short-acting Tier-2 medications within the last 90 days for approval of a short-acting Tier-3 medication; or
3. A documented allergy or contraindication to all Tier-2 medications

Special PA Approval Criteria:

1. Actiq®, Fentora®, and Onsolis®, Abstral®, Lanzanda® and Subsys™ are approved for oncology-related diagnoses only.

Approval Criteria for Greater than 12 Claims of Hydrocodone Products:

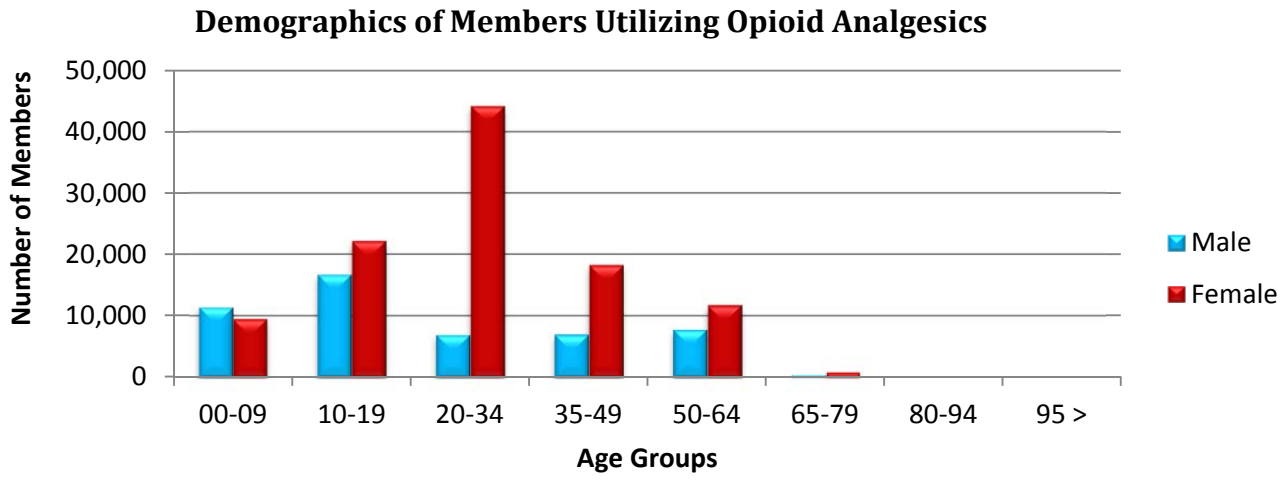
1. Members may be approved for greater than 12 claims per year if the member has a pain contract with a single prescriber. A copy of the pain contract should be submitted with the prior authorization request. Requests outside of the plan outlined in the contract will not be approved.
2. Members with a current oncology related diagnosis and hemophilia patients do not require a contract for additional approvals.
3. Immediate-release hydrocodone products will not be approved as the only therapy for chronic pain use. Members with chronic pain who require around-the-clock pain control should be on a long-acting pain medication. An additional claim may be approved to allow time for changes in therapy to be made.

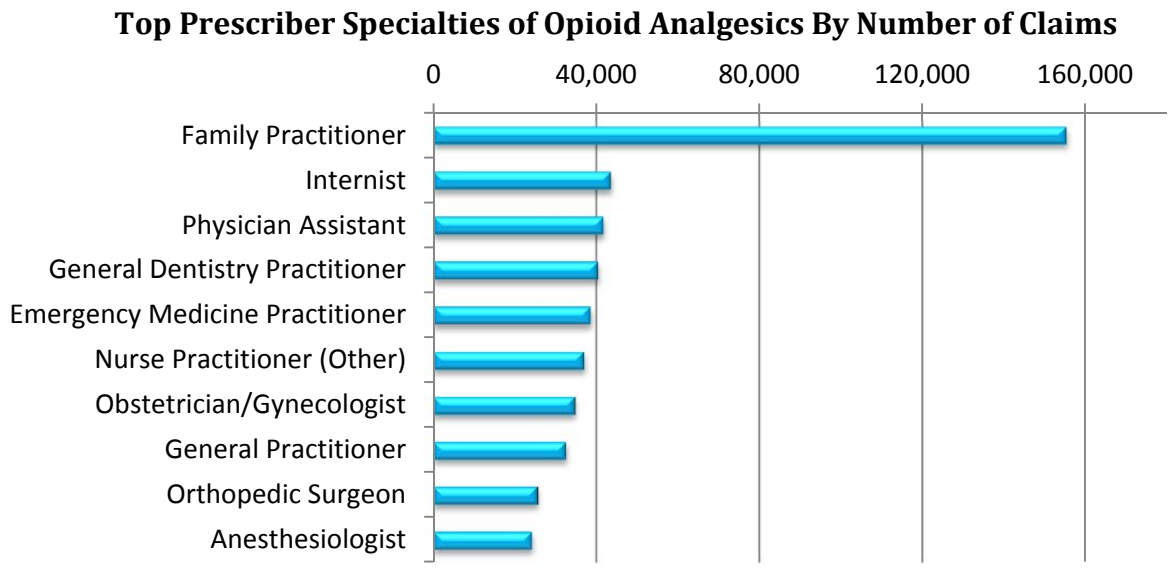
Utilization of Opioid Analgesics

Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2012	159,200	585,216	$16,506,570.22	$28.21	$1.78	39,979,888	9,271,723
2013	158,237	569,444	$15,966,300.87	$28.04	$1.72	39,259,240	9,265,457
% Change	**-0.60%**	**-2.70%**	**-3.30%**	**-0.60%**	**-3.40%**	**-1.80%**	**-0.10%**
Change	**-963**	**-15,772**	**-$540,269.35**	**-$0.17**	**-$0.06**	**-720,648**	**-6,266**

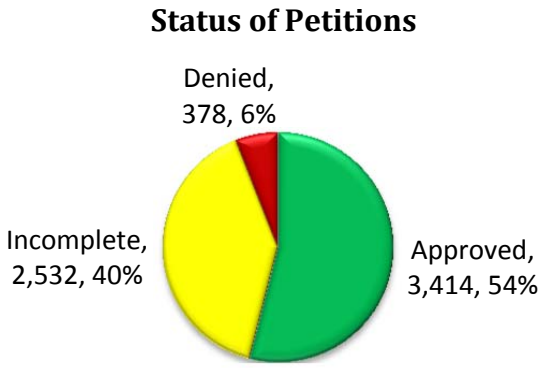
*Total number of unduplicated members.



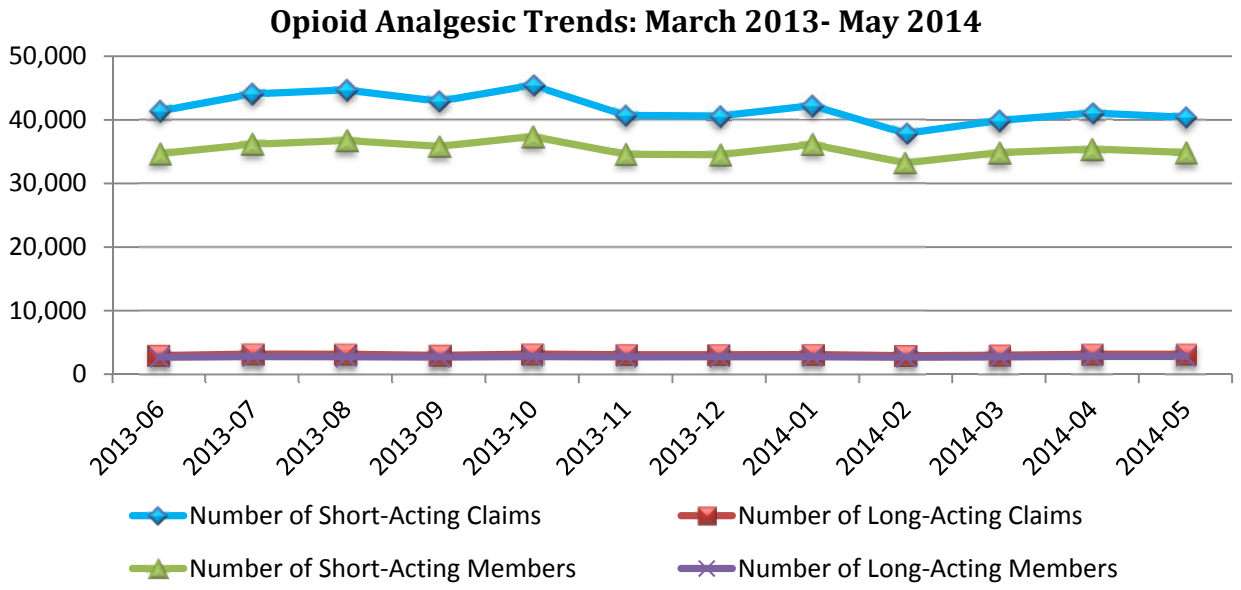


Prior Authorization of Opioid Analgesics

There was a total of 6,324 petitions submitted for opioid analgesics category during fiscal year 2013. Computer edits are in place to detect Tier-1 medications in member's recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions.



Opioid Analgesic Utilization Trends



Six Year Trend in Utilization of Opioid Analgesics

Fiscal Year	Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2008	119,047	415,908	$14,339,134.78	$34.48	$2.49	26,809,129	5,760,616
2009	124,366	419,390	$14,726,187.88	$35.11	$2.51	27,591,687	5,858,232
2010	139,509	470,949	$15,324,653.90	$32.54	$2.23	31,373,334	6,865,878
2011	150,529	515,228	$15,201,570.37	$29.50	$1.93	35,021,320	7,871,183
2012	159,200	585,216	$16,506,570.22	$28.21	$1.78	39,979,888	9,271,723
2013	158,237	569,444	$15,966,300.87	$28.04	$1.72	39,259,240	9,265,457

Top 10 Products by Claims: Fiscal Year 2013

Medication	Claims	Members	Cost	Cost/ Day	Units/ Day
HYDROCO/APAP TAB 7.5-500MG	80,047	37,372	$745,148.97	$0.71	3.4
HYDROCO/APAP TAB 10-500MG	74,088	15,786	$1,430,153.93	$0.81	3.75
TRAMADOL HCL TAB 50MG	66,939	25,862	$531,513.93	$0.44	4.11
HYDROCO/APAP TAB 10-325MG	45,766	11,680	$1,022,431.40	$0.97	4.19
HYDROCO/APAP TAB 5-500MG	39,736	26,927	$244,983.23	$0.78	3.6
HYDROCO/APAP TAB 7.5-325MG	39,117	20,326	$539,611.21	$1.08	3.89
HYDROCO/APAP TAB 5-325MG	32,650	22,459	$328,394.10	$1.32	4.19
OXYCOD/APAP TAB 5-325MG	23,931	19,547	$193,659.37	$1.32	5.49
APAP/CODEINE TAB 300-30MG	18,386	13,657	$166,950.32	$1.20	3.88
HYDROCO/APAP SOL 7.5-500MG	17,416	14,322	$222,864.87	$1.99	30.48
SUBTOTAL	**438,076**		**$5,425,711.33**		
CATEGORY TOTAL	**569,444**		**$15,966,300.87**		
PERCENT OF TOTAL	**76.93%**		**33.98%**		

Top 10 Products by Cost: Fiscal Year 2013

Medication	Claims	Members	Cost	Cost/ Day	Units/ Day
OXYCONTIN TAB 80MG CR	2,286	256	$2,552,768.70	$37.90	2.74
HYDROCO/APAP TAB 10-500MG	74,088	15,786	$1,430,153.93	$0.81	3.75
HYDROCO/APAP TAB 10-325MG	45,766	11,680	$1,022,431.40	$0.97	4.19
HYDROCO/APAP TAB 7.5-500MG	80,047	37,372	$745,148.97	$0.71	3.4
OXYCOD/APAP TAB 10-325MG	17,273	5,764	$623,030.40	$1.68	4.32
FENTANYL DIS 100MCG/HOUR	1,799	303	$613,821.31	$11.51	0.41
OXYCONTIN TAB 60MG CR	930	157	$612,352.60	$22.28	2.08
OXYCONTIN TAB 40MG CR	1,405	252	$607,776.08	$14.75	2.04
HYDROCO/APAP TAB 7.5-325MG	39,117	20,326	$539,611.21	$1.08	3.89
TRAMADOL HCL TAB 50MG	66,939	25,862	$531,513.93	$0.44	4.11
SUBTOTAL	**329,650**		**$9,278,608.53**		
CATEGORY TOTAL	**569,444**		**$15,966,300.87**		
PERCENT OF TOTAL	**57.89%**		**58.11%**		

Market News and Updates[1,2,3,4,5,6]

Anticipated Patent Expirations:

- Exalgo® (hydromorphone ER tablets)- 07/2014
- Butrans® (buprenorphine patches)- 09/2017
- Oxycontin® (oxycodone ER tablets)- 03/2025
- Nucynta® (tapentadol tablets) and Nucynta® ER (tapentadol ER tablets)- 06/2025
- Embeda® (morphine/naltrexone ER capsules)- 06/2027

FDA Update:

- **09/2013: FDA announces safety labeling changes and post-market study requirements for extended-release and long-acting opioid analgesics**
  - New boxed warning to include neonatal opioid withdrawal syndrome
    - Chronic maternal use of these products during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening and require management according to protocols developed by neonatology experts.
  - Class-wide safety labeling changes
    - Will include important new language to help health care professionals tailor their prescribing decisions based on a patient's individual needs.
    - The updated indication states that ER/LA opioids are indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.
    - The updated indication further clarifies that, because of the risks of addiction, abuse, and misuse, even at recommended doses, these drugs should be reserved for use in patients for whom alternative treatment options (e.g., non-

opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain; ER/LA opioid analgesics are not indicated for as-needed pain relief.
    - Modifications will also be made to the ER/LA Opioid Analgesics Risk Evaluation and Mitigation Strategy (REMS), to reflect the updated information. Originally approved in 2012, the ER/LA Opioid Analgesics REMS requires companies to make available to health care professionals educational programs on how to safely prescribe ER/LA opioid analgesics and to provide Medication Guides and patient counseling documents containing information on the safe use, storage, and disposal of ER/ LA opioids.
  - <u>New post market study requirements for all extended-release and long-acting (ER/LA) opioid analgesics intended to treat pain</u>
    - The goals of these post-market requirements are to further assess the known serious risks of misuse, abuse, increased sensitivity to pain (hyperalgesia), addiction, overdose, and death.

New Medications:

- **10/2013:** The FDA approved Zohydro™ ER for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.
  - FDA approval of Zohydro™ ER remains controversial. The FDA approved Zohydro™ ER despite an 11-2 vote from its own advisory panel to deny its approval because of the drug's high levels of hydrocodone and lack of abuse deterrence.
  - Attorney generals in 29 states have objected, warning in a letter to the FDA in December that the approval "has the potential to exacerbate our nation's prescription drug abuse epidemic."
- **03/2014:** The FDA approved Xartemis™ XR for the management of acute pain severe enough to require opioid treatment and for which alternative treatment options are inadequate.
- **05/2014:** Purdue Pharma filed a New Drug Application (NDA) for once-daily hydrocodone bitartrate extended-release tablets formulated to incorporate abuse-deterrent properties designed to make the product more difficult to misuse or abuse by various routes of administration (e.g., chewing, snorting, and intravenous injection).

Zohydro™ ER (Hydrocodone Bitartrate)[7]

FDA Approved: October 2013

Indications: Zohydro™ ER (hydrocodone bitartrate) is an opioid analgesic indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

- **Limitations of use:**
  - Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, reserve Zohydro™ ER for use in patients for whom alternative treatment options (e.g., nonopioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.
  - Zohydro™ ER is not indicated as an as-needed analgesic.

Dosing: Zohydro™ ER is available as 10mg, 15mg, 20mg, 30mg, 40mg, and 50mg extended-release capsules.

- Opioid naïve and opioid non-tolerant patients: initiate with 10mg by mouth every 12 hours
- Increase the dose in increments of 10mg every 12 hours every 3 to 7 days as needed
- Individualize treatment; titrate to effective and tolerable dose
- Capsules must be swallowed whole and are not to be chewed, crushed, or dissolved
- To convert to Zohydro™ ER from another opioid, use conversion factors to obtain estimated dose

Conversion Factors to Zohydro™ ER		
Prior Oral Opioid	**Oral Dose (mg)**	**Approximate Oral Conversion Factor**
hydrocodone	10	1
oxycodone	10	1
methadone	10	1
oxymorphone	5	2
hydromorphone	3.75	2.67
morphine	15	0.67
codeine	100	0.10

The conversion factors in this table are only for the conversion from one of the listed oral opioid analgesics to Zohydro™ ER. It is extremely important to monitor all patients closely when converting from methadone to other opioid agonists. The ratio between methadone and other opioid agonists may vary widely as a function of previous dose exposure. Methadone has a long half-life and tends to accumulate in the plasma.

- To calculate the estimated daily Zohydro™ ER dose using the above table:
  - For patients on a single opioid, sum the current total daily dose of the opioid and then multiply the total daily dose by the conversion factor to calculate the approximate oral hydrocodone daily dose. The daily dose should then be divided in half for administration every 12 hours.
  - Always round the dose down, if necessary, to the appropriate Zohydro ER strength(s) available.

Efficacy: The efficacy and safety of Zohydro™ ER have been evaluated in a randomized double-blind, placebo-controlled, multi-center clinical trial in opioid-experienced subjects with moderate to severe chronic low back pain. A total of 510 subjects currently on chronic opioid therapy entered an open-label conversion and titration phase (up to 6 weeks) with Zohydro™ ER dosed every 12 hours at an approximated equianalgesic dose of their pre-study opioid medication. There were 302 subjects (59%) randomized at a ratio of 1:1 into a 12-week double-blind treatment phase with their fixed stabilized dose of Zohydro™ ER (40–200 mg daily taken as 20–100 mg, every 12 hours) or a matching placebo. During the Treatment Phase, subjects were allowed to use rescue medication (hydrocodone 5 mg/500 mg acetaminophen) up to 2 doses (2 tablets) per day. There were 124 treated subjects (82%) that completed the 12-week treatment with Zohydro™ ER and 59 subjects (39%) with placebo. Zohydro™ ER provided greater analgesia compared to placebo. There was a significant difference in the mean changes from Baseline to Week 12 in average weekly pain intensity Numeric Rating Scale (NRS) scores between the two groups.

Cost:

Medication	EAC Per Tablet or Capsule	EAC Per Day	EAC for 30 Days of Therapy
Zohydro™ ER Capsules	$6.18-$7.55	$12.36-$15.10	$370.80-$453.00
Morphine ER Tablets	$0.51-$4.67+	$1.02-$9.34	$30.60-$280.20

EAC= estimated acquisition cost
+ State maximum allowable cost (SMAC) pricing
Morphine dosed BID with maximum dose of 400mg per day shown.

Xartemis™ XR (Oxycodone/Acetaminophen)[8]

FDA Approved: March 2014

Indications: Xartemis™ XR (Oxycodone/Acetaminophen) is a combination opioid agonist and acetaminophen that is indicated for the management of acute pain severe enough to require opioid treatment and for which alternative treatment options are inadequate.

- **Limitations of use:** Because of the risks of addiction, abuse, misuse, overdose, and death with opioids, even at recommended doses, reserve Xartemis™ XR for use in patients for whom alternative treatment options (e.g., non-opioid analgesics) are ineffective, not tolerated, or would be otherwise inadequate.

Dosing: Xartemis™ XR is available as 7.5mg/325mg (oxycodone/acetaminophen) extended-release tablets.

- The recommended dose of Xartemis™ XR is two tablets by mouth every 12 hours with food.
- Xartemis™ XR tablets should be swallowed whole. Do not break, chew, crush, cut, dissolve, or split the tablets. Swallow with enough water to ensure complete swallowing immediately after placing in mouth.

- Xartemis™ XR is not interchangeable with other oxycodone/acetaminophen products because of its differing pharmacokinetic profiles that affect the frequency of administration.

Efficacy: The efficacy of Xartemis™ XR was demonstrated in one multicenter, randomized, double-blind, placebo-controlled, parallel-arm, multiple-dose clinical trial comparing Xartemis™ XR and placebo in patients with acute pain following a unilateral first metatarsal bunionectomy. A total of 303 patients meeting criteria for randomization (pain intensity ≥4 on a 0 to 10 numerical pain rating scale) were randomized to receive a fixed-dose of 2 tablets of Xartemis™ XR and/or placebo every 12 hours over 48 hours. There were 36 early discontinuations (9% from Xartemis™ XR, 13% from placebo). Ibuprofen 400mg every 4 hours as needed was allowed as rescue medication. Approximately 85% of the 150 subjects treated with Xartemis™ XR and 98% of the 153 subjects treated with placebo took rescue medication at least once for pain management during the 48 hours after the first dose. Median rescue medication use was two doses for Xartemis™ XR-treated subjects and four doses for placebo-treated subjects over the 48 hours; rescue medication was used by less than 50% of the Xartemis™ XR -treated patients after the first dose interval. The median time to onset of pain relief was less than one hour for Xartemis™ XR. The primary endpoint was the summed pain intensity difference (change in pain from baseline) over 48 hours, which demonstrated improvement in pain from baseline for the Xartemis™ XR treatment group compared to placebo.

Cost:

Medication	EAC Per Tablet or Capsule	EAC Per Day	EAC for 10 Days of Therapy
Xartemis™ XR 7.5mg/325mg Tablets	$2.43	$9.72	$97.20
Oxycodone/Acetaminophen 7.5mg/325mg Tablets	$0.72[+]	$2.88-$5.76*	$28.80-$57.60
OxyContin 15mg Tablets	$3.70	$7.40	$74.00

EAC= estimated acquisition cost
+ State maximum allowable cost (SMAC) pricing
*Dosing per day based on one to two tablets four times daily.

Recommendations

The College of Pharmacy recommends the addition of Zohydro™ ER (hydrocodone bitartrate) and Xartemis™ XR (oxycodone/acetaminophen) to the Special PA category of the Opioid Analgesics Product Based Prior Authorization category with the following criteria:

Zohydro™ ER (Hydrocodone Bitartrate) Extended-Release Capsules Approval Criteria:

1. A chronic pain condition requiring daily, around-the-clock, long-term opioid treatment; and
2. A patient-specific, clinically significant reason why the member cannot use all other available long-acting Tier-2 and Tier-3 medications.
3. Tier structure rules still apply.

Xartemis™ XR (Oxycodone/APAP) Extended-Release Tablets Approval Criteria:

1. A pain condition requiring around-the-clock opioid treatment; and
2. A patient-specific, clinically significant reason for the following:
    a. Why the member cannot use any other opioid medication for treatment of acute pain; and
    b. Why the member requires a long-acting medication for an acute pain condition; and
    c. Why the member cannot use Oxycontin® (oxycodone ER) and OTC acetaminophen individual products in place of this combination product.
3. A quantity limit of 4 tablets per day will apply with a maximum approval duration of 10 days; and
4. The member must not exceed 3250mg of acetaminophen per day from all sources.
5. Tier structure rules still apply.

Opioid Analgesics			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
codeine hydrocodone/APAP (Lortab®, Norco®) hydrocodone/IBU (Vicoprofen®, Ibudone®, Reprexain™) hydromorphone (Dilaudid®) methadone(Dolophine®) morphine IR (MSIR®) oxycodone/APAP (Percocet®) oxycodone/ASA (Percodan®) oxycodone IR (Oxy IR®) tramadol/APAP (Ultracet®) tramadol (Ultram®)	**Long-Acting:** fentanyl patches (Duragesic®) morphine ER tablets (MS Contin®) **Short-Acting:** tapentadol IR (Nucynta®) oxymorphone IR (Opana®)	**Long-Acting:** morphine sulfate ER (Avinza®) morphine sulfate ER (Kadian®) morphine/naltrexone (Embeda®) oxycodone ER (OxyContin®) oxymorphone (Opana® ER)* tramadol ER (Ultram ER®, Ryzolt®) hydromorphone ER (Exalgo®) buprenorphine patch (Butrans®) tapentadol ER (Nucynta® ER) **Short-Acting:** hydrocodone/APAP (Xodol®, Zamicet®, Hycet®, Zolvit®, Liquicet®) hydrocodone/APAP/caffeine (Trezix™) oxycodone/APAP (Primlev™, Xolox®) tramadol ODT (Rybix®) oxycodone (Oxecta®)	hydrocodone bitartrate ER (Zohydro™ ER) oxycodone/APAP ER (Xartemis™ XR) **Oncology Only:** fentanyl (Actiq®) fentanyl (Fentora®) fentanyl (Onsolis® buccal film) fentanyl (Abstral®,Lazanda®) fentanyl (Subsys™) SL spray

*Brand name Opana® ER preferred. Generic oxymorphone extended release tablets require special authorization. The generic formulation is not abuse-deterrent.

Utilization Details of Opioid Analgesic Medications

Immediate Release Opioid Analgesics

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
HYDROCODONE SHORT-ACTING PRODUCTS						
HYDROCO/APAP TAB 7.5-500MG	80,047	37,372	$745,148.97	3.4	2.14	$9.31
HYDROCO/APAP TAB 10-500MG	74,088	15,786	$1,430,153.93	3.75	4.69	$19.30
HYDROCO/APAP TAB 10-325MG	45,766	11,680	$1,022,431.40	4.19	3.92	$22.34
HYDROCO/APAP TAB 5-500MG	39,736	26,927	$244,983.23	3.6	1.48	$6.17
HYDROCO/APAP TAB 7.5-325MG	39,117	20,326	$539,611.21	3.89	1.92	$13.79
HYDROCO/APAP TAB 5-325MG	32,650	22,459	$328,394.10	4.19	1.45	$10.06
HYDROCO/APAP SOL 7.5-500MG	17,416	14,322	$222,864.87	30.48	1.22	$12.80
HYDROCOD/IBU TAB 7.5-200MG	3,574	1,827	$58,929.19	3.45	1.96	$16.49
HYDROCO/APAP TAB 10-650MG	2,756	781	$39,616.39	3.6	3.53	$14.37
HYDROCO/APAP TAB 7.5-650MG	1,873	964	$15,482.47	3.25	1.94	$8.27
HYDROCO/APAP TAB 2.5-500MG	551	323	$6,712.68	3.12	1.71	$12.18
HYDROCO/APAP TAB 7.5-750MG	490	319	$3,950.40	3.39	1.54	$8.06
REPREXAIN TAB 10-200MG	183	77	$14,402.46	3.63	2.38	$78.70
IBUDONE TAB 5-200MG	160	106	$6,063.23	2.93	1.51	$37.90
IBUDONE TAB 10-200MG	145	44	$13,814.46	3.79	3.3	$95.27
HYDROCOD/IBU TAB 10-200MG	65	28	$7,809.89	3.75	2.32	$120.15
REPREXAIN TAB 2.5-200MG	47	32	$1,842.09	2.61	1.47	$39.19
REPREXAIN TAB 5-200MG	45	28	$1,414.46	3.09	1.61	$31.43
HYDROCOD/IBU TAB 2.5-200MG	21	16	$1,728.93	2.36	1.31	$82.33
HYDROCOD/IBU TAB 5-200MG	19	15	$898.44	3.35	1.27	$47.29
HYDROCO/APAP TAB 10-660MG	18	15	$231.72	3.18	1.2	$12.87
HYDROCO/APAP SOL 7.5-325MG	14	9	$2,133.22	71.03	1.56	$152.37
HYDROCO/APAP TAB 5-300MG	8	6	$677.97	5.15	1.33	$84.75
STAGESIC CAP 5-500MG	4	2	$35.24	5.1	2	$8.81
HYDROCO/APAP TAB 10-300MG	3	2	$691.73	4	1.5	$230.58
VICODIN TAB 5-300MG	1	1	$123.65	6.15	1	$123.65
HYDROCO/APAP TAB 7.5-300MG	1	1	$57.86	10	1	$57.86
SUBTOTAL	**338,798**	**111,615**	**$4,710,204.19**	**4.36**	**3.04**	**$13.90**
OXYCODONE SHORT-ACTING PRODUCTS						
OXYCOD/APAP TAB 5-325MG	23,931	19,547	$193,659.37	5.49	1.22	$8.09
OXYCOD/APAP TAB 10-325MG	17,273	5,764	$623,030.40	4.32	3	$36.07
OXYCOD/APAP TAB 7.5-325MG	8,649	5,251	$188,580.96	4.06	1.65	$21.80
OXYCODONE TAB 30MG	8,422	1,340	$451,668.68	4.65	6.29	$53.63
OXYCODONE TAB 15MG	5,973	1,302	$192,947.06	4.31	4.59	$32.30
ENDOCET TAB 10-325MG	3,468	1,269	$141,413.32	4.3	2.73	$40.78
OXYCODONE TAB 5MG	2,143	996	$36,865.66	4.68	2.15	$17.20
OXYCODONE TAB 10MG	2,130	754	$58,753.37	3.92	2.82	$27.58
ENDOCET TAB 5-325MG	1,073	893	$9,217.48	4.49	1.2	$8.59
OXYCOD/APAP TAB 10-650MG	957	408	$29,927.72	3.57	2.35	$31.27

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
OXYCODONE TAB 20MG	870	220	$47,756.72	4.29	3.95	$54.89
OXYCOD/APAP TAB 7.5-500MG	837	564	$17,392.52	3.7	1.48	$20.78
ENDOCET TAB 7.5-325MG	795	475	$22,792.50	3.84	1.67	$28.67
ENDOCET TAB 10-650MG	431	197	$16,046.45	3.61	2.19	$37.23
OXYCOD/APAP CAP 5-500MG	425	350	$3,850.79	4.01	1.21	$9.06
ROXICET TAB 5-325MG	408	382	$3,047.23	5.2	1.07	$7.47
ENDOCET TAB 7.5-500MG	206	111	$6,693.11	3.71	1.86	$32.49
OXYCODONE CAP 5MG	204	137	$11,419.43	5.14	1.49	$55.98
OXYCOD/ASA TAB 4.8-325MG	118	61	$5,648.55	3.44	1.93	$47.87
OXYCODONE CON 20MG/ML	56	24	$27,989.53	4.61	2.33	$499.81
ROXICET SOL 5-325MG/5ML	29	21	$526.87	21.9	1.38	$18.17
OXYCOD/APAP TAB 2.5-325MG	20	18	$857.40	3.98	1.11	$42.87
ENDODAN TAB 4.8-325MG	19	14	$980.40	4.33	1.36	$51.60
OXYCODONE SOL 5MG/5ML	11	10	$262.25	24.61	1.1	$23.84
XOLOX TAB 10-500MG	6	3	$1,270.63	3	2	$211.77
OXYCODONE CON 100/5ML	3	3	$842.84	3.87	1	$280.95
OXYCODONE POW HCL	2	2	$103.26	0.01	1	$51.63
OXYCOD/IBU TAB 5-400MG	1	1	$15.82	3.75	1	$15.82
OXYCODONE POW HCL	1	1	$144.33	6.18	1	$144.33
PRIMLEV TAB 10-300MG	1	1	$683.31	6	1	$683.31
SUBTOTAL	**78,462**	**33,326**	**$2,094,387.96**	**4.46**	**2.35**	**$26.69**
TRAMADOL SHORT-ACTING PRODUCTS						
TRAMADOL HCL TAB 50MG	66,939	25,862	$531,513.93	4.11	2.59	$7.94
TRAMADL/APAP TAB 37.5-325	1,552	920	$27,221.53	4.04	1.69	$17.54
SUBTOTAL	**68,491**	**26,477**	**$558,735.46**	**4.11**	**2.59**	**$8.16**
CODEINE PRODUCTS						
APAP/CODEINE TAB 300-30MG	18,386	13,657	$166,950.32	3.88	1.35	$9.08
APAP/COD SOL 120-12MG/5ML	16,282	14,190	$107,557.81	20.22	1.15	$6.61
BUT/APAP/CAF/COD CAP 30MG	930	392	$19,186.51	3.69	2.37	$20.63
APAP/CODEINE TAB 300-60MG	809	352	$16,117.58	3.36	2.3	$19.92
ASCOMP/COD CAP 30MG	360	156	$13,118.81	3.8	2.31	$36.44
APAP/CAF/DI-COD TAB 32MG	292	190	$14,287.12	3.07	1.54	$48.93
BUT/ASA/CAF/ CAP COD 30MG	290	126	$8,652.50	3.27	2.3	$29.84
APAP/CODEINE TAB 300-15MG	135	110	$1,080.15	4.24	1.23	$8.00
CAPITAL/COD SUS 120-12MG/5ML	59	55	$10,740.07	25.97	1.07	$182.04
CODEINE SULF TAB 30MG	42	31	$1,025.65	3.3	1.35	$24.42
TREZIX CAP 16MG	16	6	$1,863.63	2.54	2.67	$116.48
CODEINE SULF TAB 60MG	8	2	$626.07	4	4	$78.26
CODEINE SULF TAB 15MG	4	2	$31.05	3.69	2	$7.76
SYNALGOS-DC CAP 16MG	3	3	$216.67	4.44	1	$72.22
CODEINE SULF SOL 30MG/5ML	1	1	$17.04	30	1	$17.04
SUBTOTAL	**37,617**	**28,830**	**$361,470.98**	**9.3**	**1.3**	**$9.61**
MORPHINE SHORT-ACTING PRODUCTS						
MORPHINE SUL TAB 15MG	2,964	778	$36,347.37	3.7	3.81	$12.26

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
MORPHINE SUL TAB 30MG	1,651	339	$35,202.45	4.08	4.87	$21.32
MORPHINE SUL SOL 20MG/ML	145	65	$8,645.15	7.64	2.23	$59.62
MORPHINE SUL SOL 10MG/5ML	100	58	$1,489.29	13.42	1.72	$14.89
MORPHINE SUL INJ 10MG/ML	28	16	$866.11	4.22	1.75	$30.93
MORPHINE SUL SOL 20MG/5ML	20	13	$433.74	14.39	1.54	$21.69
MORPHINE SUL INJ 5MG/ML	7	7	$38.62	1.43	1	$5.52
MORPHINE SUL INJ 2MG/ML	6	5	$123.18	1.82	1.2	$20.53
MORPHINE POW SULFATE	4	3	$131.73	0.42	1.33	$32.93
MORPHINE SUL SOL 100/5ML	3	3	$120.25	8.37	1	$40.08
MORPHINE SUL INJ 2MG/ML	2	2	$51.07	8.33	1	$25.54
MORPHINE SUL INJ 4MG/ML	1	1	$21.23	10	1	$21.23
MORPHINE SUL INJ 15MG/ML	1	1	$13.31	8.67	1	$13.31
SUBTOTAL	**4,932**	**1,186**	**$83,483.50**	**4.04**	**4.16**	**$16.93**
HYDROMORPHONE SHORT-ACTING PRODUCTS						
HYDROMORPHON TAB 4MG	1,450	441	$28,511.69	4.27	3.29	$19.66
HYDROMORPHON TAB 2MG	864	579	$9,962.84	4.3	1.49	$11.53
HYDROMORPHON TAB 8MG	552	107	$31,465.05	3.82	5.16	$57.00
HYDROMORPHON LIQ 1MG/ML	23	7	$3,744.92	25.29	3.29	$162.82
DILAUDID TAB 4MG	16	2	$4,458.94	8.82	8	$278.68
DILAUDID TAB 8MG	13	1	$3,026.35	2.95	13	$232.80
HYDROMORPHON POW HCL	3	2	$725.25	0.3	1.5	$241.75
DILAUDID LIQ 1MG/ML	2	1	$369.20	20	2	$184.60
HYDROMORPHON INJ 50MG/5ML	2	2	$161.27	1.38	1	$80.64
HYDROMORPHON INJ 10MG/ML	1	1	$30.63	5	1	$30.63
SUBTOTAL	**2,926**	**1,043**	**$82,456.14**	**4.34**	**2.81**	**$28.18**
OXYMORPHONE SHORT-ACTING PRODUCTS						
OXYMORPHONE TAB HCL 10MG	313	64	$134,120.41	3.74	4.89	$428.50
OXYMORPHONE TAB HCL 5MG	76	26	$16,474.08	3.24	2.92	$216.76
SUBTOTAL	**389**	**85**	**$150,594.49**	**3.65**	**4.58**	**$387.13**
TAPENTADOL SHORT-ACTING PRODUCTS						
NUCYNTA TAB 100MG	129	26	$47,791.36	3.58	4.96	$370.48
NUCYNTA TAB 50MG	80	44	$13,750.18	3.09	1.82	$171.88
NUCYNTA TAB 75MG	22	13	$4,435.04	2.95	1.69	$201.59
SUBTOTAL	**231**	**75**	**$65,976.58**	**3.37**	**3.08**	**$285.61**
PENTAZOCINE PRODUCTS						
PENTAZ/NALOX TAB 50-0.5MG	1,276	638	$81,618.61	3.69	2	$63.96
PENTA/APAP TAB 25-650MG	40	23	$1,795.33	3.14	1.74	$44.88
SUBTOTAL	**1,316**	**658**	**$83,413.94**	**3.67**	**2**	**$63.38**
FENTANYL SHORT-ACTING PRODUCTS						
FENTANYL CIT INJ 0.05MG/1	24	8	$106.88	2.38	3	$4.45
FENTANYL OT LOZ 1200MCG	13	1	$24,518.63	4	13	$1,886.05
FENTANYL OT LOZ 800MCG	12	1	$16,754.84	4	12	$1,396.24
SUBSYS SPR 800MCG	9	2	$37,714.18	1.67	4.5	$4,190.46
FENTANYL OT LOZ 600MCG	7	1	$7,900.09	4	7	$1,128.58

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
FENTORA TAB 200MCG	7	3	$10,589.91	1.83	2.33	$1,512.84
FENTORA TAB 400MCG	6	2	$19,731.32	2.78	3	$3,288.55
SUBSYS SPR 600MCG	5	1	$8,385.37	1.43	5	$1,677.07
FENTORA TAB 100MCG	1	1	$3,096.71	3.73	1	$3,096.71
SUBSYS SPR 200MCG	1	1	$1,117.76	3.75	1	$1,117.76
SUBTOTAL	**85**	**18**	**$129,915.69**	**3.12**	**4.72**	**$1,528.42**
TOTAL	**533,247**	***157,222**	**$8,320,638.93**	**4.49**	**3.39**	**$15.60**

*Total number of unduplicated members

Long-Acting Opioid Analgesics

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
MORPHINE LONG-ACTING PRODUCTS						
MORPHINE SUL TAB 30MG ER	4,336	1,040	$121,908.42	2.27	4.17	$28.12
MORPHINE SUL TAB 15MG ER	3,631	1,067	$87,056.81	2.3	3.4	$23.98
MORPHINE SUL TAB 60MG ER	2,970	524	$112,241.31	2.38	5.67	$37.79
MORPHINE SUL TAB 100MG ER	1,022	169	$71,755.01	2.77	6.05	$70.21
MORPHINE SUL TAB 200MG ER	132	23	$15,097.89	2.42	5.74	$114.38
MORPHINE SUL CAP 30MG ER	91	19	$21,602.90	1.97	4.79	$237.39
MORPHINE SUL CAP 100MG ER	90	12	$106,195.76	2.81	7.5	$1,179.95
MORPHINE SUL CAP 80MG ER	78	12	$47,128.39	2.11	6.5	$604.21
MORPHINE SUL CAP 50MG ER	69	14	$27,103.77	1.93	4.93	$392.81
AVINZA CAP 90MG	49	4	$20,858.51	1	12.25	$425.68
AVINZA CAP 120MG	48	5	$23,857.91	1	9.6	$497.04
MORPHINE SUL CAP 60MG ER	47	10	$21,335.54	1.98	4.7	$453.95
MORPHINE SUL CAP 20MG ER	41	21	$10,655.63	2.41	1.95	$259.89
KADIAN CAP 200MG CR	28	3	$69,957.16	2.18	9.33	$2,498.47
KADIAN CAP 50MG CR	14	2	$7,681.77	2	7	$548.70
AVINZA CAP 60MG	14	1	$3,468.62	1	14	$247.76
AVINZA CAP 75MG	12	1	$4,369.56	1	12	$364.13
MS CONTIN TAB 60MG CR	12	1	$29,610.70	12	12	$2,467.56
KADIAN CAP 10MG CR	6	3	$837.20	1.26	2	$139.53
KADIAN CAP 30MG CR	5	1	$1,684.15	2	5	$336.83
KADIAN CAP 100MG CR	2	1	$3,402.02	4	2	$1,701.01
KADIAN CAP 40MG CR	1	1	$448.93	2	1	$448.93
KADIAN CAP 20MG CR	1	1	$309.73	2	1	$309.73
AVINZA CAP 30MG	1	1	$96.40	1	1	$96.40
SUBTOTAL	**12,700**	**2,321**	**$808,664.09**	**2.34**	**5.47**	**$63.67**
METHADONE PRODUCTS						
METHADONE TAB 10MG	3,306	485	$66,576.59	5	6.82	$20.14
METHADONE TAB 5MG	428	117	$3,990.74	2.87	3.66	$9.32
METHADONE SOL 5MG/5ML	223	89	$3,631.77	8.02	2.51	$16.29
METHADONE CON 10MG/ML	16	3	$767.92	3.22	5.33	$48.00
METHADOSE TAB 10MG	8	3	$140.35	4.2	2.67	$17.54

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
DOLOPHINE TAB 10MG	1	1	$24.29	6	1	$24.29
SUBTOTAL	**3,982**	**666**	**$75,131.66**	**4.9**	**5.98**	**$18.87**
FENTANYL LONG-ACTING PRODUCTS						
FENTANYL DIS 50MCG/HR	2,418	660	$297,121.80	0.34	3.66	$122.88
FENTANYL DIS 25MCG/HR	2,031	700	$124,525.56	0.34	2.9	$61.31
FENTANYL DIS 100MCG/H	1,799	303	$613,821.31	0.41	5.94	$341.20
FENTANYL DIS 75MCG/HR	1,582	363	$329,689.58	0.34	4.36	$208.40
FENTANYL DIS 12MCG/HR	501	215	$60,332.12	0.34	2.33	$120.42
DURAGESIC DIS 100MCG/H	28	4	$36,258.68	0.45	7	$1,294.95
DURAGESIC DIS 75MCG/HR	26	5	$21,406.13	0.39	5.2	$823.31
DURAGESIC DIS 50MCG/HR	17	2	$8,960.61	0.38	8.5	$527.09
DURAGESIC DIS 25MCG/HR	8	1	$2,038.23	0.33	8	$254.78
SUBTOTAL	**8,410**	**1,588**	**$1,494,154.02**	**0.35**	**5.3**	**$177.66**
OXYCODONE LONG-ACTING PRODUCTS						
OXYCONTIN TAB 80MG CR	2,286	256	$2,552,768.70	2.74	8.93	$1,116.70
OXYCONTIN TAB 40MG CR	1,405	252	$607,776.08	2.04	5.58	$432.58
OXYCONTIN TAB 20MG CR	1,221	273	$301,328.45	2.03	4.47	$246.79
OXYCONTIN TAB 60MG CR	930	157	$612,352.60	2.08	5.92	$658.44
OXYCONTIN TAB 30MG CR	828	180	$285,757.71	2.01	4.6	$345.12
OXYCONTIN TAB 10MG CR	433	137	$53,226.40	1.98	3.16	$122.92
OXYCONTIN TAB 15MG CR	216	76	$40,085.68	1.97	2.84	$185.58
OXYCONTIN TAB 80MG CR	4	4	$3,152.60	2.69	1	$788.15
OXYCONTIN TAB 20MG CR	3	1	$609.33	2	3	$203.11
OXYCONTIN TAB 60MG CR	1	1	$844.69	2	1	$844.69
OXYCONTIN TAB 40MG CR	1	1	$622.16	2	1	$622.16
SUBTOTAL	**7,328**	**959**	**$4,458,524.40**	**2.26**	**7.64**	**$608.42**
MEPERIDINE PRODUCTS						
MEPERIDINE SOL 50MG/5ML	900	600	$4,223.04	7.31	1.5	$4.69
MEPERIDINE TAB 50MG	661	489	$6,977.07	3.67	1.35	$10.56
MEPERITAB TAB 50MG	502	412	$5,211.88	3.96	1.22	$10.38
MEPERIDINE TAB 100MG	67	30	$1,119.20	2.88	2.23	$16.70
MEPERITAB TAB 100MG	55	32	$928.57	3.64	1.72	$16.88
DEMEROL INJ 100MG/ML	29	7	$183.73	1.23	4.14	$6.34
DEMEROL INJ 50MG/ML	24	12	$188.74	1.6	2	$7.86
MEPERIDINE INJ 100MG/ML	9	3	$194.31	2.27	3	$21.59
MEPERIDINE POW	4	3	$49.08	0.17	1.33	$12.27
DEMEROL INJ 75MG/ML	2	1	$8.46	0.1	2	$4.23
MEPERIDINE INJ 50MG/ML	1	1	$6.09	2	1	$6.09
SUBTOTAL	**2,254**	**1,532**	**$19,090.17**	**3.98**	**1.47**	**$8.47**
OXYMORPHONE LONG-ACTING PRODUCTS						
OPANA ER TAB 20MG	322	63	$137,535.78	2.06	5.11	$427.13
OPANA ER TAB 40MG	310	45	$275,830.96	2.35	6.89	$889.78
OPANA ER TAB 10MG	243	55	$56,629.23	1.98	4.42	$233.04
OPANA ER TAB 30MG	179	30	$104,695.05	1.99	5.97	$584.89

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
OXYMORPHONE TAB 15MG ER	35	6	$7,671.83	1.69	5.83	$219.20
OPANA ER TAB 5MG	18	10	$2,095.70	1.99	1.8	$116.43
OXYMORPHONE TAB 20MG ER	14	3	$4,596.63	2.12	4.67	$328.33
OPANA ER TAB 10MG	13	12	$2,621.41	2	1.08	$201.65
OXYMORPHONE TAB 30MG ER	8	4	$3,607.27	2	2	$450.91
OPANA ER TAB 20MG	8	5	$4,279.46	2.7	1.6	$534.93
OPANA ER TAB 30MG	7	5	$3,916.74	2	1.4	$559.53
OPANA ER TAB 15MG	7	4	$2,358.51	2	1.75	$336.93
OPANA ER TAB 5MG	4	3	$484.10	2	1.33	$121.03
OPANA ER TAB 40MG	4	3	$3,836.34	2.5	1.33	$959.09
OXYMORPHONE TAB 40MG ER	4	2	$4,117.14	3.5	2	$1,029.29
OXYMORPHONE TAB 10MG ER	1	1	$176.95	2	1	$176.95
SUBTOTAL	**1,177**	**173**	**$614,453.10**	**2.11**	**6.8**	**$522.05**
HYDROMORPHONE LONG-ACTING PRODUCTS						
EXALGO TAB 16MG	94	19	$89,828.97	1.58	4.95	$955.63
EXALGO TAB 12MG	29	12	$14,728.12	1.18	2.42	$507.87
EXALGO TAB 8MG	25	9	$7,480.66	1	2.78	$299.23
EXALGO TAB 32MG	9	1	$12,703.35	1.11	9	$1,411.48
SUBTOTAL	**157**	**32**	**$124,741.10**	**1.39**	**4.91**	**$794.53**
BUPRENORPHINE TRANSDERMAL PRODUCTS						
BUTRANS DIS 10MCG/HR	36	10	$7,944.98	0.14	3.6	$220.69
BUTRANS DIS 5MCG/HR	27	10	$3,942.52	0.14	2.7	$146.02
BUTRANS DIS 20MCG/HR	27	6	$9,552.82	0.14	4.5	$353.81
SUBTOTAL	**90**	**20**	**$21,440.32**	**0.14**	**4.5**	**$238.23**
TAPENTADOL LONG-ACTING PRODUCTS						
NUCYNTA ER TAB 100MG	25	14	$6,512.77	2	1.79	$260.51
NUCYNTA ER TAB 250MG	20	5	$9,456.40	2	4	$472.82
NUCYNTA ER TAB 200MG	12	3	$5,581.68	2	4	$465.14
NUCYNTA ER TAB 150MG	9	5	$3,258.30	2	1.8	$362.03
NUCYNTA ER TAB 50MG	8	6	$1,221.72	2	1.33	$152.72
SUBTOTAL	**74**	**26**	**$26,030.87**	**2**	**2.85**	$351.77
TRAMADOL LONG-ACTING PRODUCTS						
TRAMADOL HCL TAB 300MG ER	19	4	$2,818.85	1	4.75	$148.36
TRAMADOL HCL TAB 200MG ER	4	3	$470.86	1	1.33	$117.72
TRAMADOL HCL TAB 100MG ER	2	2	$142.50	1.13	1	$71.25
SUBTOTAL	**25**	**8**	**$3,432.21**	**1.01**	**3.13**	**$137.29**
TOTAL	**36,197**	***6,425**	**$7,645,661.94**	**2.13**	**5.63**	**$211.22**

*Total number of unduplicated members.

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Appendix I

Annual Review of Xolair® (Omalizumab)

Oklahoma Health Care Authority
July 2014

Manufacturer	Genentech | Novartis
Classification	Monoclonal Antibody
Status	Prescription Only

Introduction[1,2,3]

Xolair® (omalizumab), an anti-IgE antibody, was first approved in 2003 for moderate to severe persistent asthma in patients with a positive skin test or in vitro reactivity to a perennial aeroallergen and symptoms that are inadequately controlled with inhaled corticosteroids. In addition to the original indication, on March 21, 2014 the Food and Drug Administration (FDA) approved Xolair® for treatment of chronic idiopathic urticaria (CIU) in adults and adolescents (12 years of age and older) who remain symptomatic despite H1-antihistamine treatment.

Chronic idiopathic urticaria is defined as the occurrence of daily, or almost daily, wheals and itching for at least 6 weeks, with no identifiable cause. At any time, 0.5-1% of the population suffers from CIU, and most patients suffer from impaired quality of life. The peak age of CIU patients is between 20 and 40 years of age; approximately 90% of patients with CIU also have angioedema.

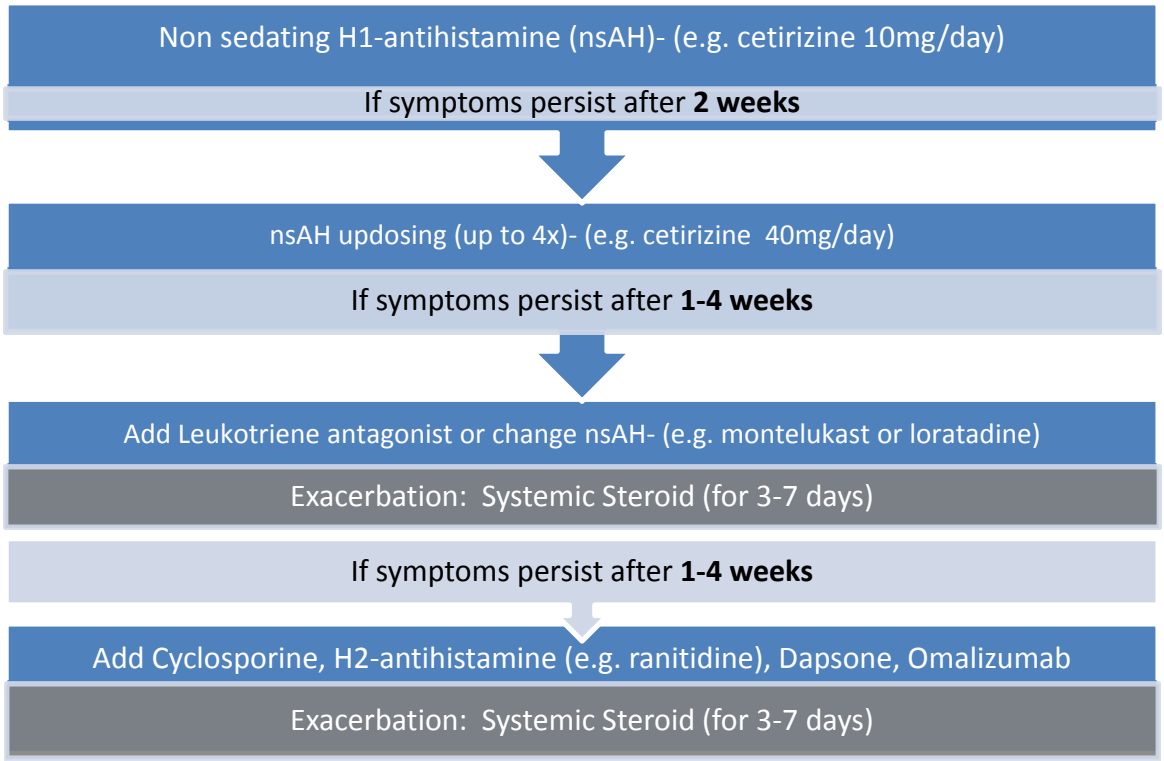
Current guidelines[1] recommend non-sedating H_1-antihistamine as first line treatment. H_1-antihistamines are effective in the majority of patients with CIU, but might not achieve complete control in all patents. For patients not responding to monotherapy with a second generation antihistamine at FDA approved doses, current European guidelines recommend up to a four-fold increase in dosage. If this is not effective, then the next line of treatment is to add a leukotriene antagonist, another non-sedating H_1-antihistamine, a H2-antagonist, or a first generation antihistamine to be taken at bedtime. If patients suffer an exacerbation, recommended treatment is a brief burst of oral corticosteroids.

Patients with chronic urticaria (CU) whose symptoms are not adequately controlled on maximal antihistamine therapy might be considered to have refractory CU and require alternative treatment. Cyclosporine and omalizumab have the greatest published experience for efficacy in patients with CU compared with other alternative agents. There is evidence from observational studies with cyclosporine, including long-term use, which suggests cyclosporine is efficacious in patients with refractory CU and capable of inducing remission. The American

[1]" European Academy of Allergy and Clinical Immunology (EAACI)/Global Allergy and Asthma European Network (GA^{2}LEN)/European Dermatology Forum (EDF)/World Allergy Organization (WAO) guideline: management of urticaria" and recently published practice parameter, "The diagnosis and management of acute and chronic urticarial:2014 update", by the American Academy of Allergy, Asthma, and Immunology (AAAAI), American College of Allergy, Asthma, and Immunology (ACAAI), and the Joint Council of Allergy, Asthma, and Immunology.

Academy of Allergy, Asthma, and Immunology (AAAAI)/American College of Allergy, Asthma, and Immunology (ACAAI) state omalizumab should be considered for refractory CU if a favorable benefit is suggested. The practitioner should take into account potential harm and cost as well as patient preferences since omalizumab is a subcutaneous injection that requires direct medical supervision and post-dose observation for a minimum of two hours.

EAACI/GA²LEN/EDF/WAO Recommended Treatment Algorithm for Chronic Urticaria**



** European Academy of Allergy and Clinical Immunology (EAACI)/Global Allergy and Asthma European Network (GA²LEN)/European Dermatology Forum (EDF)/World Allergy Organization (WAO) guideline

AAAAI/ACAAI** Recommended Step-Care Approach for Treatment of Chronic Urticaria

STEP 4
Add an alternative agent
- Omalizumab or cyclosporine
- Other anti-inflammatory agents, immunosuppressants, or biologics

STEP 3
Dose advancement of potent antihistamine (e.g., hydroxyzine or doxepin) as tolerated

STEP 2
One or more of the following:
- Dose advancement of 2nd generation antihistamine used in Step 1
- Add another second generation antihistamine (e.g. loratadine)
- Add H_2-antagonist (e.g. ranitidine)
- Add leukotriene receptor antagonist (e.g. montelukast)
- Add 1st generation antihistamine to be taken at bedtime (e.g. diphenhydramine)

STEP 1
- Monotherapy with second generation antihistamine (e.g. cetirizine)
- Avoidance of triggers (e.g., NSAIDs) and relevant physical factors if physical urticaria/angioedema syndrome is present

- Begin treatment at step appropriate for patient's level of severity and previous treatment history
- At each level of the step-approach, medication(s) should be assessed for patient tolerance and efficacy
- **"Step-down" in treatment is appropriate at any step, once consistent control of urticaria/angioedema is achieved**

**American Academy of Allergy, Asthma, and Immunology (AAAAI), American College of Allergy, Asthma, and Immunology (ACAAI), and the Joint Council of Allergy, Asthma, and Immunology

Current Prior Authorization Criteria for Persistent Asthma

Moderate to Severe Persistent Asthma Approval Criteria:

1. Member must be between 12 and 75 years of age; and
2. Member must have a diagnosis of severe persistent asthma (as per NAEPP guidelines); and
3. Member must have a positive skin test to at least one perennial aeroallergen; and
4. Member must have a pretreatment serum IgE level between 30 and 700 IU/mL; and
5. Member's weight must be between 30kg and 150kg; and
6. Member must have been on high-dose inhaled corticosteroid (as per NAEPP guidelines) for at minimum the past three months; and
7. Medication must be prescribed by either a pulmonary or an allergy/asthma specialist; and
8. Member must have been in the ER or hospitalized, due to an asthma exacerbation, twice in the past six months. Date of visits must be listed on petition. Or member must have been determined to be dependent on systemic steroids to prevent serious exacerbation; and
9. Prior Authorization request form and statement of medical necessity form must be submitted for processing

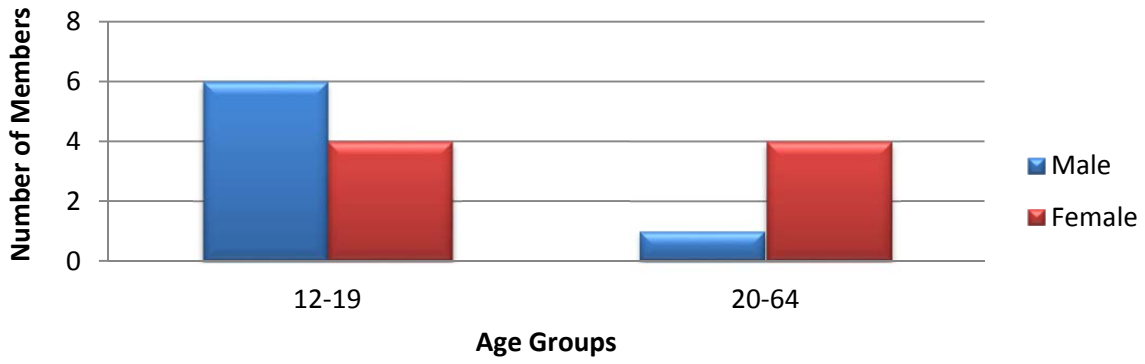
Utilization of Xolair®

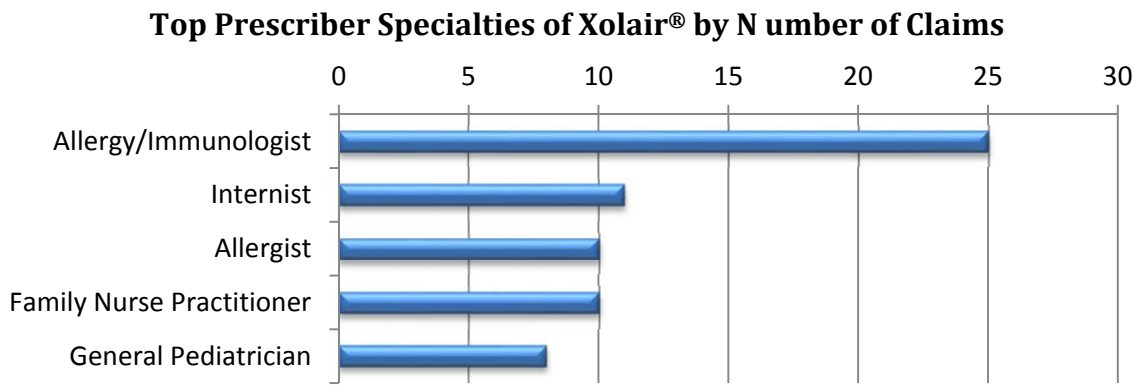
Comparison of Fiscal Years

Fiscal Year	Total Members*	Total Claims	Total Cost	Cost per Claim	Per-Diem Cost	Total Units	Total Days
2012	12	92	$188,815.06	$2,052.34	$73.07	304	2,584
2013	15	64	$147,436.95	$2,303.70	$81.77	208	1,803
% Change	**25.00%**	**-30.40%**	**-21.90%**	**12.20%**	**11.90%**	**-31.60%**	**-30.20%**
Change	**3**	**-28**	**-$41,378.11**	**$251.36**	**$8.70**	**-96**	**-781**

*Total number of unduplicated members

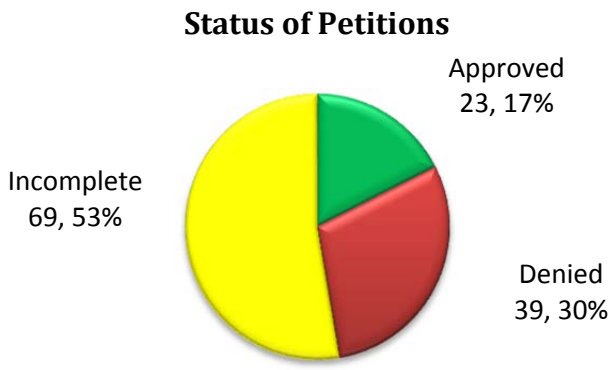
Demographics of Members Utilizing Xolair®





Prior Authorization of Xolair®

There was a total of 131 petitions submitted for Xolair® during fiscal year 2013. The following chart shows the status of the submitted petitions.



Xolair® (Omalizumab) Summary[4]

- **Indications:** Xolair® (omalizumab) is an anti-IgE antibody indicated for:
  - Moderate to severe persistent asthma in patients with positive skin test or in vitro reactivity to a perennial aeroallergen and symptoms that are inadequately controlled with inhaled corticosteroids.
  - Chronic idiopathic urticaria in adults and adolescents (12 years of age and older) who remain symptomatic despite H1-antihistamine treatment.

- **Dosing:**
  - Xolair® is available as a lyophilized, sterile powder in a single-use 5mL vial containing 150mg of omalizumab for reconstitution.
  - Xolair® is administered subcutaneously (SC) only.
  - Doses of more than 150mg should be divided among more than one injection site.
  - **Allergic Asthma:** Xolair® 150mg to 375mg SC every two or four weeks. Determine dose (mg) and dosing frequency by serum total IgE level (IU/mL), which should be measured before the start of treatment, and body weight (kg). Refer to dose determination charts in prescribing information.

- **Chronic Idiopathic Urticaria:** Xolair® 150mg or 300mg SC every four weeks. Dosing in CIU is not dependent on serum IgE level or body weight.

- **Mechanism of Action:**
  - **Allergic Asthma:** Xolair® inhibits the binding of IgE to the high-affinity IgE receptor (FcεRI) on the surface of mast cells and basophils. Reduction in surface-bound IgE on FcεRI-bearing cells limits the degree of release of mediators of the allergic response. Treatment with Xolair® also reduces the number of FcεRI receptors on basophils in atopic patients.
  - **Chronic Idiopathic Urticaria:** Xolair® binds to IgE and lowers free IgE levels. Subsequently, IgE receptors (FcεRI) on cells down-regulate. The mechanism by which these effects of Xolair® result in an improvement of CIU symptoms is unknown.

- **Contraindications:** Severe hypersensitivity reaction to Xolair® or any ingredient of Xolair®.

- **Efficacy: Chronic Idiopathic Urticaria**
  - The efficacy of Xolair® for the treatment of chronic idiopathic urticaria was evaluated in two placebo-controlled, multiple-dose clinical studies. Patients received Xolair® 75mg, 150mg, or 300mg or placebo by SC injection every four weeks in addition to their baseline level of H1 antihistamine therapy for 24 or 12 weeks, followed by a 16 week washout observation period. A total of 640 patients were included in the efficacy analyses.
  - Disease severity was measured by weekly urticaria activity score (UAS7, range 0-42) which is a composite of the weekly itch severity score (range 0-21) and the weekly hive count score (range 0-21). All patients were required to have a UAS7 of $\geq$ 16, and a weekly itch severity score of $\geq$ 8 for the 7 days prior to randomization despite having used an H1 antihistamine at an approved dose for at least 2 weeks.
  - In both CIU studies, patients who received Xolair® 150mg and 300mg had greater decreases from baseline in weekly itch severity scores and weekly hive count scores than placebo at Week 12. The 75mg dose did not demonstrate consistent evidence of efficacy and is not approved for use.
  - The appropriate duration of therapy for CIU with Xolair® has not been determined.

- **Safety:** The use of Xolair® has a black box warning for anaphylaxis. Anaphylaxis, presenting as bronchospasm, hypotension, syncope, urticaria, or angioedema of the throat or tongue, has been reported to occur after administration of Xolair®. Anaphylaxis has occurred after the first dose of Xolair® but also has occurred beyond one year after beginning treatment. Patients must be closely monitored for an appropriate period of time after Xolair® administration and be prepared to manage anaphylaxis that can be life-threatening. Patients should be informed on the signs and symptoms of anaphylaxis and should seek immediate medical care should symptoms occur.

- **Cost:**

Medication	Dose	Cost Per Unit*	Cost for 4 Weeks of Therapy
Xolair® 150mg vial	150mg-300mg every 4 weeks	$794.85¥	$794.85-$1,589.70
Cetirizine 10mg tablets	10mg-40mg daily+	$0.12	$3.36-$13.44
Loratadine 10mg tablets	10mg-40mg daily+	$0.12	$3.36-$13.44
Montelukast 10mg tablets	10mg daily	$0.33	$9.24
Cyclosporine 100mg capsules	100mg-150mg twice daily**	$2.62	$146.72-$220.08

¥ Xolair® units are per vial. All other units are per tablet.
*SMAC = state maximum allowable cost.
+Range from FDA maximum dosage to four times FDA maximum dosage.
**Based on 200mg-300mg daily dose to reflect average dosage range of 2.5 mg/kg to 4 mg/kg per day.

Recommendations

The College of Pharmacy recommends updating the prior authorization of Xolair® (omalizumab) with the following criteria for the diagnosis of chronic idiopathic urticaria:

1. Member must be ≥12 years of age; and
2. Other forms of urticaria must be ruled out; and
3. Other potential causes must be ruled out; and
4. Member must have an Urticaria Activity Score+ (UAS) ≥16; and
5. Prescriber must be an allergist, immunologist, or dermatologist; and
6. Member has tried and failed to obtain relief from other treatments* including the following trials within the last six months (member must fail all classes unless contraindicated):
   I. At least two different H1-antihistamine trials for a minimum duration of two weeks each:
      a. One trial must be a second generation antihistamine dosed four times the maximum FDA dose as recommended by EEACI/GA^{2}LEN** guidelines; and
      b. One trial must be tried in combination with an H2-antihistamine; and
   II. A 4-week trial of a leukotriene receptor antagonist in combination with an H1-antihistamine; and
   III. A 4-week trial of doxepin 10mg-50mg daily; and
   IV. An 8-week trial of cyclosporine daily titrated to maximum recommended dose (4 mg/kg daily)
7. Initial dosing will only be approved at 150mg every four weeks. If the 150mg dose yields inadequate results, then the dose may be increased to 300mg every four weeks.

+See Attachment A
*Oral corticosteroids are only used for short term management
** European Academy of Allergy and Clinical Immunology (EAACI)/Global Allergy and Asthma European Network (GA^{2}LEN)/European Dermatology Forum (EDF)/World Allergy Organization (WAO)

Attachment A

Urticaria activity score (UAS) [5, 6]

The UAS consists of the sum of the wheal number score and the itch severity score.

The wheal numbers are graded from 0 to 3 as follows:

0- Less than 10 small wheals (diameter, < 3 cm);
1- 10 to 50 small wheals or less than 10 large wheals (diameter, > 3 cm);
2- Greater than 50 small wheals or 10 to 50 large wheals;
3- Almost the whole body is covered

The severity of the itching is graded from 0 to 3 as follows:

0- None;
1- Mild;
2- Moderate;
3- Severe

Daily Scores are added to provide the weekly score.

Score	Wheals	Itch
0	0 to 10 small wheals (<3 cm in diameter)	None
1	10 to 50 wheals <3 cm in diameter or 1 to 10 wheals >3 cm in diameter	Mild
2	>50 small wheals or 10 to 50 large wheals	Moderate
3	Nearly whole body covered in wheals	Severe

Day	Daily Score- Wheals	Daily Score- Itch
Monday or Day 1		
Tuesday or Day 2		
Wednesday or Day 3		
Thursday or Day 4		
Friday or Day 5		
Saturday or Day 6		
Sunday or Day 7		
Weekly Subtotal Score		
	Wheals Weekly Score + Itch Weekly Score=	
Total Weekly UAS		

[1] Kim, Sujeong, Seunghee Baek, Bomi Shin, Sun-Young Yoon, So Young Park, Taehoon Lee, Yoon Su Lee, Yun-Jeong Bae, Hyouk Soo Kwon, You Sook Cho, Hee-Bom Moon, Tae-Bum Kim, and Salik Hussain. "Influence of Initial Treatment Modality on Long-Term Control of Chronic Idiopathic Urticaria." *PLoS ONE* 8.7 (2013): E69345. Available online at http://web.b.ebscohost.com/ehost/pdfviewer/pdfviewer?sid=6310f81e-7875-4afc-81e4-e12111d3c073%40sessionmgr198&vid=2&hid=114. Last accessed 04/18/2014.

[2] Zuberbier, T., R. Asero, C. Bindslev-Jensen, G. Walter Canonica, M. K. Church, A. M. Giménez-Arnau, C. E. H. Grattan, A. Kapp, M. Maurer, H. F. Merk, B. Rogala, S. Saini, M. Sánchez-Borges, P. Schmid-Grendelmeier, H. Schünemann, P. Staubach, G. A. Vena, and B. Wedi. "EAACI/GA²LEN/EDF/WAO Guideline: Management of Urticaria." *Allergy* 64.10 (2009): 1427-443. Available online at: http://www.ga2len.net/464D9d01.pdf. Last accessed 04/18/2014.

[3] Md, Jonathan A. Bernstein. "The Diagnosis and Management of Acute and Chronic Urticaria: 2014 Update." Available online at: http://www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Practice%20and%20Parameters/Urticaria-2014.pdf. Last accessed 06/18/2014.

[4] Xolair® Product Information. Genetech, Inc. Available online at: http://www.gene.com/download/pdf/xolair_prescribing.pdf. Last revised 03/2014. Last accessed 04/21/2014.

[5] Engin, B., and M. Ozdemir. "Prospective Randomized Non-blinded Clinical Trial on the Use of Dapsone plus Antihistamine vs. Antihistamine in Patients with Chronic Idiopathic Urticaria." Available online at: http://www.hopkinscme.edu/ofp/emeddermreview/newsletters/2012/0412.html. Last accessed 02 June 2014.

[6] Bhor U, Pande S. Scoring systems in dermatology. Indian J Dermatol Venereol Leprol [serial online] 2006 [cited 2014 Jun 2];72:315-21. Available from: http://www.ijdvl.com/text.asp?2006/72/4/315/26722. Last accessed: June 2, 2014.

Appendix J

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

FDA NEWS RELEASE

For Immediate Release: June 20, 2014
FDA approves Sivextro to treat skin infections

The U.S. Food and Drug Administration today approved Sivextro (tedizolid phosphate), a new antibacterial drug, to treat adults with skin infections.
Sivextro is approved to treat patients with acute bacterial skin and skin structure infections (ABSSSI) caused by certain susceptible bacteria, including Staphylococcus aureus (including methicillin-resistant strains (MRSA) and methicillin-susceptible strains), various Streptococcus species, and Enterococcus faecalis. Sivextro is available for intravenous and oral use.
Sivextro is the second new antibacterial drug approved by the FDA in the past month to treat ABSSSI. On May 23, the agency approved Dalvance (dalbavancin), also to treat patients with ABSSSI caused by Staphylococcus aureus and various Streptococcus species.
The application for Sivextro, intended to treat serious or life-threatening infections, was designated as a qualified infectious disease product (QIDP) and received an expedited review. Sivextro's QIDP designation also qualifies it for an additional five years of marketing exclusivity to be added to certain exclusivity periods already provided by the Food, Drug and Cosmetic Act.
Sivextro's safety and efficacy were evaluated in two clinical trials with 1,315 adults with ABSSSI. Participants were randomly assigned to receive Sivextro or linezolid, another antibacterial drug approved to treat ABSSSI. Results showed Sivextro was as effective as linezolid for the treatment of ABSSSI.
The most common side effects identified in the clinical trials were nausea, headache, diarrhea, vomiting and dizziness. The safety and efficacy of Sivextro have not been evaluated in patients with decreased levels of white blood cells (neutropenia), so alternative therapies should be considered.
Sivextro is marketed by Cubist Pharmaceuticals, based in Lexington, Massachusetts.

FDA NEWS RELEASE

For Immediate Release: June 27, 2014
FDA approves Afrezza to treat diabetes

The U.S. Food and Drug Administration today approved Afrezza (insulin human) Inhalation Powder, a rapid-acting inhaled insulin to improve glycemic control in adults with diabetes mellitus. Afrezza is a rapid-acting inhaled insulin that is administered at the beginning of each meal.
An estimated 25.8 million (18.8 million diagnosed and 7.0 million undiagnosed) people in the United States or approximately 8.3 percent of the population–have diabetes. Over time, high blood sugar levels can increase the risk for serious complications, including heart disease, blindness and nerve and kidney damage.
The drug's safety and effectiveness were evaluated in a total of 3,017 participants–1,026 participants with type 1 diabetes and 1,991 patients with type 2 diabetes. The efficacy of mealtime Afrezza in adult patients with type 1 diabetes patients was compared to mealtime insulin aspart (fast-acting insulin), both in combination with basal insulin (long-acting insulin) in a 24 week study. At week 24, treatment with basal insulin and mealtime Afrezza provided a mean reduction in HbA1c that met the pre-specified non-inferiority margin of 0.4 percent. Afrezza provided less HbA1c reduction than insulin aspart, and the difference was statistically significant. Afrezza was studied in adults with type 2 diabetes in combination with oral antidiabetic drugs; the efficacy of mealtime Afrezza in type 2 diabetes patients was compared to placebo inhalation in a 24 week study. At week 24, treatment with Afrezza plus oral antidiabetic drugs provided a mean reduction in HbA1c that was statistically significantly greater compared to the HbA1c reduction observed in the placebo group.
Afrezza is not a substitute for long-acting insulin. Afrezza must be used in combination with long-acting insulin in patients with type 1 diabetes, and it is not recommended for the treatment of diabetic ketoacidosis, or in patients who smoke.

Afrezza has a Boxed Warning advising that acute bronchospasm has been observed in patients with asthma and chronic obstructive pulmonary disease (COPD). Afrezza should not be used in patients with chronic lung disease, such as asthma or COPD because of this risk. The most common adverse reactions associated with Afrezza in clinical trials were hypoglycemia, cough, and throat pain or irritation.
The FDA approved Afrezza with a Risk Evaluation and Mitigation Strategy, which consists of a communication plan to inform health care professionals about the serious risk of acute bronchospasm associated with Afrezza.
The FDA is requiring the following post-marketing studies for Afrezza:

- a clinical trial to evaluate pharmacokinetics, safety and efficacy in pediatric patients;
- a clinical trial to evaluate the potential risk of pulmonary malignancy with Afrezza (this trial will also assess cardiovascular risk and the long-term effect of Afrezza on pulmonary function);
- two pharmacokinetic-pharmacodynamic euglycemic glucose-clamp clinical trials, one to characterize dose-response and one to characterize within-subject variability.

Afrezza is manufactured by MannKind Corporation, Danbury, Connecticut.

Safety Announcements

FDA adding general warning to testosterone products about potential for venous blood clots

[06/19/2014] The U.S. Food and Drug Administration (FDA) is requiring manufacturers to include a general warning in the drug labeling of all approved testosterone products about the risk of blood clots in the veins. Blood clots in the veins, also known as venous thromboembolism (VTE), include deep vein thrombosis (DVT) and pulmonary embolism (PE). The risk of venous blood clots is already included in the labeling of testosterone products as a possible consequence of polycythemia, an abnormal increase in the number of red blood cells that sometimes occurs with testosterone treatment. Because there have been postmarket reports of venous blood clots unrelated to polycythemia, FDA is requiring a change to drug labeling of all testosterone products to provide a more general warning regarding venous blood clots and to ensure this risk is described consistently in the labeling of all approved testosterone products.
Because these clots occur in the veins, this new warning is not related to FDA's ongoing evaluation of the possible risk of stroke, heart attack, and death in patients taking testosterone products. We are currently evaluating the potential risk of these cardiovascular events, which are related to blood clots in the arteries and are described in the Drug Safety Communication posted on January 31, 2014.
Testosterone products are FDA-approved for use in men who lack or have low testosterone levels in conjunction with an associated medical condition. Examples of these conditions include failure of the testicles to produce testosterone for reasons such as genetic problems or chemotherapy.
FDA asks health care professionals and consumers to report any adverse reactions to the FDA's MedWatch Safety Information and Adverse Event Reporting program.

Safety Announcements

FDA Drug Safety Communication: FDA review of cardiovascular risks for diabetics taking hypertension drug olmesartan not conclusive; label updates required

[6-24-2014] The U.S. Food and Drug Administration (FDA) has completed its safety review and has found no clear evidence of increased cardiovascular risks associated with use of the blood pressure medication olmesartan in diabetic patients. As a result, our recommendations for use of olmesartan (Benicar, Benicar HCT, Azor, Tribenzor, and generics) will remain the same, but we will require information about some of the studies to be included in the drug labels. Patients should discuss any questions they have with their health care professionals.
It is important to take olmesartan and other blood pressure medicines because uncontrolled high blood pressure increases the risks of cardiovascular problems such as heart disease and stroke, as well as kidney failure and other health problems. Do not stop taking olmesartan or any blood pressure medication without first discussing it with your health care professional.
This safety review was prompted by the results of the ROADMAP trial. The ROADMAP (**R**andomized **O**lmesartan and **D**iabetes **M**icroalbuminuria **P**revention) clinical trial examined the effects of olmesartan in patients with type 2 diabetes, to see whether olmesartan could delay kidney damage. There was an

unexpected finding of increased risk of cardiovascular death in the olmesartan group compared to the group taking a placebo, or sugar pill. However, the risk of non-fatal heart attack was lower in the olmesartan-treated patients.

To evaluate these findings, we reviewed additional studies, including a large study in Medicare patients. While data from the ROADMAP trial and the Medicare study have suggested that high-dose olmesartan may increase cardiovascular risk in diabetic patients, when considering the data from all trials and studies, they are not conclusive. Overall, we have determined that these studies do not clearly show an increased cardiovascular risk. Thus, the collective evidence available at this time does not support changing our recommendations for olmesartan use and does not support recommending that its use be avoided in patients with diabetes.

Olmesartan is a type of blood pressure medicine called an angiotensin receptor blocker, or ARB. In 2013, there were approximately 1.8 million patients who received a dispensed prescription for olmesartan-containing products from U.S. outpatient retail pharmacies.

We urge health care professionals and patients to report side effects involving olmesartan to the FDA MedWatch program.

Safety Announcements

FDA Drug Safety Communication: FDA warns of rare but serious hypersensitivity reactions with certain over-the-counter topical acne products

[6-25-2014] The U.S. Food and Drug Administration (FDA) is warning that certain over-the-counter (OTC) topical acne products can cause rare but serious and potentially life-threatening allergic reactions or severe irritation. Consumers should stop using their topical acne product and seek emergency medical attention immediately if they experience hypersensitivity reactions such as throat tightness; difficulty breathing; feeling faint; or swelling of the eyes, face, lips, or tongue. Consumers should also stop using the product if they develop hives or itching.

These serious hypersensitivity reactions differ from the local skin irritation that may occur at the product application site, such as redness, burning, dryness, itching, peeling, or slight swelling, that are already included in the Drug Facts labels.

Based on the information reported to FDA, we cannot determine if the serious hypersensitivity reactions were triggered by the acne products' active ingredients, benzoyl peroxide or salicylic acid, the inactive ingredients, or by a combination of both. The hypersensitivity reactions may occur within minutes to a day or longer after product use. The OTC topical acne products of concern are marketed under various brand names such as Proactiv, Neutrogena, MaxClarity, Oxy, Ambi, Aveeno, Clean & Clear, and as store brands. They are available as gels, lotions, face washes, solutions, cleansing pads, toners, face scrubs, and other products.

Manufacturers of OTC topical acne drug products have the option to add label directions for sensitivity testing for new users of their products. We encourage new users of OTC topical acne drug products to follow these directions. We are also encouraging manufacturers to add these directions to all product labels, to reduce the risk of serious hypersensitivity reactions. According to these directions, before using an OTC topical acne product for the first time, consumers should apply a small amount to one or two small affected areas of the skin for 3 days. If no discomfort occurs, then the product can be used according to the directions on the Drug Facts label. Consumers should avoid using an OTC topical acne product again if they have previously experienced a hypersensitivity reaction with its use.

Safety Announcements

FDA Drug Safety Communication: FDA recommends not using lidocaine to treat teething pain and requires new Boxed Warning

[6-26-2014] The U.S. Food and Drug Administration (FDA) warns that prescription oral viscous lidocaine 2 percent solution should not be used to treat infants and children with teething pain. We are requiring a new *Boxed Warning*, FDA's strongest warning, to be added to the drug label to highlight this information. Oral viscous lidocaine solution is not approved to treat teething pain, and use in infants and young children can cause serious harm, including death.

Health care professionals should not prescribe or recommend this product for teething pain. Parents and caregivers should follow the American Academy of Pediatrics' recommendations for treating teething pain:

- Use a teething ring chilled in the refrigerator (not frozen).
- Gently rub or massage the child's gums with your finger to relieve the symptoms.

Topical pain relievers and medications that are rubbed on the gums are not necessary or even useful because they wash out of the baby's mouth within minutes. When too much viscous lidocaine is given to infants and young children or they accidentally swallow too much, it can result in seizures, severe brain injury, and problems with the heart. Cases of overdose due to wrong dosing or accidental ingestion have resulted in infants and children being hospitalized or dying.

In 2014, FDA reviewed 22 case reports of serious adverse reactions, including deaths, in infants and young children 5 months to 3.5 years of age who were given oral viscous lidocaine 2 percent solution for the treatment of mouth pain, including teething and stomatitis, or who had accidental ingestions. In addition to the *Boxed Warning*, we are requiring revisions to the *Warnings* and *Dosage and Administration* sections of the drug label to describe the risk of severe adverse events and to include additional instructions for dosing when the drug is prescribed for approved uses.

FDA is also encouraging parents and caregivers not to use topical medications for teething pain that are available over the counter (OTC) because some of them can be harmful. We advise following the American Academy of Pediatrics' recommendations listed above to help lessen teething pain.

FDA previously communicated about safety concerns related to use of OTC topical benzocaine teething preparations. In 2011, we warned that using OTC benzocaine gels for teething or mouth pain can cause a rare but serious condition called methemoglobinemia. This condition results in a large decrease in the amount of oxygen carried through the blood. It is life-threatening and can result in death. FDA has continued to receive reports of methemoglobinemia in infants and children associated with OTC benzocaine gels and liquids since the 2011 warning was issued. OTC benzocaine gels and liquids are sold under different brand names such as Anbesol, Hurricaine, Orajel, Baby Orajel, Orabase, and various store brands.

Safety Announcements

FDA Drug Safety Communication: FDA warns that cancer drug docetaxel may cause symptoms of alcohol intoxication after treatment

[[6-20-2014] The U.S. Food and Drug Administration (FDA) is warning that the intravenous chemotherapy drug docetaxel contains ethanol, also known as alcohol, which may cause patients to experience intoxication or feel drunk during and after treatment. We are revising the labels of all docetaxel drug products to warn about this risk. Health care professionals should consider the alcohol content of docetaxel when prescribing or administering the drug to patients, particularly in those whom alcohol intake should be avoided or minimized and when using it in conjunction with other medications.

Patients should be aware that docetaxel may cause them to become intoxicated from the alcohol it contains. Patients should avoid driving, operating machinery, or performing other activities that are dangerous for one to two hours after the infusion of docetaxel. In addition, some medications, such as pain relievers and sleep aids, may interact with the alcohol in the docetaxel infusion and worsen the intoxicating effects.

Docetaxel is a prescription chemotherapy drug used to treat different kinds of cancer, including cancers of the breast, prostate, stomach, head and neck cancers, and non-small-cell lung cancer. Several forms of docetaxel are currently marketed, including generics and the brand-name products Taxotere, Docefrez, and Docetaxel Injection. The various products contain different amounts of alcohol, which is used to dissolve the active ingredients so docetaxel can be given intravenously. Health care professionals should be aware of the differences in formulations in order to monitor and counsel patients appropriately.

Current Drug Shortages Index (as of July 2, 2014):

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

Amikacin Injection

Ammonium Chloride Injection

Atropine Sulfate Injection

Barium Sulfate for Suspension
Bumetanide Injection
Bupivacaine Hydrochloride (Marcaine, Sensorcaine) Injection
Caffeine Anhydrous (125mg/mL); Sodium Benzoate (125mg/mL) Injection[12]
Calcium Gluconate Injection
Cefazolin Injection
Chloramphenicol Sodium Succinate Injection
Chromic Chloride Injection
Cidofovir Injection
Clindamycin Phosphate (Cleocin) Injection
Copper Injection
Cyanocobalamin (Vitamin B12) Injection
Daunorubicin Hydrochloride Solution for Injection
Dexamethasone Sodium Phosphate Injection
Dexmethylphenidate Hydrochloride (Focalin) Tablet
Dextrose 5% Injection Bags
Dextrose 50% Injection
Doxorubicin (Adriamycin) Lyophilized Powder
Ephedrine Sulfate Injection
Epinephrine 1mg/mL (Preservative Free)[13]
Epinephrine Injection
Erythrocin Lactobionate Lyophilized Powder for Injection
Ethiodol (Ethiodized Oil) Ampules
Fentanyl Citrate (Sublimaze) Injection
Haloperidol Lactate Injection
Heparin Sodium Injection
Indigo Carmine Injection
Leucovorin Calcium Lyophilized Powder for Injection
Leuprolide Acetate Injection
Lidocaine Hydrochloride (Xylocaine) Injection
Liotrix (Thyrolar) Tablets
Lorazepam (Ativan) Injection
Magnesium Sulfate Injection
Mecasermin [rDNA origin] (Increlex) Injection
Methazolamide (Neptazane) Tablets
Methyldopate Hydrochloride Injection
Methylin Chewable Tablets
Methylphenidate Hydrochloride ER Capsules/Tablets
Methylphenidate Hydrochloride Tablets
Methylprednisolone Sodium Succinate Injection
Morphine Sulfate (Astramorph PF, Duramorph, Infumorph) Injection (Preservative Free)
Multi-Vitamin Infusion (Adult and Pediatric)
Nalbuphine Hydrochloride (Nubain) Injection
Nitroglycerin (Nitronal) Injection
Nitroglycerin in 5% Dextrose Injection
Ondansetron (Zofran) Injection
Pancuronium Bromide Injection
Papaverine Hydrochloride Injection
Phosphate (Glycophos) Injection
Piperacillin and Tazobactam (Zosyn) Injection

Potassium Acetate Injection, USP 2mEq/mL[15]
Potassium Chloride Injection
Potassium Phosphate Injection
Procainamide HCL Injection
Reserpine Tablets
Rifampin for Injection
Secretin Synthetic Human (ChiRhoStim) Injection
Selenium Injection
Sincalide (Kinevac) Lyophilized Powder for Injection
Sodium Chloride 0.9% Injection Bags
Sodium Chloride 23.4% Injection
Sodium Phosphate Injection
Succinylcholine (Anectine, Quelicin) Injection
Sufentanil Citrate (Sufenta) Injection
Tesamorelin (Egrifta) Injection Kit
Tetracycline Capsules
Thiotepa (Thioplex) for Injection
Tiopronin (Thiola)
Tobramycin Solution for Injection
Trace Elements
Verapamil Hydrochloride Injection, USP
Vitamin A Palmitate (Aquasol A) Injection
Zinc Injection