Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
September 9, 2015
4 p.m.

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

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 – September 9, 2015

DATE: September 1, 2015

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

Call to Order

Public Comment Forum

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

Update on Medication Coverage Authorization Unit/FDA Safety Alerts – Appendix B

Action Item – Vote to Prior Authorize Hysingla® ER (Hydrocodone Bitartrate Extended-Release) – Appendix C

Action Item – Vote to Prior Authorize Various Special Formulations: Sitavig® (Acyclovir Buccal Tablets), Rasuvo® (Methotrexate Injection), Otrexup™ (Methotrexate Injection), Onmel® (Itraconazole Oral Tablets), & Purixan® (Mercaptopurine Oral Suspension) – Appendix D

Action Item – Vote to Prior Authorize Namzaric™ (Memantine Extended-Release/Donepezil) – Appendix E

Action Item – Vote to Prior Authorize Irenka™ (Duloxetine) – Appendix F

Action Item – Vote to Prior Authorize Corlanor® (Ivabradine) – Appendix G

30-Day Notice to Prior Authorize Tykerb® (Lapatinib), Halaven® (Eribulin), Ixempra® (Ixabepilone), Kadcyla® (Ado-trastuzumab), Afinitor® (Everolimus), & Perjeta® (Pertuzumab) – Appendix H

30-Day Notice to Prior Authorize Orkambi™ (Lumacaftor/Ivacaftor) – Appendix I

Action Item – Annual Review of Synagis® (Palivizumab) – Appendix J

Annual Review of Antihyperlipidemics and 30-Day Notice to Prior Authorize Epanova® (Omega-3-Carboxylic Acids), Praluent® (Alirocumab), and Repatha™ (Evolocumab) – Appendix K

Annual Review of Anticoagulants and Platelet Aggregation Inhibitors and 30-Day Notice to Prior Authorize Savaysa™ (Edoxaban) – Appendix L

FDA and DEA Updates – Appendix M

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – September 9, 2015 @ 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. July 8, 2015 DUR Minutes – Vote
   B. July 8, 2015 DUR Recommendations Memorandum

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

4. **Update on Medication Coverage Authorization Unit/FDA Safety Alerts – See Appendix B**
   A. Medication Coverage Activity for July 2015
   B. Pharmacy Help Desk Activity for July 2015
   C. Medication Coverage Activity for August 2015
   D. Pharmacy Help Desk Activity for August 2015
   E. FDA Safety Alerts

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

5. **Action Item – Vote to Prior Authorize Hysingla® ER (Hydrocodone Bitartrate Extended-Release) – See Appendix C**
   A. College of Pharmacy Recommendations

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

6. **Action Item – Vote to Prior Authorize Various Special Formulations: Sitavig® (Acyclovir Buccal Tablets), Rasuvo® (Methotrexate Injection), Otrexup™ (Methotrexate Injection), Onmel® (Itraconazole Oral Tablets), & Purixan® (Mercaptopurine Oral Suspension) – See Appendix D**
   A. College of Pharmacy Recommendations

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

7. **Action Item – Vote to Prior Authorize Namzaric™ (Memantine Extended-Release/Donepezil) – See Appendix E**
   A. College of Pharmacy Recommendations

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

8. **Action Item – Vote to Prior Authorize Irenka™ (Duloxetine) – See Appendix F**
   A. College of Pharmacy Recommendations

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

9. Action Item – Vote to Prior Authorize Corlanor® (Ivabradine) – See Appendix G

A. College of Pharmacy Recommendations

Items to be presented by Dr. Schmidt, Dr. Borders, Dr. Medina, Dr. Muchmore, Chairman:

10. 30-Day Notice to Prior Authorize Tykerb® (Lapatinib), Halaven® (Eribulin), Ixempra® (Ixabepilone), Kadcyla® (Ado-trastuzumab), Afinitor® (Everolimus), & Perjeta® (Pertuzumab) – See Appendix H

A. Introduction
B. Utilization of Oncology Medications
C. Utilization of Breast Cancer Medications
D. Market News and Updates
E. Product Summaries
F. Recommendations
G. Utilization Details of Breast Cancer Medications

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

11. 30-Day Notice to Prior Authorize Orkambi™ (Lumacaftor/Ivacaftor) – See Appendix I

A. Introduction
B. Orkambi™ (Lumacaftor/Ivacaftor) Product Summary
C. College of Pharmacy Recommendations

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

12. Action Item – Annual Review of Synagis® (Palivizumab) – See Appendix J

A. Current Prior Authorization Criteria
B. Utilization of Palivizumab
C. Prior Authorization of Palivizumab
D. Referrals to Care Management Services
E. Market News and Updates
F. Guidance for Palivizumab Prophylaxis
G. Palivizumab Claims Analysis
H. College of Pharmacy Recommendations

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

13. Annual Review of Antihyperlipidemics and 30-Day Notice to Prior Authorize Epanova® (Omega-3-Carboxylic Acids), Praluent® (Alirocumab), and Repatha™ (Evolocumab) – See Appendix K

A. Current Prior Authorization Criteria
B. Utilization of Antihyperlipidemics
C. Prior Authorization of Antihyperlipidemics
D. Market News and Updates
E. Epanova® (Omega-3-Carboxylic Acids) Product Summary
F. Praluent® (Alirocumab) Product Summary
G. Repatha™ (Evolocumab) Product Summary
H. Place in Therapy: PCSK9 Inhibitors
I. Cost Comparison: High-Intensity Statins and PCSK9 Inhibitors
J. College of Pharmacy Recommendations
K. Utilization Details of Statins and Zetia® (Ezetimibe)
L. Utilization Details of Lovaza® (Omega-3-Acid Ethyl Esters) and Vascepa® (Icosapent Ethyl)
M. Utilization Details of Juxtapid® (Lomitapide) and Kynamro® (Mipomersen)
N. Attachment A: Diagnosis of Heterozygous Familial Hypercholesterolemia (HeFH)
O. Attachment B: Framingham Heart Study & Framingham Risk Score
P. Draft PCSK9 Inhibitor Prior Authorization Form

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

14. Annual Review of Anticoagulants and Platelet Aggregation Inhibitors and 30-Day Notice to Prior Authorize Savaysa™ (Edoxaban) – See Appendix L

A. Current Prior Authorization Criteria
B. Utilization of Anticoagulants and Platelet Aggregation Inhibitors
C. Prior Authorization of Anticoagulants and Platelet Aggregation Inhibitors
D. Oral Anticoagulants and Platelet Aggregation Inhibitors: Utilization Trends
E. Market News and Updates
F. Savaysa™ (Edoxaban) Product Summary
G. College of Pharmacy Recommendations
H. Utilization Details of Anticoagulants
I. Utilization Details of Platelet Aggregation Inhibitors

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

15. FDA and DEA Updates – See Appendix M

Items to be presented by Dr. Muchmore, Chairman:

16. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF JULY 8, 2015

BOARD MEMBERS:	PRESENT	ABSENT
Theresa Garton, M.D.	x	
Carla Hardzog-Britt, M.D.	x	
Anetta Harrell, Pharm.D.	x	
Ashley Huddleston, 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 Winegardner, 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	
Erin Ford, Pharm.D.; Clinical Pharmacist		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
Ashley Teel, Pharm.D.; Clinical Pharmacist	x	
Grace Hsu, Pharm.D.; Clinical Pharmacist	x	
Jacquelyn Travers, Pharm.D.; Academic Detailing Pharmacist	x	
Graduate Students: Christina Bulkley, Pharm.D.	x	
David George, Pharm.D.		x
Tammy Lambert, Pharm.D.		x
Timothy Pham, Pharm.D.	x	
Visiting Pharmacy Student(s): Marisa Irving	x	

	PRESENT	ABSENT
Marlene Asmussen, R.N.; Population Care Management Director	x	
Burl Beasley, D.Ph.; M.P.H.; M.S. Pharm	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	
Jill Ratterman, D.Ph.; Clinical Pharmacist	x	
Garth Splinter, M.D.; MBA; Medicaid Director	x	
Joseph Young, Deputy General Counsel IV	x	
Kerri Wade, Pharmacy Operations Manager	x	

OTHERS PRESENT:		
Mark DeClerk, Lilly	Dan Keeney, BDSI	Jim Fowler, AstraZeneca
Jason Schwier , Amgen	Phillip Lafferty, Celgene	Jim Chapman, AbbVie
Mindy Brown, Celgene	James McAdams, OREXO	Rick Ulasewich, DSI
Richard Ponder, J&J	Kelly Eldridge, Teva	Brian Maves, Pfizer
Aaron Zimmerman, Teva Pharm	Elizabeth Ariano, Indivior	Audrey Rattan, Alkermes
Ron Schnare, Shire	Jon Maguire, GSK	

PRESENT FOR PUBLIC COMMENT:	
Cynthia Patterson	Bio Delivery
M. Lane Peyton, M.D.	Rivus

AGENDA ITEM NO. 1: CALL TO ORDER

1A: ROLL CALL

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 2: PUBLIC COMMENT FORUM

2A: AGENDA NO. 16 SPEAKER: CYNTHIA PATTERSON

2B: AGENDA NO. 16 SPEAKER: M. LANE PEYTON, M.D.

ACTION: NONE REQUIRED

AGENDA ITEM NO. 3: APPROVAL OF DUR BOARD MINUTES

3A: JUNE 10, 2015 DUR MINUTES – VOTE

3B: JUNE 10, 2015 DUR RECOMMENDATIONS MEMORANDUM

Materials included in agenda packet; presented by Dr. Muchmore

Dr. Harrell moved to approve; seconded by Dr. Hardzog-Britt

ACTION: MOTION CARRIED

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

4A: MEDICATION COVERAGE ACTIVITY FOR JUNE 2015

4B: PHARMACY HELP DESK ACTIVITY FOR JUNE 2015

4C: SOONERPSYCH PROGRAM UPDATE

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NO ACTION REQUIRED

AGENDA ITEM NO. 5: VOTE TO PRIOR AUTHORIZE AVYCAZ™ (CEFTAZIDIME/AVIBACTAM) AND ZERBAXA™ (CEFTOLOZANE/TAZOBACTAM)

5A: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Holderread

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: VOTE TO PRIOR AUTHORIZE COPAXONE® (GLATIRAMER ACETATE) 40MG/ML

6A: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Holderread

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: VOTE TO PRIOR AUTHORIZE INVEGA TRINZA™ (3-MONTH PALIPERIDONE PALMITATE INJECTION)

7A: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nawaz
Dr. Rhymer moved to approve; seconded by Dr. Harrell
ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: VOTE TO PRIOR AUTHORIZE CHOLBAM™ (CHOLIC ACID)

8A: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nawaz
Ms. Varalli-Claypool moved to approve; seconded by Dr. Huddleston
ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: VOTE TO PRIOR AUTHORIZE NATPARA® (PARATHYROID HORMONE INJECTION)

9A: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nawaz
Dr. Hardzog-Britt moved to approve; seconded by Ms. Varalli Claypool
ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: VOTE TO PRIOR AUTHORIZE ZENZEDI® (DEXTROAMPHETAMINE), EVEKEO™ (AMPHETAMINE), AND APTENSIO XR™ (METHYLPHENIDATE EXTENDED-RELEASE)

10A: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Adams
Dr. Harrell moved to approve; seconded by Dr. Rhymer
ACTION: MOTION CARRIED

AGENDA ITEM NO. 11: VOTE TO PRIOR AUTHORIZE XTORO™ (FINAFLOXACIN) AND OFLOXACIN OTIC

11A: OFLOXACIN OTIC SOLUTION UPDATE

11B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Adams
Ms. Varalli-Claypool moved to approve; seconded by Dr. Rhymer
ACTION: MOTION CARRIED

AGENDA ITEM NO. 12: VOTE TO PRIOR AUTHORIZE HETLIOZ® (TASIMELTEON) AND BELSOMRA® (SUVOREXANT)

12A: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Adams
Dr. Rhymer moved to approve; seconded by Ms. Varalli-Claypool
ACTION: MOTION CARRIED

AGENDA ITEM NO. 13: ANNUAL REVIEW OF ANTIDEPRESSANT MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE IRENKA™ (DULOXETINE)

13A: CURRENT PRIOR AUTHORIZATION CRITERIA
13B: UTILIZATION OF ANTIDEPRESSANTS
13C: PRIOR AUTHORIZATION OF ANTIDEPRESSANTS
13D: MARKET NEWS AND UPDATES
13E: IRENKA™ (DULOXETINE) PRODUCT SUMMARY
13F: COLLEGE OF PHARMACY RECOMMENDATIONS

13G: UTILIZATION DETAILS OF ANTIDEPRESSANTS
Materials included in agenda packet; presented by Dr. Adams
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: ANNUAL REVIEW OF ALZHEIMER'S MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE NAMZARIC™ (MEMANTINE EXTENDED-RELEASE/DONEPEZIL)
14A: CURRENT PRIOR AUTHORIZATION CRITERIA
14B: UTILIZATION OF ALZHEIMER'S MEDICATIONS
14C: PRIOR AUTHORIZATION OF ALZHEIMER'S MEDICATIONS
14D: MARKET NEWS AND UPDATES
14E: NAMZARIC™ (MEMANTINE EXTENDED-RELEASE/DONEPEZIL) PRODUCT SUMMARY
14F: COLLEGE OF PHARMACY RECOMMENDATIONS
14G: UTILIZATION DETAILS OF ALZHEIMER'S MEDICATIONS
Materials included in agenda packet; presented by Dr. Adams
ACTION: NONE REQUIRED

AGENDA ITEM NO. 15: 30-DAY NOTICE TO PRIOR AUTHORIZE CORLANOR® (IVABRADINE)
15A: INTRODUCTION
15B: CORLANOR® (IVABRADINE) PRODUCT SUMMARY
15C: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Teel
ACTION: NONE REQUIRED

AGENDA ITEM NO. 16: ANNUAL REVIEW OF OPIOID ANALGESICS & BUPRENORPHINE PRODUCTS AND 30-DAY NOTICE TO PRIOR AUTHORIZE HYSINGLA® ER (HYDROCODONE BITARTRATE EXTENDED-RELEASE)
16A: CURRENT PRIOR AUTHORIZATION CRITERIA
16B: UTILIZATION OF OPIOID ANALGESICS & BUPRENORPHINE PRODUCTS
16C: PRIOR AUTHORIZATION OF OPIOID ANALGESICS & BUPRENORPHINE PRODUCTS
16D: OPIOID ANALGESIC UTILIZATION TRENDS
16E: MARKET NEWS AND UPDATES
16F: HYSINGLA® ER (HYDROCODONE BITARTRATE EXTENDED-RELEASE) PRODUCT SUMMARY
16G: COLLEGE OF PHARMACY RECOMMENDATIONS
16H: UTILIZATION DETAILS OF OPIOID ANALGESICS AND BUPRENORPHINE PRODUCTS
Materials included in agenda packet; presented by Holderread
ACTION: NONE REQUIRED

AGENDA ITEM NO. 17: 30-DAY NOTICE TO PRIOR AUTHORIZE VARIOUS SPECIAL FORMULATIONS: SITAVIG® (ACYCLOVIR BUCCAL TABLETS), RASUVO® (METHOTREXATE INJECTION), OTREXUP™ (METHOTREXATE INJECTION), ONMEL™ (ITRACONAZOLE ORAL TABLETS), & PURIXAN® (MERCAPTOPURINE ORAL SUSPENSION)
17A: INTRODUCTION
17B: PRODUCT SUMMARIES
17C: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Holderread
ACTION: NONE REQUIRED

AGENDA ITEM NO. 18: ANNUAL REVIEW OF GROWTH HORMONE
18A: CURRENT PRIOR AUTHORIZATION CRITERIA
18B: UTILIZATION OF GROWTH HORMONE

18C: PRIOR AUTHORIZATION OF GROWTH HORMONE
18D: MARKET NEWS AND UPDATES
18E: COLLEGE OF PHARMACY RECOMMENDATIONS
18F: UTILIZATION DETAILS OF GROWTH HORMONE
Materials included in agenda packet; presented by Dr. Holderread
ACTION: NONE REQUIRED

AGENDA ITEM NO. 19: FDA AND DEA UPDATES
Materials included in agenda packet; presented by Dr. Cothran
ACTION: NONE REQUIRED

AGENDA ITEM NO. 20: ADJOURNMENT
The meeting was adjourned at 5:15 pm

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

Memorandum

Date: July 09, 2015

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

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

Subject: DUR Board Recommendations From Meeting of July 08, 2015

Recommendation 1: Vote to Prior Authorize Avycaz™ (Ceftazidime/Avibactam) and Zerbaxa™ (Ceftolozane/Tazobactam)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Avycaz™ (ceftazidime/avibactam) and Zerbaxa™ (ceftolozane/tazobactam) with the following criteria:

Avycaz™ (Ceftazidime/Avibactam) Approval Criteria:

1. An FDA approved diagnosis of one of the following infections caused by designated susceptible microorganisms:
    a. Complicated intra-abdominal infections (cIAI), used in combination with metronidazole; or
    b. Complicated urinary tract infections (cUTI), including Pyelonephritis; and
2. Member must be 18 years of age or older; and
3. For the diagnosis of cIAI, Avycaz™ must be used in combination with metronidazole; and
4. A patient-specific, clinically significant reason why the member cannot use an appropriate penicillin-beta lactamase inhibitor combination (e.g. piperacillin-tazobactam), a carbapenam (e.g. ertapenem, meropenem, imipenem-cilastatin), a cephalosporin (e.g. ceftriaxone, ceftazidime) in combination with metronidazole, or other cost effective therapeutic equivalent medication(s).
5. A quantity limit of 42 vials per 14 days will apply.

Zerbaxa™ (Ceftolozane/Tazobactam) Approval Criteria:

1. An FDA approved diagnosis of one of the following infections caused by designated susceptible microorganisms:
    a. Complicated intra-abdominal infections (cIAI), used in combination with metronidazole; or
    b. Complicated urinary tract infections (cUTI), including Pyelonephritis; and
2. Member must be 18 years of age or older; and
3. For the diagnosis of cIAI, Zerbaxa™ must be used in combination with metronidazole; and
4. A patient-specific, clinically significant reason why the member cannot use an appropriate penicillin-beta lactamase inhibitor combination (e.g. piperacillin-tazobactam), a carbapenam (e.g. ertapenem, meropenem, imipenem-cilastatin), a cephalosporin (e.g. ceftriaxone, ceftazidime) in combination with metronidazole, or other cost effective therapeutic equivalent medication(s).
5. A quantity limit of 42 vials per 14 days will apply.

Recommendation 2: Vote to Prior Authorize Copaxone® (Glatiramer Acetate) 40mg/mL

MOTION CARRIED by unanimous approval.

Based on federal rebate pricing and net cost, the College of Pharmacy recommends the prior authorization of Copaxone® (glatiramer acetate) 40mg with the criteria presented below. A pre-emptive educational initiative will be sent to prescriber and pharmacy providers before these prior authorizations become effective.

Copaxone® (Glatiramer Acetate) Approval Criteria:

1. An FDA approved diagnosis of relapsing, remitting Multiple Sclerosis; and
2. Approvals will not be granted for concurrent use with other disease modifying therapies; and
3. Approvals for the 40mg strength of Copaxone® will require a patient-specific, clinically significant reason why the member cannot use the 20mg strength; and
4. Compliance will be checked for continued approval every six months.

Recommendation 3: Vote to Prior Authorize Invega Trinza™ (3-Month Paliperidone Palmitate Injection)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following changes to the Atypical Antipsychotic Product Based Prior Authorization (PBPA) category:

1. Moving aripiprazole tablets to Tier-1 when the state maximum allowable cost is comparable to other Tier-1 generic medications.

2. After moving aripiprazole tablets to Tier-1, the College of Pharmacy recommends requiring a trial of aripiprazole as one of the Tier-1 trials for authorization of a Tier-2 medication.
    a. If an aripiprazole tablets trial is inappropriate for the member, a patient-specific, clinically significant reason would need to be provided; or
    b. An FDA approved diagnosis not covered by aripiprazole.
3. Additionally, after moving aripiprazole tablets to Tier-1, the College of Pharmacy recommends adding a required trial of aripiprazole to the approval criteria for atypical antipsychotics as adjunctive treatment for major depressive disorder.
4. Lastly, the College of Pharmacy recommends placing Invega Trinza™ into Tier-3. Current criteria for this category will apply. Invega Trinza™ is currently rebated to Tier-2, but will be placed in Tier-3 if the manufacturer chooses not to participate in supplemental rebates.

Atypical Antipsychotic Tier-2 Approval Criteria:

1. Trials of two Tier-1 medications at least 14 days in duration each, titrated to recommended dose, that did not yield adequate response or resulted in intolerable adverse effects.
    a. One of the Tier-1 trials must include a trial with aripiprazole unless member has a patient-specific, clinically significant reason why aripiprazole is not appropriate or an FDA approved diagnosis not covered by aripiprazole.
    b. Clozapine does not count towards a Tier-1 trial.

Atypical Antipsychotic Tier-3 Approval Criteria:

1. Trials of two Tier-1 medications at least 14 days in duration each, titrated to recommended dose, that did not yield adequate response or resulted in intolerable adverse effects; and
    a. One of the Tier-1 trials must include a trial with aripiprazole unless member has a patient-specific, clinically significant reason why aripiprazole is not appropriate or an FDA approved diagnosis not covered by aripiprazole.
    b. Clozapine does not count towards a Tier-1 trial.
2. Trials of two Tier-2 medications, at least 14 days in duration each, titrated to recommended dose, that did not yield adequate response or resulted in intolerable adverse effects.
3. A manual prior authorization may be submitted for consideration of a Tier-3 medication when the member has had at least four trials of Tier-1 and Tier-2 medications (two trials must be from Tier-1) that did not yield an adequate response or resulted in intolerable adverse effects.
4. Use of Versacloz™ (clozapine oral suspension) and Fazaclo® (clozapine orally disintegrating tablet) requires a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation.

Approval Criteria for Atypical Antipsychotics as Adjunctive Treatment for Major Depressive Disorder:

Authorization of Seroquel XR® (quetiapine extended-release) or Symbyax® (olanzapine/fluoxetine) for a diagnosis of major depressive disorder requires current use of an

antidepressant, and previous trials with at least two other antidepressants from both categories (an SSRI and duloxetine) and a trial of aripiprazole tablets that did not yield adequate response. Tier structure applies.

Atypical Antipsychotics*		
Tier-1	**Tier-2**	**Tier-3+**
aripiprazole (Abilify®)	aripiprazole (Abilify Maintena®)	clozapine (Fazaclo®)
clozapine (Clozaril®)¥	asenapine (Saphris®)	clozapine oral suspension (Versacoz™)
olanzapine (Zyprexa®)	iloperidone (Fanapt™)	olanzapine/fluoxetine (Symbyax®)
quetiapine (Seroquel®)	lurasidone (Latuda®)	
risperidone (Risperdal®)	paliperidone (Invega®)	
risperidone (Risperdal Consta®)	paliperidone (Invega® Sustenna®)	
ziprasidone (Geodon®)	**paliperidone (Invega Trinza™)∞**	
	quetiapine ER (Seroquel XR®)	

*Tier structure based on supplemental rebate participation.
+ May be rebated to Tier-2 status only.
¥ Does not count toward a Tier-1 trial.
∞ In addition to tier trials, use of Invega Trinza™ requires members to have been adequately treated with the 1-month paliperidone extended-release injection (Invega® Sustenna®) for at least four months.
ER = extended-release

Recommendation 4: Vote to Prior Authorize Cholbam™ (Cholic Acid)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Cholbam™ (cholic acid) with the following criteria:

Cholbam™ (Cholic Acid) Approval Criteria:

1. An FDA approved diagnosis of one of the following:
    a. Treatment of bile acid disorders due to single enzyme defects (SEDs); or
    b. Adjunctive treatment of peroxisomal disorders (PDs) including Zellweger spectrum disorders in patients who exhibit manifestations of liver disease, steatorrhea, or complications from decreased fat-soluble vitamin absorption; and
2. Treatment with Cholbam™ should be initiated and monitored by a hepatologist or pediatric gastroenterologist; and
3. The prescriber must verify that AST, ALT, GGT, alkaline phosphatase, bilirubin and INR will be monitored every month for the first three months, every three months for the next nine months, every six months during the next three years and annually thereafter; and
4. Cholbam™ should be discontinued if liver function does not improve within three months of starting treatment, if complete biliary obstruction develops, or if there are persistent clinical or laboratory indicators of worsening liver function or cholestasis; and

5. Initial approvals will be for the duration of three months to monitor for compliance and liver function tests.
6. Continuation approvals will be granted for the duration of one year.
7. A quantity limit of 120 capsules per 30 days will apply. Quantity limit requests will be based on the member's recent weight taken within the last 30 days.

Recommendation 5: Vote to Prior Authorize Natpara® (Parathyroid Hormone Injection)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Natpara® (parathyroid hormone injection) with the following criteria:

Natpara® (Parathyroid Hormone Injection) Approval Criteria:

1. An FDA approved diagnosis as an adjunct to calcium and vitamin D to control hypocalcemia in patients with hypoparathyroidism; and
    a. Natpara® is not FDA approved for hypoparathyroidism caused by calcium-sensing receptor mutations.
    b. Natpara® is not FDA approved for hypoparathyroidism due to acute post-surgery.
2. Magnesium deficiency must be ruled out; and
3. Member must have pretreatment serum calcium above 7.5mg/dL before starting Natpara®; and
4. Prescriber must verify the member has sufficient 25-hydroxyvitamin D level per standard of care; and
5. Member must be unable to be adequately well-controlled on calcium supplements and active forms of vitamin D alone; and
6. Health care provider and dispensing pharmacy must be certified through the Natpara® Risk Evaluation and Mitigation Strategies (REMS) Program; and
7. A quantity limit of two cartridges (each package contains two 14-day cartridges) per 28 days will apply. The maximum covered dose will be 100mcg per day.

Recommendation 6: Vote to Prior Authorize Zenzedi® (Dextroamphetamine), Evekeo™ (Amphetamine), and Aptensio XR™ (Methylphenidate Extended-Release)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following changes to the ADHD & Narcolepsy Medications Product Based Prior Authorization (PBPA) category:

1. Place Zenzedi® (dextroamphetamine) into the Special Prior Authorization (PA) category.
    a. The existing criteria for other dextroamphetamine products in the Special PA category will apply.

2. Place Evekeo™ (amphetamine) into the Special PA category based on estimated acquisition cost and FDA approved indications.
    a. Evekeo™ (amphetamine) will require a covered diagnosis; and
    b. A patient-specific, clinically significant reason why the member cannot use all other available stimulant medications.
    c. A quantity limit of 90 tablets per 30 days will apply.
3. Place Aptensio XR™ (methylphenidate ER) into Tier-3 based on estimated acquisition cost.
    a. The existing criteria for this category will apply.
    b. A quantity limit of 30 capsules per 30 days will apply.
4. Add specific criteria for the new indication of binge eating disorder (BED) for Vyvanse® (lisdexamfetamine).

ADHD & Narcolepsy Medications Tier-2 Approval Criteria:

1. A covered diagnosis; and
2. A trial with at least one long-acting Tier-1 stimulant:
    a. Trials should have been within the last 180 days; and
    b. Trials should have been dosed up to maximum recommended dose or documented adverse effects at higher doses should be included; and
    c. If trials are not in the member's claim history, the pharmacy profile should be submitted or detailed information regarding dates and doses should be included along with the signature from the prescriber.

ADHD & Narcolepsy Medications Tier-3 Approval Criteria:

1. A covered diagnosis; and
2. A trial with at least one long-acting Tier-1 stimulant; and
3. A trial with at least one long-acting Tier-2 stimulant that did not yield adequate response:
    a. Trials should have been within the last 365 days; and
    b. Trials should have been dosed up to maximum recommended dose or documented adverse effects at higher doses should be included; and
    c. If trials are not in the member's claim history, the pharmacy profile should be submitted or detailed information regarding dates and doses should be included along with the signature from the prescriber.
4. A clinical exception may apply for special formulation products when there is a patient-specific, clinically significant reason why the member cannot use the available long-acting capsule formulation.
5. Use of Kapvay® (clonidine extended-release tablets) requires:
    a. An FDA approved diagnosis; and
    b. Recent trials with a long-acting Tier-1 stimulant and a long-acting Tier-2 stimulant, and a trial of Intuniv® and Strattera® within the past six months, unless contraindicated, that did not yield adequate results; and
    c. A patient-specific, clinically significant reason why the member cannot use clonidine immediate release tablets.

ADHD & Narcolepsy Medications Special Prior Authorization (PA) Approval Criteria:

1. Desoxyn®, Dexedrine®, Dexedrine Spansules®, Evekeo®, ProCentra® Solution, and Zenzedi® Criteria:
    a. A covered diagnosis; and
    b. A patient-specific, clinically significant reason why member cannot use all other available stimulant medications.
2. Daytrana®, Quillivant XR®, and Methylin® Chewable Tablets and Solution Criteria:
    a. An FDA approved diagnosis; and
    b. A patient-specific, clinically significant reason why member cannot use all other available formulations of long-acting stimulant medications that can be used for members who cannot swallow capsules or tablets.
3. Provigil®, Nuvigil®, and Xyrem® Criteria:
    a. An FDA approved diagnosis; and
    b. Use of Provigil® or Nuvigil® requires a patient-specific, clinically significant reason why the member cannot use stimulant medications to improve wakefulness during the daytime.
    c. Use of Xyrem® requires recent trials with Tier-1 and Tier-2 stimulants from different chemical categories, and trials with both Provigil® and Nuvigil® within the past six months, unless contraindicated, that did not yield adequate results.
    d. The diagnosis of obstructive sleep apnea requires concurrent treatment for the obstructive sleep apnea.
    e. The diagnosis of shift work sleep disorder requires the member's work schedule to be included with the prior authorization request.

ADHD & Narcolepsy Medications Additional Criteria:

1. Doses exceeding 1.5 times the FDA maximum are not covered.
2. Prior Authorization is required for all tiers for members greater than 20 years of age and for members 0-4 years of age. All prior authorization requests for members under the age of 5 years must be reviewed by an OHCA contracted psychiatrist.
3. Vyvanse® (Lisdexamfetamine) Approval Criteria: Binge Eating Disorder (BED)
    a. An FDA approved diagnosis of moderate-to-severe binge eating disorder; and
    b. Member must be 18 years or older; and
    c. Vyvanse® for the diagnosis of BED must be prescribed by a psychiatrist; and
    d. Authorizations will not be granted for the purpose of weight loss without the diagnosis of BED or for the diagnosis of obesity alone. The safety and effectiveness of Vyvanse® for the treatment of obesity have not been established; and
    e. A quantity limit of 30 capsules per 30 days will apply; and
    f. Initial approvals will be for the duration of three months. Continued authorization will require prescriber documentation of improved response/effectiveness of Vyvanse®.

ADHD & Narcolepsy Medications			
Tier-1*	**Tier-2***	**Tier-3***	**Special PA**
Amphetamine			Daytrana™ (methylphenidate ER) Desoxyn® (methamphetamine) Dexedrine® (dextroamphetamine) Dexedrine Spansules® (dextroamphetamine ER) **Evekeo™ (amphetamine sulfate)** Methylin® (methylphenidate soln & chew tabs) Nuvigil® (armodafinil) ProCentra™ (dextroamphetamine) Provigil® (modafinil) Quillivant XR® (methylphenidate ER) Xyrem® (sodium oxybate) **Zenzedi® (dextroamphetamine)**
Short-Acting			
Adderall® (amphetamine/ dextroamphetamine)			
Long-Acting			
Vyvanse® (lisdexamfetamine)+	Adderall XR® brand name only (amphetamine/ dextroamphetamine ER)	amphetamine/ dextroamphetamine ER (generic Adderall XR®)	
Methylphenidate			
Short-Acting			
Focalin® (dexmethylphenidate) Methylin® (methylphenidate) Ritalin® (methylphenidate)			
Long-Acting			
Metadate CD® brand name only (methylphenidate ER) Metadate ER® (methylphenidate ER) Methylin ER® (methylphenidate ER) Ritalin SR® (methylphenidate ER)	Focalin XR® (dexmethylphenidate ER) Ritalin LA® brand name only (methylphenidate ER)	**Aptensio XR™ (methylphenidate ER)** Concerta® (methylphenidate ER) methylphenidate ER (generic Metadate CD®) methylphenidate ER (generic Ritalin LA®)	
Non-Stimulants			
Intuniv® (guanfacine ER) Strattera® (atomoxetine)		Kapvay® (clonidine ER)	

*Tier structure based on State Maximum Allowable Cost (SMAC) and/or supplemental rebate participation.
+Unique criteria applies for the diagnosis of binge eating disorder (BED).
ER = Extended-Release
SR = Sustained-Release
Soln = Solution

Recommendation 7: Vote to Prior Authorize Xtoro™ (Finafloxacin) and Ofloxacin Otic

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following changes to the Otic Anti-Infectives Product Based Prior Authorization (PBPA) category:

1. Place Xtoro™ (finafloxacin) into Tier-2. The existing criteria for this category will apply.
2. Move ofloxacin otic solution to Tier-2 based on an increased state maximum allowable cost (SMAC).
    a. The existing criteria for this category will apply.
    b. Initiate an educational mailing regarding these tier changes, which will include the option of utilizing ofloxacin ophthalmic solution for otic conditions as well other Tier-1 otic anti-infectives.

Otic Anti-Infectives		
Tier-1	**Tier-2**	**Special PA**
acetic acid (VoSol®, Acetasol®)	chloroxylenol/benzocaine/HC (Trioxin®)	acetic acid/HC (Acetasol® HC, VoSol® HC)
ciprofloxacin/dexamethasone (Ciprodex®)	chloroxylenol/pramoxine/zinc/ glycerin (Zinotic®, Zinotic® ES)	antipyrine/benzocaine/ glycerin/zinc (Neotic®)
neomycin/polymyxin B/HC (Cortisporin®, Pediotic®)	ciprofloxacin (Cetraxal®)	
	ciprofloxacin/HC (Cipro® HC)	
	finafloxacin (Xtoro™)	
	neomycin/colistin/HC/ thonzonium (Cortisporin® TC, Coly-Mycin® S)	
	ofloxacin (Floxin® Otic)	

Tier structure based on supplemental rebate participation and/or state maximum allowable cost (SMAC).
HC = hydrocortisone

Otic Anti-Infectives Tier-2 Approval Criteria:

1. Member must have an adequate 14-day trial of at least two Tier-1 medications; or
2. Approval may be granted if there is a unique FDA approved indication not covered by Tier-1 medications or infection by an organism not known to be covered by any of the Tier-1 medications.

Otic Anti-Infectives Special Prior Authorization (PA) Approval Criteria:

1. Diagnosis of acute otitis externa; and
2. Recent (within 6 months) trials with all other commonly used topical otic anti-infectives that have failed to resolve infection; or
3. Allergy to all available products and failure of acetic acid alone.

Recommendation 8: Vote to Prior Authorize Hetlioz® (Tasimelteon) and Belsomra® (Suvorexant)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following changes to the Insomnia Medications Product Based Prior Authorization (PBPA) category:

1. The addition of Belsomra® (suvorexant) to Tier-3 based on estimated acquisition cost. The current criteria for this category will apply.
2. Moving Lunesta® (eszopiclone) to Tier-1 based on generic availability and state maximum allowable cost.
3. The creation of a Special Prior Authorization (PA) category for unique dosage formulations and medications with limited indications. Authorization for unique dosage formulations would require a patient-specific, clinically significant reason for use in place of the lower tiered formulations.
4. The prior authorization of Hetlioz® (tasimelteon) with the criteria listed below.

Hetlioz® (Tasimelteon) Approval Criteria:

1. An FDA approved diagnosis of Non-24-Hour Sleep-Wake Disorder (Non-24); and
2. Member must be 18 years of age or older; and
3. Member must be totally blind; and
4. A failed trial of appropriately timed doses of melatonin.
5. Initial approvals will be for the duration of 12 weeks. For continuation, the prescriber must include information regarding improved response/effectiveness of this medication.
6. A quantity limit of 30 capsules for 30 days will apply.

Insomnia Medications			
Tier-1	**Tier-2**	**Tier-3**	**Special PA***
estazolam (ProSom®)	zolpidem CR (Ambien® CR)	ramelteon (Rozerem®)	doxepin (Silenor®)
eszopiclone (Lunesta®)		**suvorexant (Belsomra®)**	**tasimelteon (Hetlioz®)+**
flurazepam (Dalmane®)			temazepam (Restoril®) 7.5mg and 22.5mg
temazepam (Restoril®) 15mg and 30mg			zolpidem SL tablets (Edluar®)
triazolam (Halcion®)			zolpidem SL tablets (Intermezzo®)
zaleplon (Sonata®)			zolpidem oral spray (Zolpimist®)
zolpidem (Ambien®)			

*Unique dosage formulations require a special reason for use in place of Tier-1 formulations.
+ Individual criteria specific to tasimelteon.

Recommendation 9: Annual Review of Antidepressant Medications and 30-Day Notice to Prior Authorize Irenka™ (Duloxetine)

NO ACTION REQUIRED.

Recommendation 10: Annual Review of Alzheimer's Medications and 30-Day Notice to Prior Authorize Namzaric™ (Memantine Extended-Release/Donepezil)

NO ACTION REQUIRED.

Recommendation 11: 30-Day Notice to Prior Authorize Corlanor® (Ivabradine)

NO ACTION REQUIRED.

Recommendation 12: Annual Review of Opioid Analgesics & Buprenorphine Products and 30-Day Notice to Prior Authorize Hysingla® ER (Hydrocodone Bitartrate Extended-Release)

NO ACTION REQUIRED.

Recommendation 13: 30-Day Notice to Prior Authorize Various Special Formulations: Sitavig® (Acyclovir Buccal Tablets), Rasuvo® (Methotrexate Injection), Otrexup™ (Methotrexate Injection), Onmel™ (Itraconazole Oral Tablets), & Purixan® (Mercaptopurine Oral Suspension)

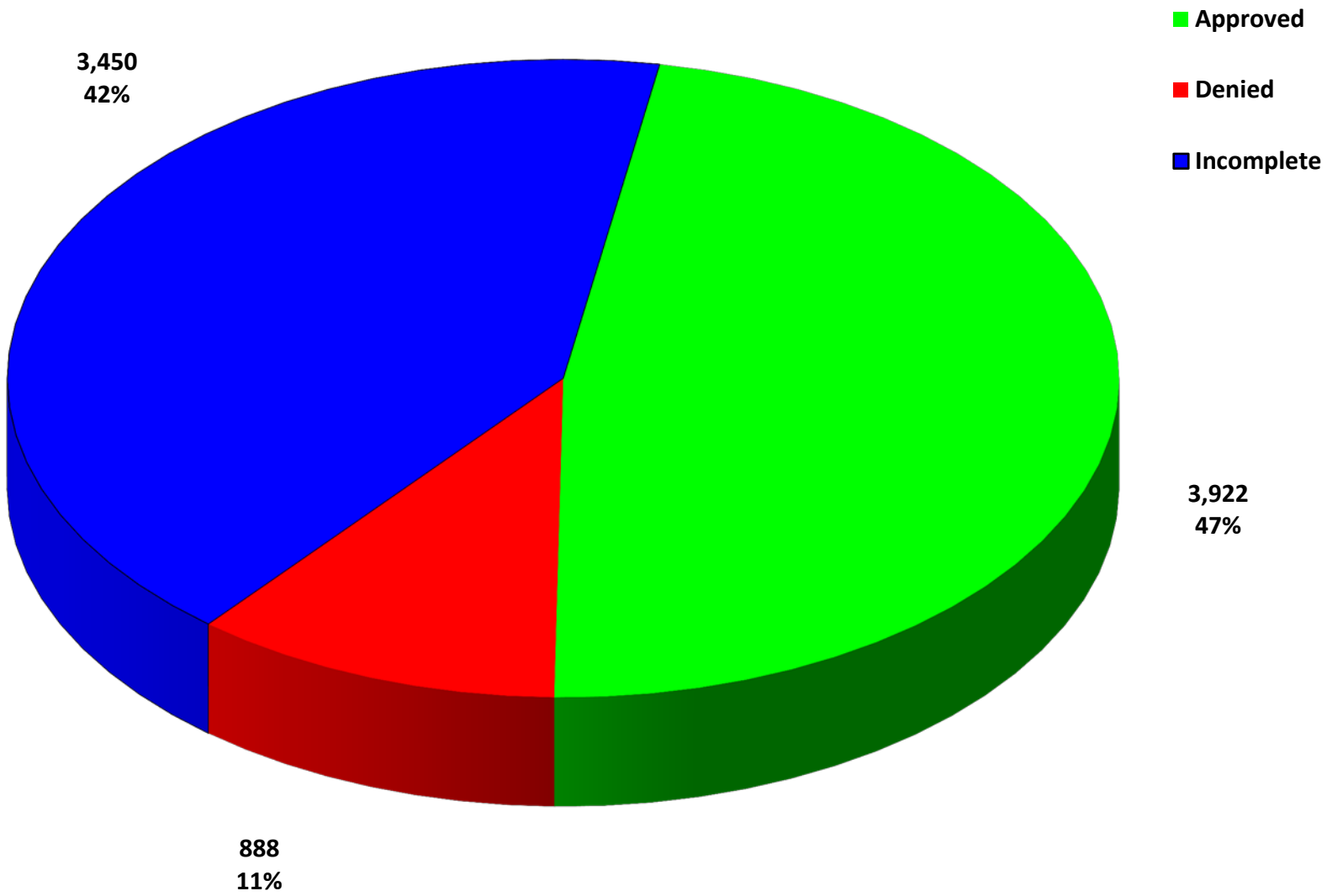
NO ACTION REQUIRED.

Recommendation 14: Annual Review of Growth Hormone

NO ACTION REQUIRED.

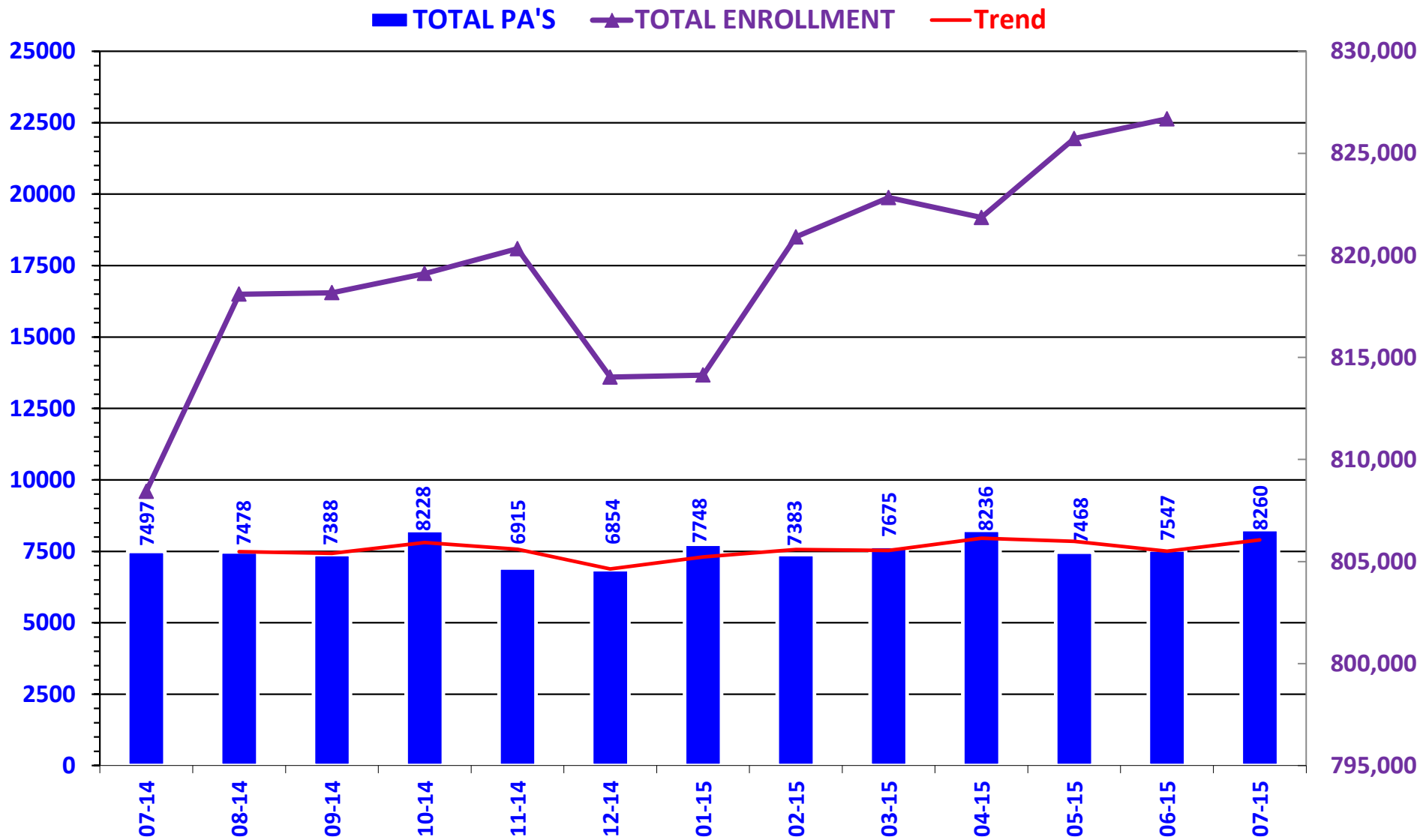
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: JULY 2015



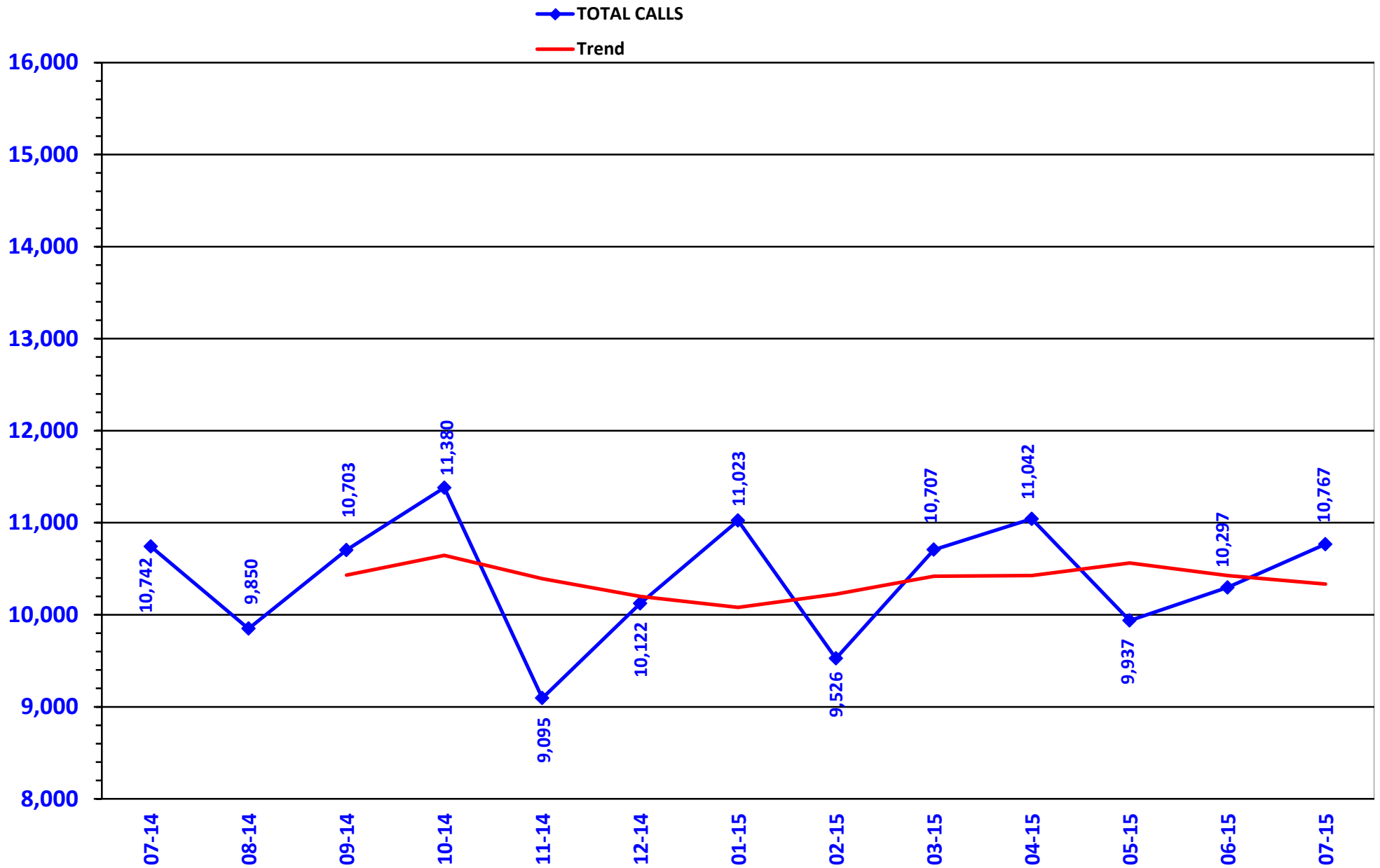
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: JULY 2014 – JULY 2015



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
JULY 2014 – JULY 2015



Prior Authorization Activity
7/1/2015 Through 7/31/2015

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	344	153	16	175	359
Analgesic - NonNarcotic	19	0	3	16	0
Analgesic, Narcotic	381	226	22	133	169
Angiotensin Receptor Antagonist	29	3	2	24	360
Antiasthma	204	90	20	94	336
Antibiotic	56	23	2	31	93
Anticoagulant	10	4	1	5	297
Anticonvulsant	88	32	15	41	335
Antidepressant	102	19	18	65	343
Antidiabetic	177	78	18	81	350
Antifungal	17	2	6	9	9
Antigout	13	7	2	4	361
Antihistamine	138	109	10	19	355
Antimigraine	43	12	10	21	230
Antiulcers	165	26	45	94	126
Anxiolytic	65	42	3	20	293
Atypical Antipsychotics	559	239	29	291	342
Benign Prostatic Hypertrophy	13	1	4	8	361
Biologics	76	40	9	27	334
Bladder Control	43	11	9	23	360
Blood Thinners	148	97	2	49	322
Botox	34	24	7	3	344
Cardiovascular	30	17	3	10	260
Chronic Obstructive Pulmonary Disease	23	5	3	15	358
Contraceptive	13	10	0	3	262
Dermatological	95	10	48	37	121
Diabetic Supplies	745	335	38	372	233
Endocrine & Metabolic Drugs	62	37	8	17	128
Erythropoietin Stimulating Agents	37	18	5	14	111
Fibromyalgia	104	26	32	46	356
Fish Oils	17	2	6	9	361
Gastrointestinal Agents	97	31	21	45	101
Growth Hormones	78	54	5	19	147
Hepatitis C	165	89	35	41	8
HFA Rescue Inhalers	57	26	4	27	354
Insomnia	43	11	8	24	173
Insulin	30	4	3	23	282
Linzess, Amitiza, and Relistor	72	9	23	40	207
Multiple Sclerosis	85	30	12	43	215
Muscle Relaxant	77	19	23	35	94
Nasal Allergy	81	12	19	50	312
Neurological Agents	38	26	1	11	348
NSAIDs	201	36	38	127	256
Ocular Allergy	40	10	1	29	147
Ophthalmic Anti-infectives	10	1	0	9	176
Osteoporosis	19	8	2	9	337
Other*	287	57	85	145	232
Otic Antibiotic	56	2	6	48	17
Pediculicide	150	84	7	59	19
Prenatal Vitamins	29	0	4	25	0
Statins	71	20	7	44	359
Stimulant	825	385	48	392	334
Suboxone/Subutex	220	146	4	70	79
Testosterone	66	18	17	31	325
Topical Antifungal	35	2	6	27	107

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Topical Corticosteroids	77	0	17	60	0
Vitamin	63	16	29	18	254
Pharmacotherapy	64	58	0	6	242
Emergency PAs	0	0	0	0	
Total	**6,886**	**2,852**	**821**	**3,213**	

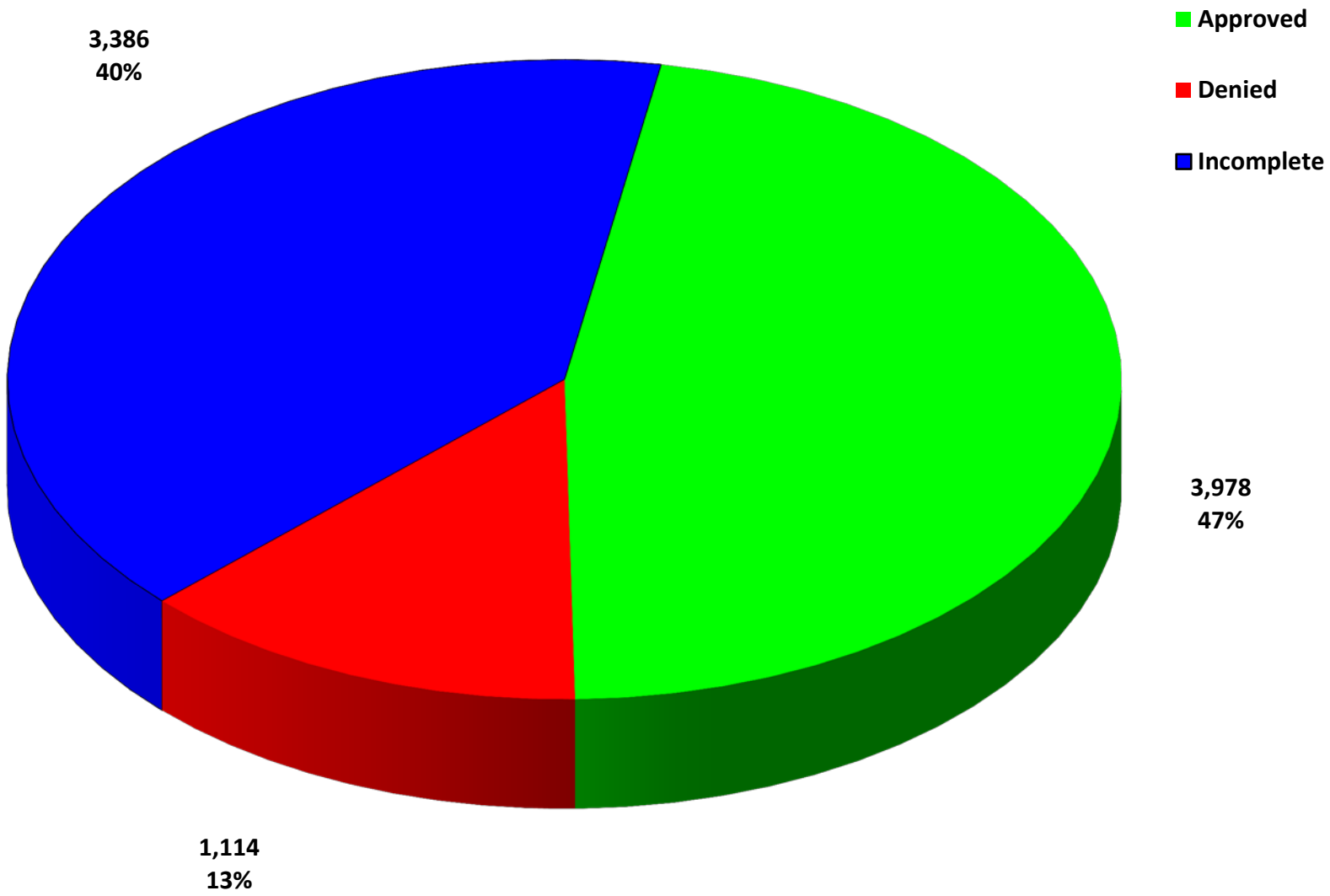
Overrides					
Brand	70	56	4	10	275
Cumulative Early Refill	2	2	0	0	98
Diabetic Supplies	35	19	2	14	173
Dosage Change	351	317	3	31	5
High Dose	3	2	0	1	193
Ingredient Duplication	43	33	0	10	13
Lost/Broken Rx	100	90	6	4	4
NDC vs Age	21	21	0	0	223
Nursing Home Issue	67	64	0	3	4
Opioid Quantity	10	8	2	0	90
Other*	29	25	1	3	3
Quantity vs. Days Supply	626	420	41	165	259
STBS/STBSM	16	14	1	1	76
Stolen	16	14	0	2	3
Third Brand Request	32	14	11	7	20
Overrides Total	**1,374**	**1,070**	**67**	**237**	
Total Regular PAs + Overrides	**8,260**	**3,922**	**888**	**3,450**	

Denial Reasons	
Unable to verify required trials.	2,926
Does not meet established criteria.	879
Lack required information to process request.	518

Other PA Activity	
Duplicate Requests	619
Letters	5,590
No Process	10
Changes to existing PAs	589
Helpdesk Initiated Prior Authorizations	847
PAs Missing Information	62

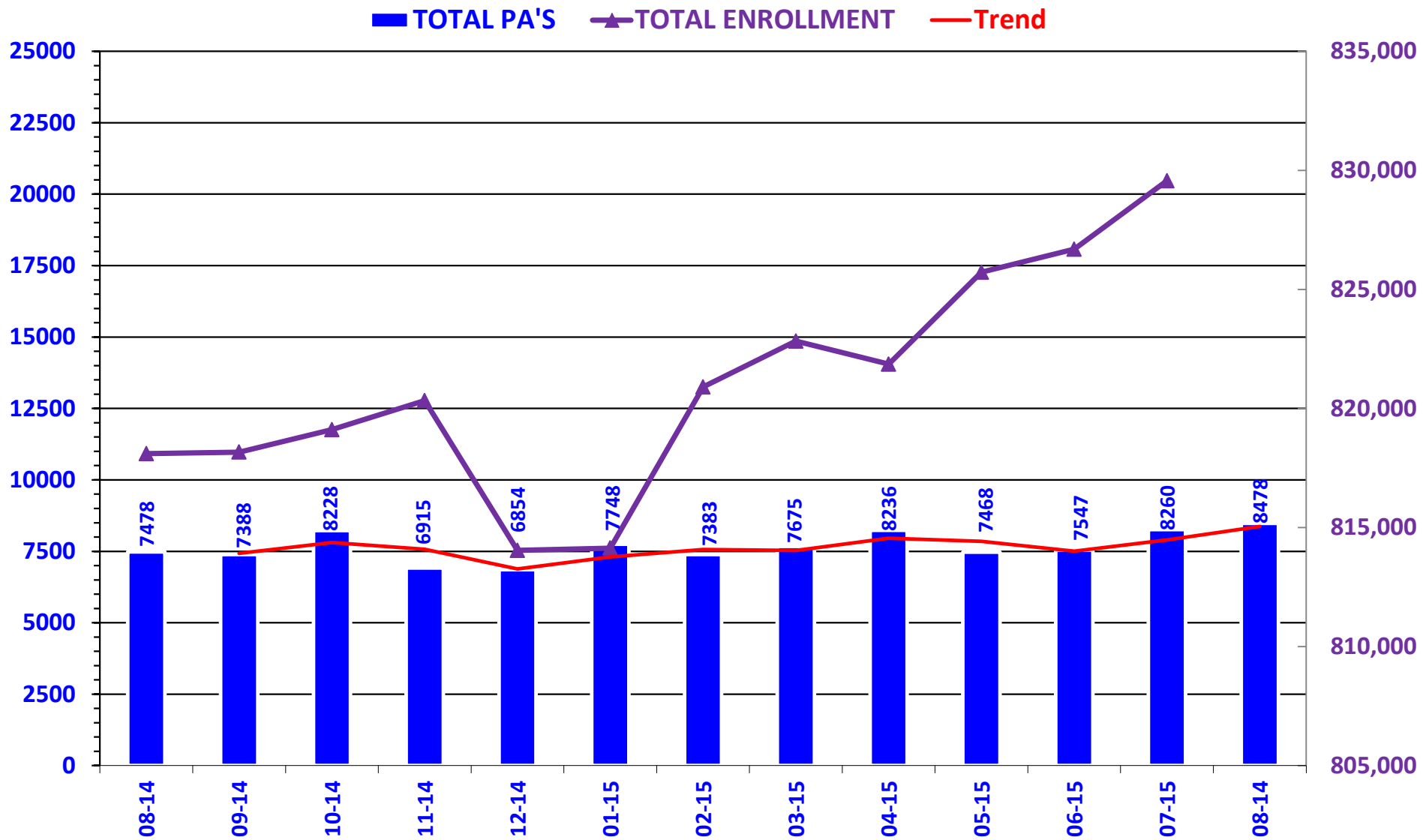
* Includes any therapeutic category with less than 10 prior authorizations for the month.

PRIOR AUTHORIZATION ACTIVITY REPORT: AUGUST 2015



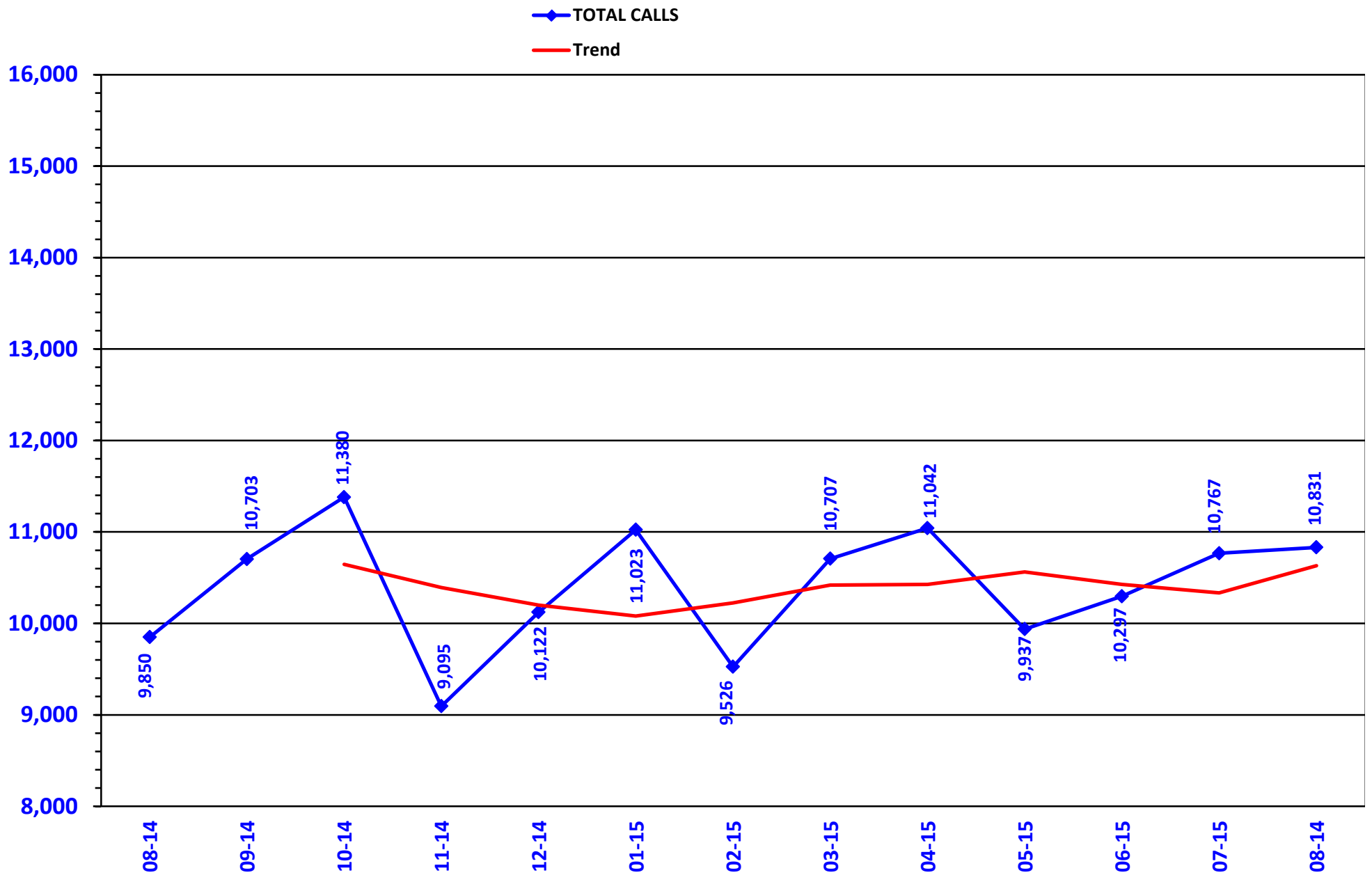
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: AUGUST 2014 – AUGUST 2015



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
AUGUST 2014 – AUGUST 2015



Prior Authorization Activity
8/1/2015 Through 8/31/2015

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	376	158	44	174	351
Analgesic - NonNarcotic	18	0	7	11	0
Analgesic, Narcotic	418	199	55	164	162
Angiotensin Receptor Antagonist	28	5	7	16	360
Antiasthma	199	86	31	82	344
Antibiotic	58	22	5	31	96
Anticonvulsant	86	32	11	43	305
Antidepressant	88	18	15	55	349
Antidiabetic	187	82	21	84	359
Antigout	14	3	2	9	360
Antihistamine	136	102	9	25	353
Antimigraine	50	14	9	27	215
Antiulcers	195	34	67	94	134
Anxiolytic	76	39	7	30	297
Atypical Antipsychotics	526	231	45	250	350
Benign Prostatic Hypertrophy	10	0	5	5	0
Biologics	67	21	20	26	341
Bladder Control	52	16	13	23	360
Blood Thinners	120	81	10	29	341
Botox	30	23	3	4	359
Cardiovascular	38	23	7	8	359
Chronic Obstructive Pulmonary Disease	11	2	4	5	361
Contraceptive	19	14	2	3	306
Dermatological	116	24	58	34	73
Diabetic Supplies	643	319	32	292	236
Endocrine & Metabolic Drugs	54	37	6	11	140
Erythropoietin Stimulating Agents	22	13	5	4	115
Fibromyalgia	155	37	49	69	352
Gastrointestinal Agents	98	29	29	40	73
Glaucoma	10	0	2	8	0
Growth Hormones	74	49	10	15	150
Hepatitis C	155	80	23	52	9
HFA Rescue Inhalers	66	33	2	31	347
Insomnia	41	8	10	23	178
Insulin	32	8	4	20	315
Linzess, Amitiza, and Relistor	93	18	25	50	177
Multiple Sclerosis	79	22	12	45	212
Muscle Relaxant	94	15	32	47	96
Nasal Allergy	106	13	28	65	254
Neurological Agents	68	46	9	13	335
NSAIDs	187	26	42	119	257
Ocular Allergy	42	11	9	22	230
Ophthalmic Anti-infectives	10	1	5	4	8
Osteoporosis	22	12	3	7	345
Other*	300	58	79	163	198
Otic Antibiotic	32	5	2	25	6
Pediculicide	171	102	9	60	18
Prenatal Vitamins	14	0	0	14	0
Statins	77	18	13	46	342
Stimulant	1,011	460	82	469	342
Suboxone/Subutex	196	150	3	43	84
Testosterone	65	8	21	36	302
Topical Antifungal	42	1	7	34	179

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Topical Corticosteroids	86	0	26	60	0
Vitamin	59	8	33	18	288
Pharmacotherapy	47	45	0	2	228
Emergency PAs	0	0	0	0	
Total	**7,069**	**2,861**	**1,069**	**3,139**	

Overrides					
Brand	64	39	7	18	249
Cumulative Early Refill	11	8	0	3	31
Diabetic Supplies	11	9	0	2	30
Dosage Change	312	296	1	15	7
High Dose	3	3	0	0	116
Ingredient Duplication	47	36	1	10	20
Lost/Broken Rx	117	108	0	9	4
NDC vs Age	29	28	0	1	231
Nursing Home Issue	47	44	1	2	4
Opioid Quantity	14	12	1	1	456
Other*	59	50	2	7	14
Quantity vs. Days Supply	685	477	32	176	278
STBS/STBSM	7	7	0	0	65
Stolen	7	6	0	1	3
Temporary Unlock	4	4	0	0	10
Third Brand Request	28	19	1	8	42
Overrides Total	**1,409**	**1,117**	**45**	**247**	
Total Regular PAs + Overrides	**8,478**	**3,978**	**1,114**	**3,386**	

Denial Reasons	
Unable to verify required trials.	2,853
Does not meet established criteria.	1,085
Lack required information to process request.	547

Other PA Activity	
Duplicate Requests	516
Letters	5,234
No Process	6
Changes to existing PAs	514
Helpdesk Initiated Prior Authorizations	868
PAs Missing Information	53

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

Retrospective Drug Evaluation: Focus on Safety

Overview of FDA Safety Alerts

Oklahoma Health Care Authority
September 2015

Introduction[1,2,3,4,5,6,7,8,9]

The following are recent FDA safety alerts included for the Drug Utilization Review (DUR) Board's consideration. SoonerCare specific data may be presented where applicable. The College will make recommendations as well as take recommendations from the DUR Board.

Date	Drug	Issue
03/03/2015	**Testosterone**	**Risk of heart attack and stroke**
Issue Details: The FDA released a drug safety communication cautioning that the benefit and safety of testosterone for low testosterone levels due to aging has not been established and may lead to increased risk of heart attacks and strokes. **FDA Recommendations:** The FDA is requiring that the labeling of prescription testosterone products include information to clarify the approved use of testosterone medications. Additionally, the FDA required label changes outlining the possible increased risk of heart attacks and strokes in patients taking testosterone. Prescribers should warn their patients about these risks when initiating or continuing testosterone therapy and only prescribe testosterone therapy for men with low testosterone levels caused by certain medical conditions and confirmed by laboratory tests. **SoonerCare Action:** In June of 2013, the DUR Board voted to strengthen the approval criteria for testosterone coverage. Members are now required to have two low morning testosterone levels below 300ng/dL in addition to having labs showing abnormal gonadotropins and/or other information necessary to demonstrate diagnosis. **Pharmacy Claims evaluation:** A review of SoonerCare pharmacy claims data from calendar year 2014 shows 189 SoonerCare members with paid claims for testosterone, down from calendar year 2013 when 329 members used testosterone. The decrease in utilization is likely due to the criteria change in 2013.		

Date	Drug	Issue
03/09/2015	**varenicline (Chantix®)**	**Risk of alcohol interaction, risk of seizure, side effects on mood, behavior, or thinking**
Issue Details: The FDA issued a Drug Safety Communication regarding varenicline. The smoking cessation medication can change reactions to alcohol involving decreased tolerance with increased drunkenness, unusual or aggressive behavior, and/or no memory of actions. Use of varenicline also caused seizures in patients with no previous history of seizures, or an increase in seizures in previously well controlled patients. Studies showing possible increased neuropsychiatric side effects on mood, behavior, or thinking were reviewed and though they		

did not show varenicline as the cause, they did not review all possible effects and had limitations.
FDA Recommendations: Changes to the *Warning and Precautions* section of the product label have been made to include information about alcohol reactions, risk of seizure, and mood changes.
Pharmacy Claims Evaluation: During calendar year 2014, a total of 2,042 SoonerCare members had a paid claim for varenicline. No issues related to varenicline adverse effects were reported to the College of Pharmacy.

Date	Drug	Issue
03/23/2015	**ledipasvir/sofosbuvir (Harvoni®) and sofosbuvir (Sovaldi®)**	**Risk of serious bradycardia when combined with amiodarone**

Issue Details: Gilead Sciences, manufacturer of ledipasvir/sofosbuvir and sofosbuvir, reported serious treatment-related adverse events, including bradycardia, pacemaker intervention, and even death, in patients taking amiodarone with ledipasvir/sofosbuvir or sofosbuvir. Symptoms occurred within 24 hours of starting ledipasvir/sofosbuvir or sofosbuvir.
FDA Recommendations: The FDA required a product label update for the antivirals to include information about serious slowing of the heart rate, known as symptomatic bradycardia, in patients taking amiodarone and ledipasvir/sofosbuvir or sofosbuvir together. In patients who have no alternative treatment options, cardiac monitoring for 48 hours after starting ledipasvir/sofosbuvir or sofosbuvir is required. Additionally, daily heart-rate monitoring for two weeks in an outpatient or home setting should be performed. For patients whose amiodarone is discontinued just prior to starting ledipasvir/sofosbuvir or sofosbuvir, the same monitoring is recommended because of the long half-life of amiodarone.
SoonerCare Action: The member Intent to Treat Contract and the Initiation Prior Authorization Form for both ledipasvir/sofosbuvir and sofosbuvir have been updated to include this interaction. Prior authorization requests for ledipasvir/sofosbuvir or sofosbuvir are not approved without additional documentation from the prescriber if the member has paid claims for amiodarone in their recent SoonerCare pharmacy claims history.
Pharmacy Claims Evaluation: A review of SoonerCare pharmacy claims data from July 1, 2014 to December 31, 2014 did not reveal concomitant use of amiodarone and ledipasvir/sofosbuvir or sofosbuvir.

Date	Drug	Issue
03/30/2015	**ferumoxytol (Feraheme®)**	**Risk of serious allergic reactions**

Issue Details: Since its approval in 2009 for treatment of iron deficiency anemia in adults with chronic kidney disease, ferumoxytol has caused life-threatening allergic reactions, including death. These reactions have occured despite correct use within the medication's FDA approved indication and despite precautions (therapies and emergency resuscitation

measures) being in place to reduce potential reactions and/or treat allergic reactions that do occur.

FDA Recommendations: The FDA has strengthened warnings by adding a boxed warning to the product label regarding the serious, potentially fatal allergic reactions. The label also includes a contraindication for the use of ferumoxytol in patients who have had a previous allergic reaction to other intravenous iron products. The boxed warning includes recommendations to health care professionals regarding the administration and monitoring of ferumoxytol.

SoonerCare Action: Current prior authorization criteria restrict use of ferumoxytol to members with iron deficiency anemia and who have chronic kidney disease. The criteria has been updated to include the contraindication for use of ferumoxytol in patients who have had a previous allergic reaction to other intravenous iron products.

Pharmacy Claims Evaluation: A total of five SoonerCare members have had approved prior authorization requests for ferumoxytol since 2013.

Date	Drug	Issue
05/15/2015	**SGLT2 inhibitors:** **canagliflozin (Invokana™)** **dapagliflozin (Farxiga™)** **empagliflozin (Jardiance®)**	**Risk of ketoacidosis**

Issue Details: The FDA released a Drug Safety Communication and Podcast regarding ketoacidosis in Type II diabetics. Twenty cases have been identified through the FDA Adverse Event Reporting System (FAERS) in patients being treated with SGLT2 (sodium-glucose cotransporter-2) inhibitors. All cases required emergency room visits or hospitalizations to treat the ketoacidosis. These medications are available alone, in combination with metformin (dapagliflozin-metformin [Xigduo™], canagliflozin-metformin [Invokamet™]), or in combination with a DPP-4 (dipeptidyl peptidase-4) inhibitor (empagliflozin/linagliptin [Glyxambi®]).

FDA Recommendations: The FDA is investigating these findings and will make a determination regarding changes to prescribing information. Prescribers should evaluate their patients for signs of ketoacidosis, including dyspnea, nausea, vomiting, abdominal pain, confusion, and unusual fatigue or sleepiness. If the diagnosis of ketoacidosis is confirmed, the SGLT2 inhibitor should be discontinued.

Pharmacy Claims Evaluation: During calendar year 2014, a total of 96 SoonerCare members had paid claim(s) for an SGLT2 inhibitor or SGLT2 inhibitor combination product. No issues related to SGLT2 inhibitor adverse effects were reported to the College of Pharmacy.

Date	Drug	Issue
06/24/2015	**methylphenidate transdermal (Daytrana®)**	**Permanent skin color changes**

Issue Details: The FDA issued a Drug Safety Communication regarding the possible development of chemical leukoderma, the permanent loss of skin color, with the use of methylphenidate transdermal patches. Fifty-one cases of the condition were reported to the FAERS database from 4/2006 to 12/2014. While leukoderma is not physically harmful, it is disfiguring and may be distressful to patients. The condition was reported to have started two months to four years following the initial use of methylphenidate transdermal patches. Most of the skin color loss occurred at the site of application, though others reported developing patches of leukoderma in areas where a patch was never used.
FDA Recommendations: The drug label has been updated with a new warning for potential chemical leukoderma.
Pharmacy Claims Evaluation: During calendar year 2014, a total of 217 members had paid claims for methylphenidate transdermal patches. No issues related to methylphenidate transdermal patches adverse effects were reported to the College of Pharmacy.

Date	Drug	Issue
07/09/2015	**Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)**	**Increased risk of heart attack or stroke**

Issue Details: Based on a review of new safety information, the FDA issued a Drug Safety Communication regarding the increased risk of heart attack or stroke in patients taking non-aspirin NSAIDs.
FDA Recommendations: The FDA is recommending the strengthening of existing non-aspirin NSAID labels for prescription NSAIDs, as well as the Drug Facts labels for over-the-counter (OTC) NSAIDs. The prescription NSAID labels will be revised to reflect the following information:

- The risk of heart attack or stroke can occur as early as the first week of using an NSAID, and may increase with longer use.
- The risk is greater at higher doses.
- It is less clear if the risk is similar for all NSAIDs; there is insufficient data to determine if the risk is higher or lower for any particular NSAID.
- NSAIDs can increase the risk of heart attack or stroke in patients with or without heart disease or risk factors for heart disease.
- In general there is a greater likelihood of heart attack or stroke following NSAID use in patients who already have heart disease because they have a higher risk at baseline.
- Patients treated with NSAIDs following a first heart attack were more likely to die in the first year after the heart attack compared to patients who were not treated with NSAIDs after their first heart attack.
- There is an increased risk of heart failure with NSAID use.

SoonerCare Action: The College of Pharmacy is exploring educational opportunities regarding the appropriate use of NSAIDs among SoonerCare members. Potential educational

interventions include articles in the member and provider newsletter as well as letters to prescribers and pharmacies.
Claims Evaluation: During calendar year 2014, a total of 102,112 members had paid claims for NSAIDs. Comorbidities including cardiovascular disease diagnoses will be examined in members utilizing NSAIDs. CVD diagnoses in this population may be a guide for educational targeting.

Date	Drug	Issue
07/30/2015	**vortioxetine (Brintellix®)** **ticagrelor (Brilinta®)**	**Prescribing and dispensing errors resulting from brand name confusion**

Issue Details: The FDA released a Drug Safety Communication warning health care professionals that reports of confusion between the antidepressant Brintellix® and the platelet aggregation inhibitor Brilinta® have resulted in the wrong medication being prescribed or dispensed.
FDA Recommendations: Health care professionals can reduce the risk of name confusion by including the generic name of the medication, in addition to the brand name, the strength of the medication, and the indication for use when prescribing these medications.
Pharmacy Claims Evaluation: During calendar year 2014, a total of 80 members had paid claims for vortioxetine or ticagrelor.

Date	Drug	Issue
08/04/2015	**fingolimod (Gilenya®)**	**Risk of progressive multifocal leukoencephalopathy (PML)**

Issue Details: The FDA issued a Drug Safety Communication regarding a confirmed case of PML as well as another probable case in patients taking fingolimod who had not been previously treated with an immunosuppressant for multiple sclerosis. PML is a rare and serious brain infection caused by the John Cunningham (JC) virus. Prior to the recent cases of PML, a case of PML was reported in 2013 in a patient who had previously been treated with immunosuppressive therapy, and therefore fingolimod could not be conclusively linked at that time.
FDA Recommendations: The product label has been modified to include information regarding the recent cases of PML. Patients taking fingolimod should contact their prescriber right away if they experience symptoms such as new or worsening weakness; increased trouble using their arms or legs; or changes in thinking, eyesight, strength, or balance. Patients should not stop taking fingolimod without first discussing it with their prescriber. Health care professionals should stop fingolimod and perform a diagnostic evaluation if PML is suspected.
Pharmacy Claims Evaluation: During calendar year 2014, 26 SoonerCare members had paid claims for fingolimod. All paid claims for fingolimod were prescribed by a neurologist or mid-level practitioner working with a neurologist.

[1] FDA Drug Safety Communication (testosterone) available online at http://www.fda.gov/Drugs/DrugSafety/ucm436259.htm. Last revised: 5/14/2015. Last accessed: 8/21/2015.
[2] Drug Safety Communication (Chantix®) available online at http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm437415.htm Last revised: 3/16/2015. Last accessed: 8/11/2015.
[3] FDA Drug Safety Communication (Harvoni®/Sovaldi®) available online at http://www.fda.gov/drugs/drugsafety/ucm439484.htm. Last revised: 4/6/2015. Last accessed. 8/20/2015.
[4] FDA Drug Safety Communication (Feraheme®) available online at http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm440479.htm. Last revised: 3/31/2015. Last accessed. 8/11/2015.
[5] FDA Drug Safety Communication (SGLT2 Inhibitors) available online at: http://www.fda.gov/drugs/drugsafety/ucm446845.htm. Last revised: 5/19/2015. Last accessed: 8/11/2015
[6] FDA Drug Safety Communication (Daytrana®) available online at http://www.fda.gov/downloads/Drugs/DrugSafety/UCM452496.pdf Last revised: 6/24/2015. Last accessed: 8/11/2015.
[7] Label revision (Nonsteroidal Anti-Inflammatory Drugs) available online at http://www.fda.gov/Drugs/DrugSafety/ucm451800.htm. Last revised: 7/17/2015. Last accessed: 8/11/2015.
[8] FDA Drug Safety Communication (Brintellix®/Brilinta®) available online at http://www.fda.gov/Drugs/DrugSafety/ucm456341.htm. Last revised: 07/30/2015.. Last accessed: 8/21/2015
[9] FDA Drug Safety Communication (Gilenya®) available online at http://www.fda.gov/Drugs/DrugSafety/ucm456919.htm. Last revised: 8/7/2015. Last accessed: 8/11/2015.

Appendix C

Vote to Prior Authorize Hysingla® ER (Hydrocodone Bitartrate Extended-Release)

Oklahoma Health Care Authority
September 2015

Recommendations

The College of Pharmacy recommends the following changes to the Opioid Analgesic Product Based Prior Authorization (PBPA) category:

1. The addition of Hysingla® ER (hydrocodone bitartrate extended-release tablets) to Tier-3. Current criteria for this category will apply.
    a. Hysingla® ER is currently rebated to Tier-2, but will be placed in Tier-3 if the manufacturer chooses not to participate in supplemental rebates.
2. Moving Zohydro™ ER (hydrocodone bitartrate extended-release capsules) from the Special Prior Authorization (PA) category to Tier-3 based on reformulation with abuse-deterrent properties and to encourage supplemental rebate participation.

Opioid Analgesics*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
ASA/butalbital/caffeine/codeine (Fiorinal with Codeine®) codeine codeine/APAP hydromorphone (Dilaudid®) hydrocodone/APAP (Norco®) hydrocodone/IBU (Vicoprofen®, Ibudone®, Reprexain™) hydromorphone (Dilaudid®) methadone (Dolophine®) morphine IR (MSIR®) oxycodone/APAP (Percocet®) oxycodone/ASA (Percodan®) oxycodone ER 10mg, 15mg, 20mg only (Oxycontin®) oxycodone IR (Oxy IR®) oxycodone/ibuprofen (Combunox™) tramadol/APAP (Ultracet®) tramadol (Ultram®)	**Long-Acting:** buprenorphine (Butrans®) fentanyl patches (Duragesic®) **hydrocodone bitartrate ER (Hysingla® ER)** morphine ER tablets (MS Contin®) oxycodone ER (Oxycontin®) **Short-Acting:** oxymorphone IR (Opana®) tapentadol IR (Nucynta®)	**Long-Acting:** **hydrocodone bitartrate ER (Zohydro™ ER)** hydromorphone ER (Exalgo®) morphine sulfate ER (Avinza®) morphine sulfate ER (Kadian®) morphine/naltrexone (Embeda®) oxymorphone ER (Opana® ER)+ tapentadol ER (Nucynta® ER) tramadol ER (Ultram ER®, Ryzolt®) **Short-Acting:** hydrocodone/APAP (Xodol®, Zamicet®, Liquicet®) hydrocodone/APAP/caffeine (Trezix™) oxycodone/APAP (Primlev™, Xolox®) oxycodone (Oxecta®)	**Short-Acting:** Unique strengths of hydrocodone/APAP **Long-Acting:** oxycodone/APAP ER (Xartemis™ XR) **Oncology Only:** fentanyl (Actiq®) fentanyl (Fentora®) fentanyl (Onsolis® buccal film) fentanyl (Abstral®,Lazanda®) fentanyl (Subsys™ SL spray)

APAP: Acetaminophen, ASA: Aspirin, IBU: Ibuprofen, IR: Immediate-Release, ER: Extended-Release, SL: Sublingual
*Tier Structure based on supplemental rebate participation and/or state maximum allowable cost (SMAC). Tier-2 medications are subject to move to Tier-3.
+Brand name Opana® ER preferred. Generic oxymorphone extended-release tablets require special authorization. The generic formulation is not abuse-deterrent.

Appendix D

Vote to Prior Authorize Various Special Formulations: Sitavig® (Acyclovir Buccal Tablets), Rasuvo® (Methotrexate Injection), Otrexup™ (Methotrexate Injection), Onmel® (Itraconazole Oral Tablets), & Purixan® (Mercaptopurine Oral Suspension)

Oklahoma Health Care Authority
September 2015

Recommendations

The College of Pharmacy recommends the prior authorization of Sitavig® (acyclovir buccal tablets), Otrexup™ (methotrexate injection), Rasuvo® (methotrexate injection), Onmel™ (itraconazole oral tablets), & Purixan® (mercaptopurine oral suspension) with the following criteria:

1. **Sitavig® (Acyclovir Buccal Tablets) Approval Criteria:**
   a. An FDA approved diagnosis of recurrent herpes labialis (cold sores); and
   b. A patient-specific, clinically significant reason why the member cannot use acyclovir or valacyclovir oral tablets.

2. **Rasuvo® (Methotrexate Injection) & Otrexup™ (Methotrexate Injection) Approval Criteria:**
   a. An FDA approved diagnosis of one of the following:
      i. Adults with severe, active rheumatoid arthritis (RA); or
      ii. Children with active polyarticular juvenile idiopathic arthritis (pJIA); or
      iii. Severe, recalcitrant, disabling psoriasis confirmed by biopsy or dermatologic consultation; and
   b. Members with a diagnosis of RA or pJIA must have had an adequate trial of full dose NSAIDs; and
   c. A patient-specific, clinically significant reason why the oral tablets or the generic injectable formulation cannot be used.

3. **Onmel® (Itraconazole Oral Tablets) Approval Criteria:**
   a. An FDA approved diagnosis of onychomychosis of the toenail caused by *Trichophyton rubrum* or *T. mentagrophytes;* and
   b. A patient-specific, clinically significant reason why itraconazole 100mg oral capsules cannot be used in place of Onmel® 200mg tablets.

4. **Purixan® (Mercaptopurine Oral Suspension) Approval Criteria:**
   a. An FDA approved diagnosis of acute lymphoblastic leukemia (ALL); and
   b. An age restriction on members older than 10 years of age will apply. Members younger than 10 years of age and younger would not require prior authorization for Purixan® therapy; and
   c. Members older than 10 years of age would require a patient-specific, clinically significant reason why the oral tablet formulation cannot be used.

Appendix E

Vote to Prior Authorize Namzaric™ (Memantine Extended-Release/Donepezil)

Oklahoma Health Care Authority
September 2015

Recommendations

The College of Pharmacy recommends the prior authorization of Namzaric™ (memantine ER/donepezil) with the following criteria:

Alzheimer's Medications Approval Criteria:

1. Special formulation products including oral solutions, transdermal patches, and other convenience formulations require prior authorization with the following approval criteria:
    a. A patient-specific, clinically significant reason why the special formulation is necessary in place of the regular formulation.
2. An age restriction for ages 0-50 years applies to all Alzheimer's medications. Members older than 50 years of age can receive regular formulations without prior authorization. Members age 50 years or younger will require prior authorization with the following criteria:
    a. An FDA approved diagnosis; or
    b. Other patient specific, clinically significant information supporting the use of the medication.
3. Namzaric™ (Memantine ER/Donepezil) Approval Criteria:
    a. Member must have a patient-specific, clinically significant reason why the separate products cannot be used in place of this combination product; and
    b. A quantity limit of 30 capsules per 30 days will apply.

Appendix F

Vote to Prior Authorize Irenka™ (Duloxetine)

Oklahoma Health Care Authority
September 2015

Recommendations

The College of Pharmacy recommends placing Irenka™ (duloxetine 40mg delayed-release capsules) into the Special Prior Authorization (PA) category of the Antidepressant Product Based Prior Authorization (PBPA) category. The existing criteria for this category will apply. Additionally, use of Irenka™ for the diagnosis of diabetic peripheral neuropathy or chronic musculoskeletal pain will require a patient-specific, clinically significant reason why the member cannot use two duloxetine 20mg capsules in place of Irenka™ 40mg capsules.

Antidepressants*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
Selective Serotonin Reuptake Inhibitors (SSRIs)			
citalopram (Celexa®)			fluoxetine 60mg tablets
escitalopram (Lexapro®)			fluoxetine DR (Prozac® Weekly™)
fluoxetine (Prozac®, Sarafem®)			fluvoxamine CR (Luvox CR®)
fluvoxamine (Luvox®)			paroxetine CR (Paxil CR®)
paroxetine (Paxil®)			paroxetine (Pexeva®)
sertraline (Zoloft®)			
Dual Acting Antidepressants			
bupropion (Wellbutrin®, Wellbutrin SR®, Wellbutrin XL®)	vilazodone (Viibryd®)	desvenlafaxine (Khedezla®)	bupropion ER (Aplenzin®)
duloxetine (Cymbalta®)		desvenlafaxine (Pristiq®)	bupropion ER (Forfivo XL®)
mirtazapine (Remeron®, Remeron® SolTab™)		levomilnacipran (Fetzima®)	**duloxetine 40mg (Irenka™)**
trazodone (Desyrel®)		nefazodone (Serzone®)	trazodone ER (Oleptro®)
venlafaxine (Effexor®, Effexor XR® capsules)			venlafaxine ER tablets (Effexor XR® tablets)
Monoamine Oxidase Inhibitors (MAOIs)			
		phenelzine (Nardil®)	
		selegiline (Emsam®)	
		tranylcypromine (Parnate®)	
Unique Mechanisms of Action			
	vortioxetine (Brintellix®)		

*Tier structure based on supplemental rebate participation and/or state maximum allowable cost (SMAC).
CR = Controlled-Release DR = Delayed-Release ER = Extended-Release

Antidepressant Tier-2 Approval Criteria:

1. Member must have a documented, recent (within six months) trial of two Tier-1 medications at least four weeks in duration and titrated to recommended dosing, that did not provide an adequate response. Tier-1 selection must include at least one medication from the SSRI category and one trial with duloxetine; or
2. Prior stabilization on the Tier-2 medication documented within the last 100 days. A past history of success on the Tier-2 medication will also be considered with adequate documentation; or
3. A unique FDA-approved indication not covered by Tier-1 medications or other medications from a different therapeutic class; or
4. A petition may be submitted for consideration whenever a unique patient-specific situation exists.

Antidepressant Tier-3 Approval Criteria:

1. Member must have a documented, recent (within six months) trial with two Tier-1 medications (one medication from the SSRI category and one trial with duloxetine) and a trial of a Tier-2 medication at least four weeks in duration and titrated to recommended dosing, that did not provide an adequate response; or
2. Prior stabilization on the Tier-3 medication documented within the last 100 days. A past history of success on the Tier-3 medication will also be considered with adequate documentation; or
3. A unique FDA-approved indication not covered by a lowered tiered medication or other medications from a different therapeutic class; or
4. A petition may be submitted for consideration whenever a unique patient-specific situation exists.

Antidepressant Special Prior Authorization (PA) Approval Criteria:

1. Use of any Special PA medication will require a patient-specific, clinically significant reason why the member cannot use other available generic Tier-1 medications; or
2. A petition may be submitted for consideration whenever a unique patient-specific situation exists.
3. Tier structure rules still apply.
4. When Irenka™ (Duloxetine 40mg) is being requested for non-depression related diagnoses, the criteria below will apply:
    a. An FDA approved diagnosis of diabetic peripheral neuropathy or chronic musculoskeletal pain; and
    b. A patient-specific, clinically significant reason why the member cannot use two duloxetine 20mg capsules in place of Irenka™ 40mg capsules; and
    c. A quantity limit of 30 capsules per 30 days will apply.

Appendix G

Vote to Prior Authorize Corlanor® (Ivabradine)

Oklahoma Health Care Authority
September 2015

Recommendations

The College of Pharmacy recommends the prior authorization of Corlanor® (ivabradine) with the following criteria:

Corlanor® (Ivabradine) Approval Criteria:

1. An FDA approved diagnosis of symptomatic stable, chronic worsening heart failure; and
2. The prescriber must verify that the member has left ventricular ejection fraction ≤ 35%; and
3. The prescriber must verify that the member is in sinus rhythm with a resting heart rate ≥ 70 beats per minute; and
4. The member must be on maximal/maximally tolerated doses of beta-blockers or have a contraindication to beta-blockers; and
5. A quantity limit of 60 tablets per 30 days will apply.

Appendix H

30-Day Notice to Prior Authorize Tykerb® (Lapatinib), Halaven® (Eribulin), Ixempra® (Ixabepilone), Kadcyla® (Ado-trastuzumab), Afinitor® (Everolimus), & Perjeta® (Pertuzumab)

Oklahoma Health Care Authority
September 2015

Introduction[1,2,3,4,5]

According to the National Cancer Institute, in 2015 an estimated 1,658,370 new cases of cancer will be diagnosed in the U.S. Breast cancer is the most common cancer found in women with an estimated 231,840 new cases in 2015. The most common type of breast cancer is ductal carcinoma, which begins in the cells of the ducts. Breast cancer can also begin in the cells of the lobules and in other tissues in the breast. Invasive breast cancer is breast cancer that has spread from where it began in the ducts or lobules to surrounding tissue. Traditional chemotherapy has long been used to treat breast cancer, but in more recent years targeted chemotherapy is being developed to specifically take advantage of gene changes in cells that cause cancer [e.g. drugs that target Human Epidermal Receptor Type 2 (HER2), anti-angiogenesis drugs, etc.].

These targeted cancer drugs come at a high price for many reasons. They include:

1) The high cost of drug development and performing all regulatory studies (phase 1, 2, and 3 clinical trials);
2) The treatment paradigm for incurable cancers where patients are treated with every approved agent (sequentially or in combination), creating a virtual monopoly because the use of one drug does not automatically mean that the others are no longer needed;
3) The older (sometimes generic) version of treatment may be viewed as substandard treatment;
4) The seriousness of a cancer diagnosis leads to patients and physicians that are willing to pay higher prices of treatment, even with potentially marginal improvements in outcome;
5) The health care systems provide an incentive to administer more chemotherapy (fee-for-service);
6) There are legal barriers that prevent agencies such as the FDA from taking economic and cost-effectiveness considerations into account when approving new drugs.

An article in the *Journal of the National Cancer Institute* lists the following principles to address controlling cancer care costs:

1) Low prices alone may indicate skimping on effective treatment rather than identifying high-value care. Reliable quality measures can help distinguish high-value care from inexpensive but low-value care.

2) Interventions must consider total costs for cancer care. Shifting costs, for example, away from chemotherapy and outpatient supportive care toward increased hospitalization for symptoms is not a solution.
3) Eliminating the use of services that either have no supporting evidence of superior outcomes or good evidence of similar outcomes but higher costs will reduce costs without harming patients.
4) Communication with patients about the risks, benefits, and costs of alternative therapies is critical because patients are suspicious of efforts to reduce costs, often justifiably.

Use of evidence-based expert consensus guidelines is imperative in the treatment of cancers. The National Comprehensive Cancer Network (NCCN) Compendium contains authoritative, scientifically derived information designed to support decision-making about the appropriate use of drugs and biologics in patients with cancer. These evidence-based guidelines should be used for optimal outcomes of cancer patients.

Utilization of Oncology Medications: Calendar Year 2014

Comparison of Calendar Years: Oncology Medications (Pharmacy Claims)

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2013	2,906	13,807	$8,633,336.38	$625.29	$20.43	913,906	422,656
2014	2,786	13,822	$9,118,034.29	$659.68	$22.15	844,131	411,628
% Change	**-4.10%**	**0.10%**	**5.60%**	**5.50%**	**8.40%**	**-7.60%**	**-2.60%**
Change	**-120**	**15**	**$484,697.91**	**$34.39**	**$1.72**	**-69,775**	**-11,028**

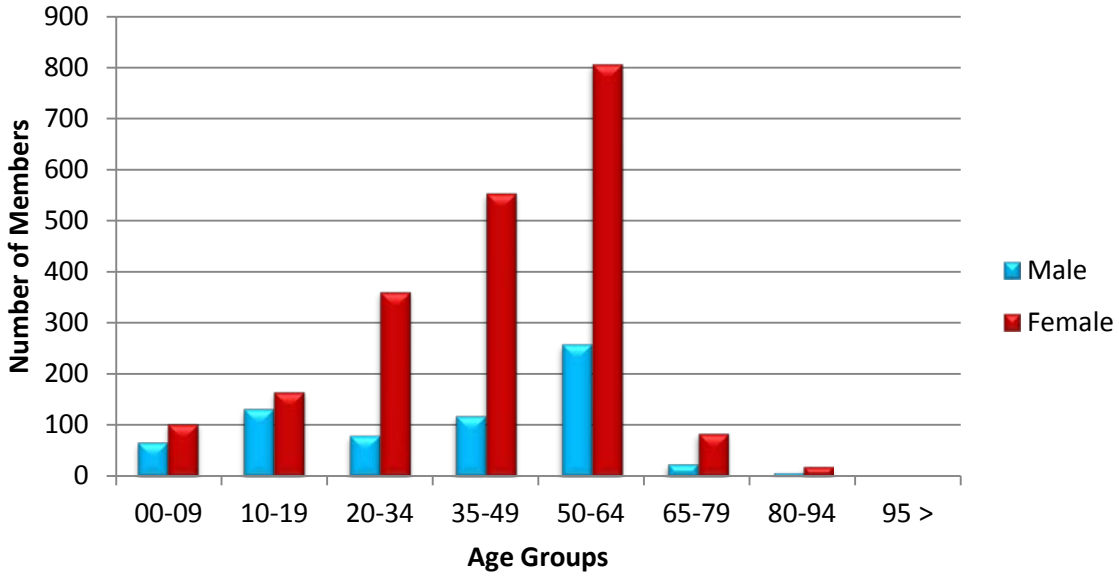
*Total number of unduplicated members.

Calendar Year 2014 Utilization of Oncology Medications: Medical Claims

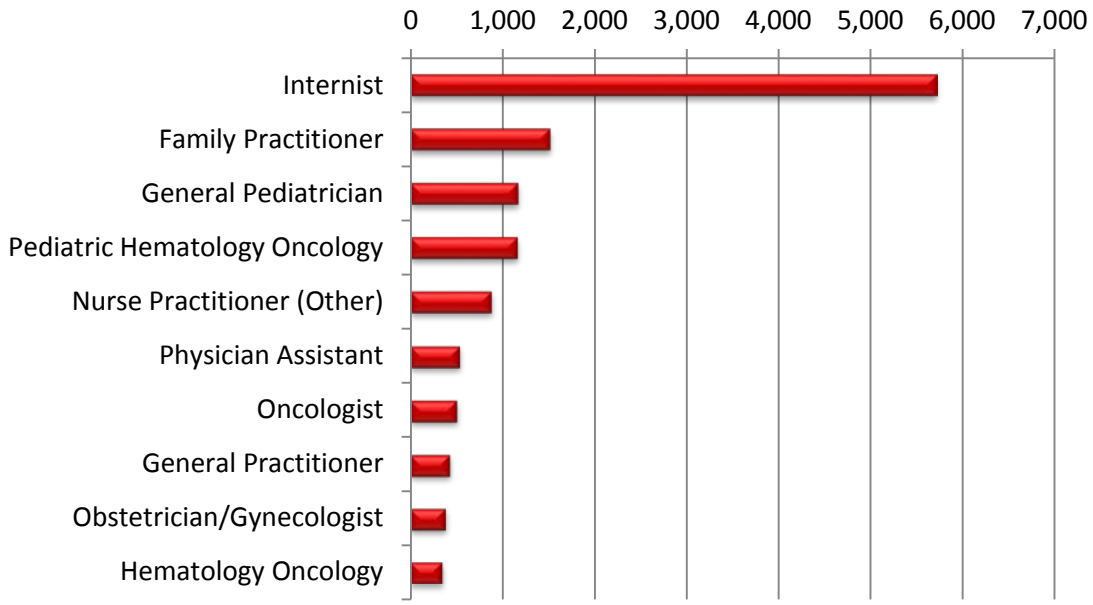
*Total Members	Total Claims	Total Cost	Cost/Claim	Total Units
1,327	7,447	$12,592,787.99	$1,690.99	571,870.4

*Total number of unduplicated members.

Demographics of Members Utilizing Oncology Medications: Pharmacy Claims



Top Prescriber Specialties of Oncology Medications By Number of Claims: Pharmacy Claims



Utilization of Breast Cancer Medications: Calendar Year 2014

Comparison of Calendar Years:
Breast Cancer Medications (Pharmacy Claims)

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2013	1,022	4,867	$2,087,580.52	$428.93	$12.15	186,661	171,845
2014	929	4,458	$2,519,250.20	$565.11	$16.12	168,669	156,315
% Change	**-9.10%**	**-8.40%**	**20.70%**	**31.70%**	**32.70%**	**-9.60%**	**-9.00%**
Change	**-93**	**-409**	**$431,669.68**	**$136.18**	**$3.97**	**-17,992**	**-15,530**

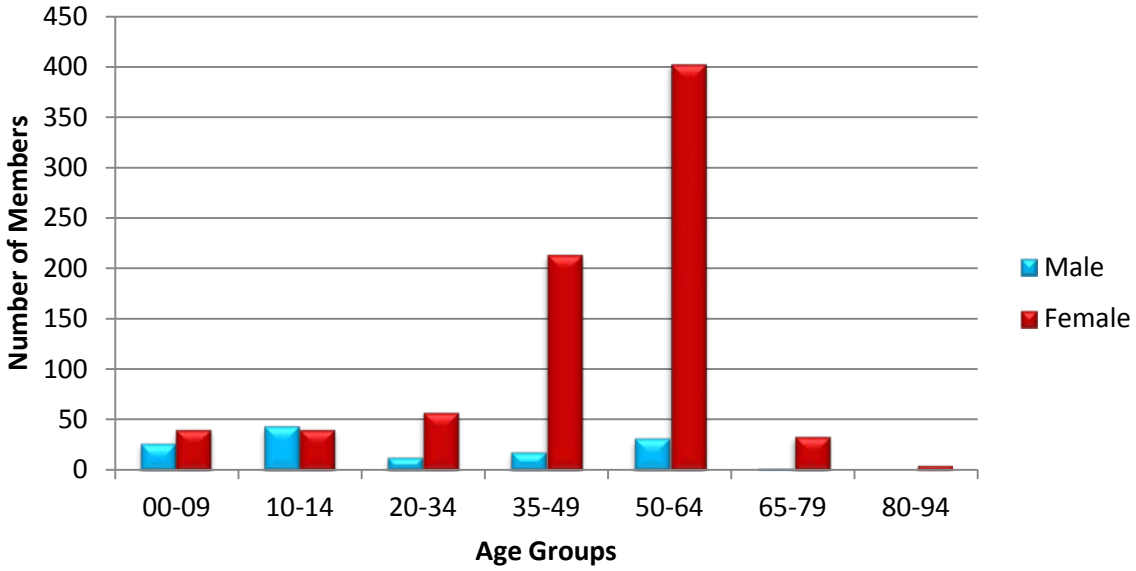
*Total number of unduplicated members.

Calendar Year 2014 Utilization of Breast Cancer Medications: Medical Claims

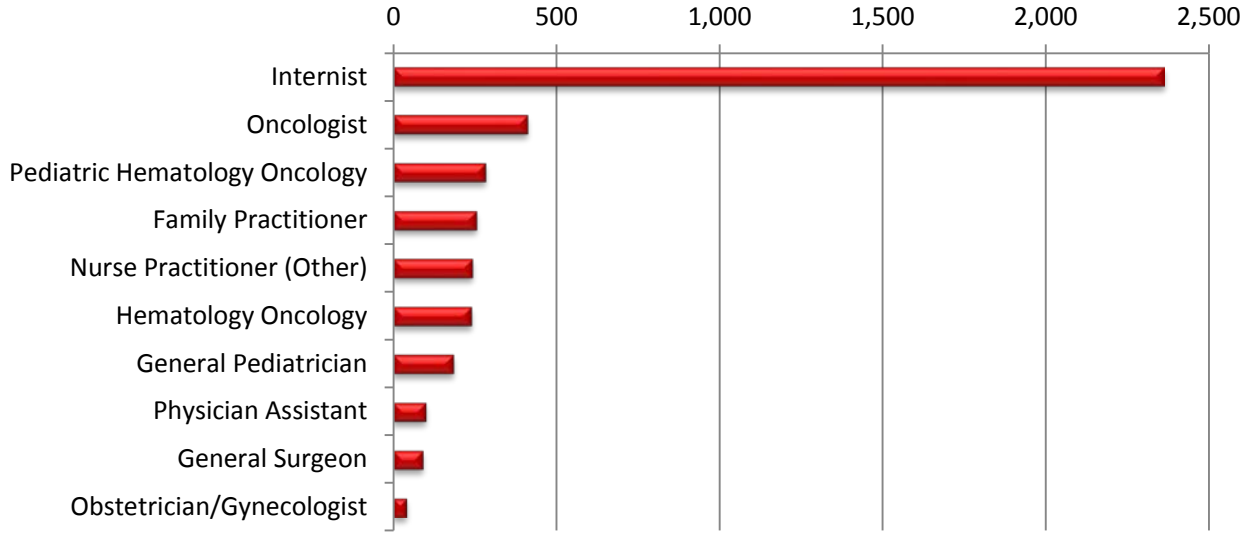
*Total Members	Total Claims	Total Cost	Cost/Claim	Total Units
1,090	5,880	$7,490,565.43	$1,273.91	303,064.4

*Total number of unduplicated members.

Demographics of Members Utilizing Breast Cancer Medications: Pharmacy Claims



Top Prescriber Specialties of Breast Cancer Medications By Number of Claims: Pharmacy Claims



Market News and Updates

NCCN guidelines for the treatment of breast cancer are continually updated, but the major indications are reflected in the product summaries. None of the medications listed will have their patent expire in the next 12 months.

Product Summaries

Tykerb® (lapatinib)

- Lapatinib is a kinase inhibitor indicated for the following:
  - In combination with capecitabine for the treatment of patients with advanced metastatic breast cancer whose tumors overexpress HER2 and who have received prior therapy including an anthracycline, a taxane, and trastuzumab
  - *Limitation of use: Patients should have disease progression on trastuzumab prior to initiation of treatment with lapatinib in combination with capecitabine.*
  - In combination with letrozole for the treatment of postmenopausal women with hormone receptor positive metastatic breast cancer that overexpresses the HER2 receptor for whom hormonal therapy is indicated
  - Lapatinib in combination with an aromatase inhibitor has not been compared to a trastuzumab-containing chemotherapy regimen for the treatment of metastatic breast cancer.

Halaven® (eribulin)

- Eribulin is a mictrotubule inhibitor indicated for the following:
  - Treatment of patients with metastatic breast cancer who have previously received at least two chemotherapeutic regimens for the treatment of metastatic disease

- Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting.

Ixempra® (ixabepilone)

- Ixabepilone is a mictrotubule inhibitor with low susceptibility to tumor resistance mechanisms indicated for the following:
  - In combination with capecitabine for the treatment of metastatic or locally advanced breast cancer in patients after failure of an anthracycline and a taxane
    - May be used in combination in taxane only resistance if anthracylines not indicated
  - Monotherapy is indicated for the treatment of metastatic or locally advanced breast cancer.

Kadcyla® (ado-trastuzumab)

- Ado-trastuzumab is a HER-2 targeted monoclonal antibody conjugated with a microtubule inhibitor indicated for the following:
  - Treatment of patients with HER-2 positive metastatic breast cancer who previously received trastuzumab and a taxane (separately or in combination)
  - *Limitation of use: Patients should have received prior therapy for metastatic disease or have had disease progression within six months of completing adjuvant therapy*

Afinitor® (everolimus)

- Everolimus is an oral kinase inhibitor indicated for the following:
  - Postmenopausal women with advanced hormone receptor-positive, HER2-negative breast cancer in combination with exemestane after failure of treatment with letrozole or anastrozole

Perjeta® (pertuzumab)

- Pertuzumab is a recombinant humanized monoclonal antibody targeting HER2 indicated for the following:
  - HER2-positive metastatic breast cancer in combination with trastuzumab and docetaxel
  - Neoadjuvant treatment in locally advanced, inflammatory, or early stage HER2-positive breast cancer in combination with trastuzumab and docetaxel

Recommendations

Tykerb® (Lapatinib) Approval Criteria:

1. An FDA approved diagnosis of metastatic or recurrent breast cancer; and
2. Positive expression of Human Epidermal Receptor Type 2 (HER2); and
3. Tykerb® must be used in combination with one of the following:
   a. Herceptin (trastuzumab); or
   b. Xeloda (capecitabine); or

c. An aromatase inhibitor [e.g. Aromasin® (exemestane), Femara® (letrozole) or Arimidex® (anastrozole)] if also estrogen receptor positive (ER positive)

Halaven® (Eribulin) Approval Criteria:

1. Diagnosis of metastatic breast cancer; and
2. Previously received at least two chemotherapeutic regimens for the treatment of metastatic disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting.

Ixempra® (Ixabepilone) Approval Criteria:

1. Diagnosis of metastatic or locally advanced breast cancer; and
2. Usage as either:
   a. Combination with capecitabine after failure of an anthracycline and a taxane
      i. May be used in combination in taxane only resistance if anthracylines not indicated; or
   b. Monotherapy after failure of an anthracycline, a taxane, and capecitabine

Kadcyla® (Ado-Trastuzumab) Approval Criteria:

1. Positive expression of Human Epidermal Receptor Type 2 (HER2); and
2. Diagnosis of metastatic breast cancer; and
3. Has previously received trastuzumab and a taxane, separately or in combination; and
4. Patients should also have either:
   a. Received prior therapy for metastatic disease; or
   b. Developed disease recurrence during or within six months of completing adjuvant therapy

Afinitor® (Everolimus) Approval Criteria:

1. Diagnosis of advanced breast cancer; and
2. Negative expression of Human Epidermal Receptor Type 2 (HER2); and
3. Hormone receptor-positive (ER positive); and
4. Used in combination with exemestane; and
5. Must have failed treatment with, has a contraindication to, or intolerant to letrozole or anastrozole

Perjeta® (Pertuzumab) Approval Criteria:

1. Positive expression of Human Epidermal Receptor Type 2 (HER2); and
2. Usage for either:
   a. Metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease; or
   b. Neoadjuvant treatment of patients with locally advanced, inflammatory, or early stage breast cancer (either greater than 2cm in diameter or node positive); and
3. Used in combination with trastuzumab and docetaxel (neoadjuvant treatment may also contain other agents as well in addition to trastuzumab and docetaxel)

Utilization Details of Breast Cancer Medications: Calendar Year 2014

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
TAMOXIFEN PRODUCTS					
TAMOXIFEN TAB 20MG	974	207	$21,932.90	4.71	$22.52
TAMOXIFEN TAB 10MG	140	30	$2,216.01	4.67	$15.83
SUBTOTAL	**1,114**	**227**	**$24,148.91**	**4.91**	**$21.68**
AROMATASE INHIBITOR PRODUCTS					
ANASTROZOLE TAB 1MG	863	201	$11,158.85	4.29	$12.93
LETROZOLE TAB 2.5MG	591	142	$7,253.04	4.16	$12.27
EXEMESTANE TAB 25MG	291	63	$110,301.50	4.62	$379.04
AROMASIN TAB 25MG	15	3	$4,523.97	5	$301.60
ARIMIDEX TAB 1MG	12	1	$135.46	12	$11.29
SUBTOTAL	**1,772**	**383**	**$133,372.82**	**4.63**	**$75.27**
METHOTREXATE PRODUCTS					
METHOTREXATE INJ 25MG/ML	495	166	$9,333.20	2.98	$18.85
METHOTREXATE INJ 50MG/2ML	356	95	$4,063.31	3.75	$11.41
METHOTREXATE INJ 25MG/ML	58	19	$635.21	3.05	$10.95
METHOTREXATE INJ 250/10ML	48	26	$624.06	1.85	$13.00
METHOTREXATE INJ 100/4ML	7	2	$63.25	3.5	$9.04
METHOTREXATE INJ 200/8ML	1	1	$13.00	1	$13.00
SUBTOTAL	**965**	**257**	**$14,732.03**	**3.75**	**$15.27**
CAPECITABINE PRODUCTS					
CAPECITABINE TAB 500MG	117	42	$388,142.65	2.79	$3,317.46
XELODA TAB 500MG	87	34	$303,970.29	2.56	$3,493.91
CAPECITABINE TAB 150MG	8	3	$3,618.96	2.67	$452.37
XELODA TAB 150MG	7	5	$6,384.40	1.4	$912.06
SUBTOTAL	**219**	**61**	**$702,116.30**	**3.59**	**$3,206.01**
EVEROLIMUS PRODUCTS					
AFINITOR TAB 10MG	96	20	$950,194.31	4.8	$9,897.86
AFINITOR TAB 5MG	17	5	$163,494.55	3.4	$9,617.33
AFINITOR TAB 7.5MG	7	1	$68,997.77	7	$9,856.82
AFINITOR DIS TAB 2MG	5	1	$48,177.65	5	$9,635.53
SUBTOTAL	**125**	**25**	**$1,230,864.28**	**5**	**$9,846.91**
BEVACIZUMAB PRODUCTS					
AVASTIN INJ 400/16ML	47	6	$172,520.97	7.83	$3,670.66
AVASTIN INJ	36	8	$58,053.04	4.5	$1,612.58
SUBTOTAL	**83**	10	**$230,574.01**	**8.3**	**$2,778.00**
CARBOPLATIN PRODUCTS					
CARBOPLATIN INJ 150/15ML	46	5	$931.29	9.2	$20.25
SUBTOTAL	**46**	**5**	**$931.29**	**9.2**	**$20.25**
DOXORUBICIN PRODUCTS					

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
DOXORUBICIN INJ 2MG/ML	40	15	$1,902.83	2.67	$47.57
SUBTOTAL	**40**	**15**	**$1,902.83**	**2.67**	**$47.57**
LAPATINIB PRODUCTS					
TYKERB TAB 250MG	33	7	$157,077.41	4.71	$4,759.92
SUBTOTAL	**33**	**7**	**$157,077.41**	**4.71**	**$4,759.92**
CYCLOPHOSPHAMIDE PRODUCTS					
CYCLOPHOSPH INJ 500MG	27	8	$11,797.64	3.38	$436.95
CYCLOPHOSPH INJ 1GM	17	5	$10,687.40	3.4	$628.67
SUBTOTAL	**44**	**13**	**$22,485.04**	**3.38**	**$511.02**
FLUOROURACIL PRODUCTS					
FLUOROURACIL INJ 5GM/100M	12	3	$757.54	4	$63.13
FLUOROURACIL INJ 2.5G/50M	5	2	$287.74	2.5	$57.55
SUBTOTAL	**17**	**3**	**$1,045.28**	**5.67**	**$61.49**
TOTAL	**4,458**	**929***	**$2,519,250.20**	**4.8**	**$565.11**

*Total number of unduplicated members.

Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM
J9395 FULVESTRANT INJECTION	92	21	$136,142.47	$1,479.81
J8520 CAPECITABINE ORAL	32	2	$35,574.12	$1,111.69
J9070 CYCLOPHOSPHAMIDE	564	166	$347,721.70	$616.53
J9171 DOCETAXEL INJECTION	495	136	$487,596.41	$985.04
J9000 DOXORUBICIN INJECTION	500	154	$9,285.09	$18.57
J9178 EPIRUBICIN INJECTION	17	5	$1,353.80	$79.64
J9190 FLUOROURACIL INJECTION	851	142	$9,856.22	$11.58
J9260 METHOTREXATE INJECTION	188	68	$150.67	$0.80
J9264 PACLITAXEL PROTEIN BOUND	165	33	$412,787.27	$2,501.74
J9265 PACLITAXEL INJECTION	1,133	227	$37,893.08	$33.44
J9355 TRASTUZUMAB INJECTION	692	97	$2,765,560.31	$3,996.47
J9045 CARBOPLATIN INJECTION	796	226	$26,932.64	$33.83
J9306 PERTUZUMAB INJECTION	123	29	$643,524.00	$5,231.90
J9354 ADO-TRASTUZUMAB INJECTION	16	3	$143,408.40	$8,963.03
J9035 BEVACIZUMAB INJECTION	965	274	$2,134,727.87	$2,212.15
J9060 CISPLATIN INJECTION	692	157	$9,085.58	$13.13
J9201 GEMCITABINE	418	74	$26,125.78	$62.50
J9179 ERIBULIN MESYLATE INJECTION	59	9	$184,001.40	$3,118.67
J9207 IXABEPILONE INJECTION	14	4	$76,286.65	$5,449.05
J9390 VINORELBINE TARTRATE INJECTION	49	9	$2,551.97	$52.08
TOTAL	**5,880+**	**1,090***	**$7,490,565.43**	**$1,273.91**

+Total number of unduplicated claims.

*Total number of unduplicated members.

[1] National Cancer Institute. SEER Cancer Statistics. Retrieved July 20, 2015, from http://www.cancer.gov/about-cancer/what-is-cancer/statistics.

[2] American Cancer Society. *What's new in breast cancer research and treatment*? Retrieved July 20, 2015, from http://www.cancer.org/cancer/breastcancer/detailedguide/breast-cancer-new-research.

[3] Siddiqui M and Rajkumar SV. The high cost of cancer drugs and what we can do about it. Mayo Clin Proc 2012;87:935-943.

[4] NCCN. *NCCN drugs & biologics compendium (NCCN Compendium)*. Retrieved August 6, 2015, from http://www.nccn.org/professionals/drug_compendium/content/contents.asp.

[5] Ramsey SD, Ganz PA, Shankaran V, et al. Addressing the American health-care cost crisis: Role of the oncology community. J Natl Cancer Inst 2013;105:1777-8.

Appendix I

30-Day Notice to Prior Authorize Orkambi™ (Lumacaftor/Ivacaftor)

Oklahoma Health Care Authority
September 2015

Introduction[1,2]

Cystic Fibrosis (CF) is a life-threatening, genetic disease that causes persistent lung infections and progressively limits the ability to breathe. In people with CF, a defective gene causes a thick buildup of mucus in the lungs, pancreas, and other organs. In the lungs, the mucus clogs the airways and traps bacteria leading to infections, extensive lung damage, and eventually, respiratory failure. In the pancreas, the mucus prevents the release of digestive enzymes that allow the body to break down food and absorb vital nutrients.

CF affects roughly 30,000 people in the United States; approximately 1,000 new cases of cystic fibrosis are diagnosed each year. More than 1,800 mutations of the cystic fibrosis transmembrane regulator (CFTR) gene have been found. Homozygous F508del mutation is the most common genetic mutation seen, occurring in about 8,500 people in the United States. With an F508del mutation, CFTR proteins are deficient meaning too few of the regulators reach the cell surface.

General standards of medication management of CF are pancreatic enzyme supplements, multivitamins (including fat-soluble vitamins), mucolytics, antibiotics (nebulized, inhaled, oral, or intravenous), bronchodilators, anti-inflammatory agents, and agents devised to potentially reverse the abnormalities in chloride transport (i.e. ivacaftor). Orkambi™ (lumacaftor/ivacaftor) is a medication approved by the FDA in July 2015 for CF patients with two copies of the F508del mutation in their CFTR gene.

Orkambi™ (Lumacaftor/Ivacaftor) Product Summary[3,4,5,6]

Indications: Orkambi™ (lumacaftor/ivacaftor) is indicated for patients with CF age 12 years and older who are homozygous for the F508del mutation in the CFTR gene. If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of the F508del mutation on both alleles of the CFTR gene.

Dosing:

- Lumacaftor/ivacaftor is available as a 200mg/125mg tablet.
- The recommended dosing is 400mg/250mg (2 tablets) orally every 12 hours.
- Lumacaftor/ivacaftor should be taken with fat-containing food (i.e. eggs, avocado, nuts, butter).

Mechanism of Action: Lumacaftor improves the conformational stability of F508del-CFTR, resulting in increased processing and trafficking of mature protein to the cell surface. Ivacaftor is a CFTR potentiator that facilitates increased chloride transport by potentiating the channel-open probability (or gating) of the CFTR protein at the cell surface.

Contraindications: None

Special Populations:

- Pregnancy: Lumacaftor/ivacaftor is Pregnancy Category B. There are no adequate and well-controlled trials of lumacaftor or ivacaftor in pregnant women.
- Lactation: It is not currently known if lumacaftor or ivacaftor is excreted into breast milk, however excretion is expected. The manufacturer recommends that caution be used if administered to a breast-feeding woman.
- Pediatric Use: Lumacaftor/ivacaftor is not approved for patients younger than 12 years.
- Geriatric Use: Clinical trials of lumacaftor/ivacaftor did not include sufficient numbers of patients 65 years of age and older to determine whether they respond differently than younger patients.
- Hepatic Impairment: No dose adjustment is necessary for patients with mild hepatic impairment (Child-Pugh Class A). A dose reduction to two tablets in the morning and one tablet in the evening (lumacaftor 600mg/ivacaftor 375mg total daily dose) is recommended for patients with moderate hepatic impairment (Child-Pugh Class B). Studies have not been conducted in patients with severe hepatic impairment (Child-Pugh Class C), but exposure is expected to be higher than in patients with moderate hepatic impairment. Therefore, use with caution at a maximum dose of one tablet in the morning and one tablet in the evening (lumacaftor 400mg/ivacaftor 250mg total daily dose), or less, in patients with severe hepatic impairment after weighing the risks and benefits of treatment.
- Renal Impairment: Lumacaftor/ivacaftor has not been studied in patients with mild, moderate, or severe renal impairment or in patients with end-stage renal disease. No dose adjustment is necessary for patients with mild-to-moderate renal impairment. Caution is recommended while using lumacaftor/ivacaftor in patients with severe renal impairment (creatinine clearance less than or equal to 30 mL/min) or end-stage renal disease.

Safety:

- Liver-Related Events: Worsening of liver function, including hepatic encephalopathy, in patients with advanced liver disease has been reported in some patients with CF while receiving lumacaftor/ivacaftor. Serious adverse reactions related to elevated transaminases have been reported in patients with CF while receiving lumacaftor/ivacaftor. Use with caution in patients with advanced liver disease and only if the benefits are expected to outweigh the risks.
- Respiratory Events: Respiratory events (e.g. chest discomfort, dyspnea, and respiratory abnormalities) were observed more commonly in patients during initiation of lumacaftor/ivacaftor compared to those who received placebo. Clinical experience in patients with percent predicted FEV_1 ($ppFEV_1$) <40% is limited, and additional monitoring of these patients is recommended during initiating of therapy.
- Drug Interactions:
    - Lumacaftor is a strong inducer of CYP3A. Administration of lumacaftor/ivacaftor may decrease systemic exposure of medicinal products that are substrates of CYP3A, which may decrease therapeutic effect. Co-administration with sensitive

CYP3A substrates (e.g. tacrolimus, cyclosporine, midazolam) with a narrow therapeutic index is not recommended.

- Ivacaftor is a substrate of CYP3A4 and CYP3A5 isoenzymes. Use of lumacaftor/ivacaftor with strong CYP3A inducers, such as rifampin, significantly reduces ivacaftor exposure, which may reduce therapeutic effectiveness. Therefore, co-administration with strong CYP3A inducers (e.g. rifampin, St. John's wort) is not recommended.
- Lumacaftor/ivacaftor may substantially decrease hormonal contraceptive exposure, reducing their effectiveness and increasing the incidence of menstruation-associated reactions. Hormonal contraceptives, including oral, injectable, transdermal, and implantable, should not be relied upon as an effective method of contraception when co-administered with lumacaftor/ivacaftor.

Adverse Drug Reactions:

Adverse Reaction	Lumacaftor/Ivacaftor N = 369	Placebo N = 370
Dyspnea	13%	8%
Nasopharyngitis	13%	11%
Nausea	13%	8%
Diarrhea	12%	8%
Upper Respiratory Tract Infection	10%	5%

Efficacy:

- TRANSPORT and TRAFFIC were two randomized control trials (*N*=1108) conducted in patients with CF that were homozygous for the F508del CFTR mutation and had a baseline FEV_1 between 40-90%. Both studies were 24 weeks in duration. Lumacaftor/ivacaftor showed significant improvements in the primary endpoint of efficacy, absolute change from baseline in $ppFEV_1$ at week 24. The difference between active treatment and placebo with respect to the mean absolute percentage of predicted FEV_1 ranged from 2.6 to 4.0 percentage points ($P<0.001$), which correspond to a mean relative treatment difference of 4.3 to 6.7% ($P<0.001$).
- Secondary pooled analyses showed that the rate of pulmonary exacerbations was lower in the lumacaftor/ivacaftor group compared to placebo. The relative change in baseline FEV_1 and changes in BMI were higher in the lumacaftor/ivacaftor group compared to placebo. These were all statistically significant. The absolute change in Cystic Fibrosis Questionnaire-Revised (CFQ-R) score, measuring health-related quality of life, was lower in the lumacaftor/ivacaftor group compared to placebo, but was not statistically significant.
- The incidence of adverse events was generally similar in the lumacaftor/ivacaftor and placebo groups. The rate of discontinuation due to an adverse event was 4.2% among patients who received lumacaftor/ivacaftor versus 1.6% among those who received placebo.

Utilization: Three members have utilized lumacaftor/ivacaftor since its approval on July 2nd, 2015.

Cost Comparison:

Orkambi™ (Lumacaftor/Ivacaftor) vs. Recommended Maximum Kalydeco® (Ivacaftor) Dose for Cystic Fibrosis				
Medication Name	**Strength**	**Cost Per Unit***	**Cost Per Month*,+**	**Cost Per Year*,+**
Orkambi™	**200mg/125mg**	**$187.85**	**$21,039.20**	**$252,470.40**
Kalydeco®	150mg	$450.61	$25,234.16	$302,809.92

*Cost based on Estimated Acquisition Cost (EAC).

+Cost based on recommended dosing.

Kalydeco® is not indicated in the F508del mutation in the CFTR gene, but is indicated in the following CFTR mutations: *G551D*, *G1244E*, *G1349D*, *G178R*, *G551S*, *R117H*, *S1251N*, *S1255P*, *S549N*, or *S549R.*

Recommendations

The College of Pharmacy recommends prior authorization of Orkambi™ (lumacaftor/ivacaftor) with the following criteria:

Orkambi™ (Lumacaftor/Ivacaftor) Approval Criteria:

1. An FDA approved diagnosis of cystic fibrosis (CF) in patients who are homozygous for the F508del mutation in the CFTR gene detected by genetic testing; and
2. If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of the F508del mutation on both alleles of the CFTR gene; and
3. Orkambi™ will not be approved for patients with CF other than those homozygous for the F508del mutation; and
4. Documentation must be provided showing baseline FEV_1 between 40-90%; and
5. Member must be 12 years of age or older; and
6. Members using Orkambi™ must be supervised by a pulmonary specialist; and
7. The prescriber must verify that ALT, AST, and bilirubin will be assessed prior to initiating Orkambi™, every three months during the first year of treatment, and annually thereafter; and
8. Members must not be taking any of the following medications concomitantly with Orkambi™: rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin, and St. John's wort; and
9. A quantity limit of four tablets per day or 112 tablets per 28 days will apply.
10. Initial approval will be for the duration of three months, after which time, compliance and information regarding efficacy, such as improvement in FEV_1, will be required for continued approval.

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[1] "About Cystic Fibrosis." Cystic Fibrosis Foundation. Available online at: https://www.cff.org/What-is-CF/About-Cystic-Fibrosis/. Last revised 07/2015. Last accessed 07/2015.

[2] Sharma GD. Cystic Fibrosis Treatment and Management. In: Medscape. Bye MR (Ed). Available online at: http://emedicine.medscape.com/article/1001602-treatment. Last revised 07/2015. Last accessed 07/2015.

[3] Orkambi monograph. Lexi-Comp Online™, Pediatric Lexi-Drugs Online™, Hudson, Ohio: Lexi-Comp, Inc.; 2015; July 24, 2015.

[4] Orkambi. Drug Facts and Comparisons. eFacts [online]. 2015. Available from Wolters Kluwer Health, Inc. Accessed July 24, 2015.

[5] Orkambi package insert. Boston, MA: Vertex Pharmaceuticals Incorporated; 2015 July.

[6] Wainwright CE, Elborn JS, Ramsey BW, et al. Lumacaftor-Ivacaftor in Patients with Cystic Fibrosis Homozygous for Phe508del CFTR. *N Engl J Med* 2015; 373(3): 220-231.

Appendix J

Fiscal Year 2015 Annual Review of Synagis® (Palivizumab)

Oklahoma Health Care Authority
September 2015

Current Prior Authorization Criteria

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

Synagis® (Palivizumab) Approval Criteria:

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

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

B. Length of treatment: Palivizumab is approved for use only during RSV season. Approval dates will be November 1st through March 31st.

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

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

Utilization of Palivizumab: Fiscal Year 2015

Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Total Units	Total Days
2014	659	2,458	$5,375,581.42	$2,186.97	$73.03	2,112
2015	476	2,213	$4,797,391.82	$2,167.82	$72.25	1,887
% Change	-27.80%	-10.00%	-10.80%	-0.90%	-1.10%	-10.70%
Change	-183	-245	-$578,189.60	-$19.15	-$0.78	-225

*Total number of unduplicated members.

Pharmacy Claim Details for Season 2014-2015

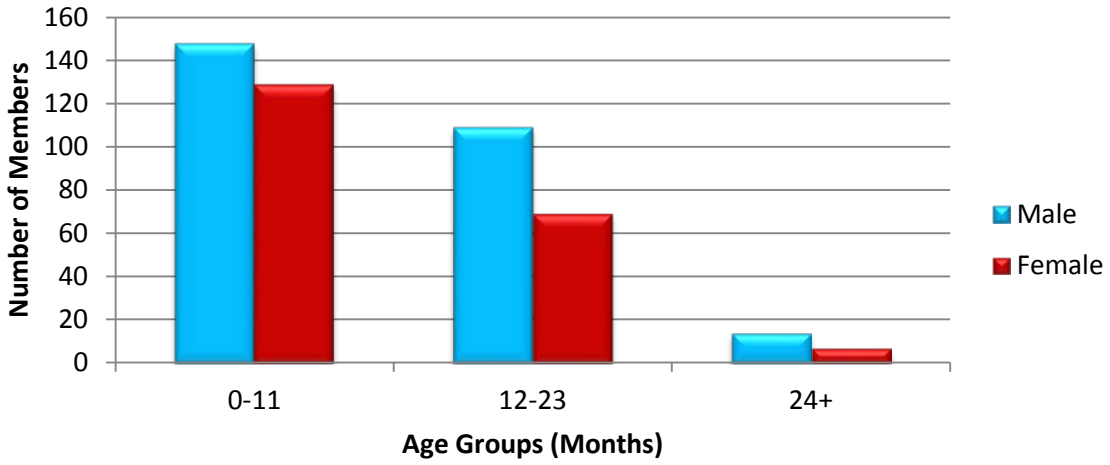
Product Utilized	Total Claims	Total Members	Total Cost	Claims/ Member	Cost/ Claim	% Cost
SYNAGIS INJ 100MG/ML	1,475	427	$3,807,073.222	3.45	$2,581.07	79.36%
SYNAGIS INJ 50MG/0.5ML	738	335	$990,318.60	2.2	$1,341.90	20.64%
Total	2,213	476*	$4,797,391.82	4.65	$2,167.82	100%

*Total number of unduplicated members.

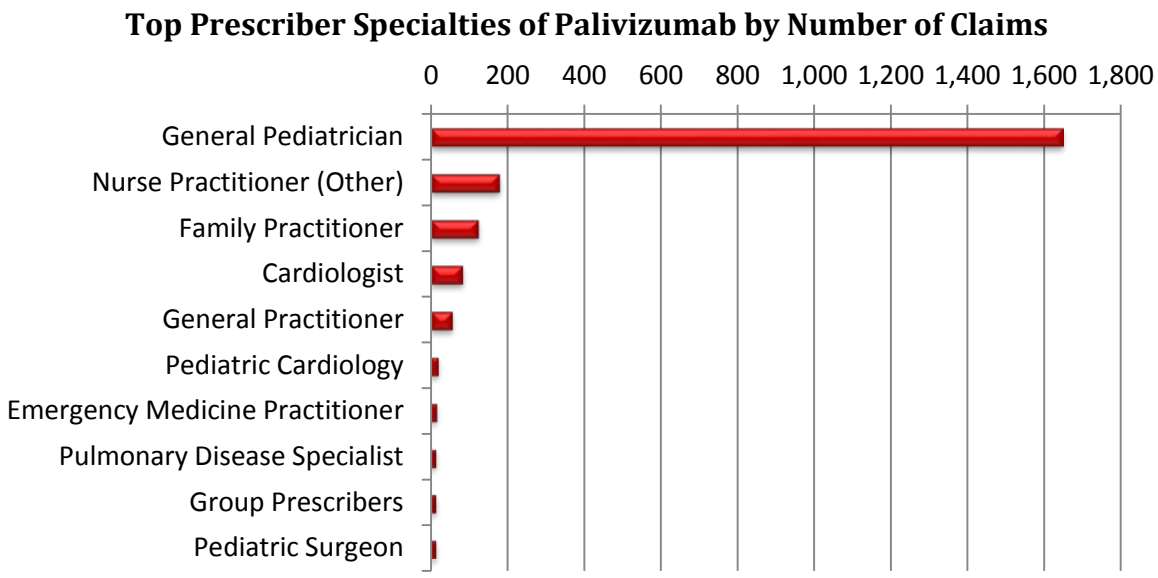
Cost per Vial

Vial Size	Cost per Vial
Synagis® (palivizumab) 100mg/ml vial	$2,542.74
Synagis® (palivizumab) 50mg/ml vial	$1,348.08

Demographics of Members Utilizing Palivizumab

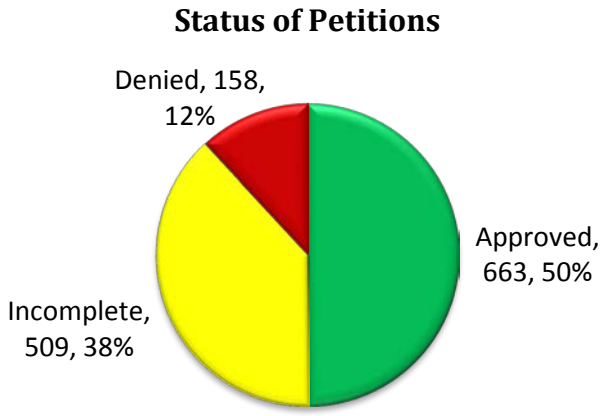


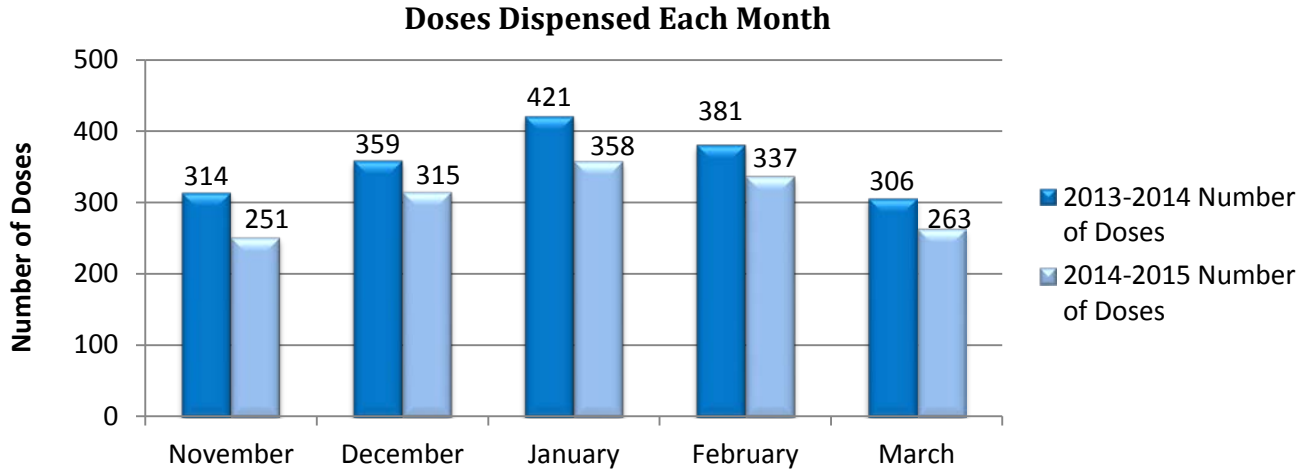
All age groups saw a decrease in utilization compared to the 2013-2014 palivizumab season. The 0-11 month age group saw a 32.93% decrease in utilization. The 12-23 month age group saw an 8.72% decrease in utilization, and the 24+ month age group saw a 12.50% decrease in utilization.

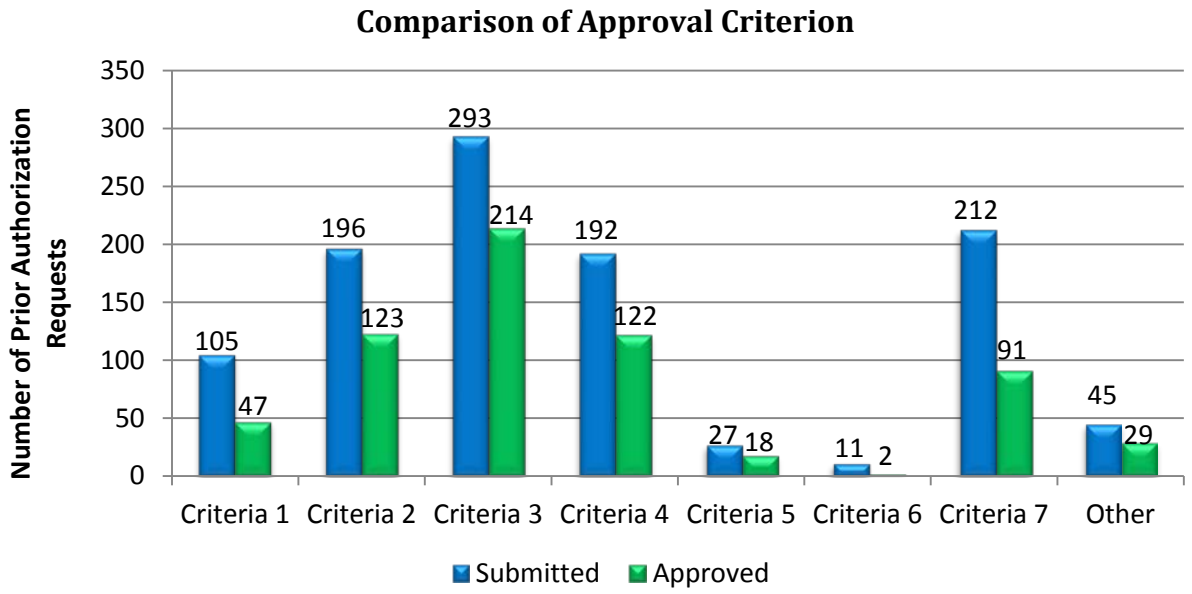


Prior Authorization of Palivizumab

There were 1,330 palivizumab prior authorization requests submitted for 701 unique members during fiscal year 2015. The following chart shows the status of the submitted petitions.







Please see the current criteria listed on the first page of this report.

Referrals to Care Management Services

OHCA Care Management Services are available to assist with infants felt to be at increased risk of non-compliance. Nurse Care Managers contact the parents to discuss and educate them about the importance of getting palivizumab each month, along with other safety issues. The following message is sent back to the prescriber and the pharmacy with each approved petition:

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

Additionally, members are referred to Care Management Services if the member's palivizumab claims history shows 45 days or more between palivizumab doses or between initial prior authorization approval and palivizumab dosing. For the 2014-2015 RSV season, 92 children were referred for Care Management Services.

Market News and Updates[1,2,3]

Pipeline News:

- **August 2015:** New research revealed a RSV virus-like particle (VLP) vaccine induced a neutralizing antibody response and subsequently protected rats when exposed to the live virus. The VLPs resemble the virus but do not contain the viral genome and can't replicate. The researchers concluded that the RSV-VLP vaccine showed promise as a safe and effective vaccine for RSV.
- **August 2015:** Novavax announced positive results from their phase-2 RSV F-protein vaccine clinical trial in older adults. The trial was a randomized, placebo-controlled trial of 1,600 adults in the United States. Findings showed statistically significant vaccine efficacy in prevention of all symptomatic RSV disease (44%) and RSV disease with symptoms of lower respiratory tract infection (46%) in older adults.

Guideline Updates:

- **July 2014:** The American Academy of Pediatrics (AAP) released *Updated Guidance for Palivizumab Prophylaxis Among Infants and Young Children at Increased Risk of Hospitalization for Respiratory Syncytial Virus Infection*. The following table (Table 1) highlights differences in the updated guidance for palivizumab prophylaxis compared to previous guidance.

Table 1

Risk Group/Topic	Previous Guidance	Updated Guidance
Preterm Infants (no CLD) & Prophylaxis	• Previously, prophylaxis was recommended for infants with preterm birth before 32 weeks gestation. • Infants with certain risk factors born at 32 weeks, 0 days to 34 weeks, 6 days were eligible.	• In the first year of life, palivizumab prophylaxis is recommended for infants born before 29 weeks, 0 days' gestation. • Palivizumab prophylaxis is **not** recommended for otherwise healthy infants born at or after 29 weeks, 0 days' gestation.
Preterm Infants (with CLD) & Prophylaxis	• Previously no definition of chronic lung disease was provided.	• In the **first year of life**, palivizumab prophylaxis is recommended for preterm infants with chronic lung disease of prematurity defined as <32 weeks, 0 days' gestation and a requirement for >21% oxygen for at least 28 days after birth.
Infants with CHD & Prophylaxis	• Previously prophylaxis was recommended in the second year of life for this cohort. • In addition, consultation with a cardiologist currently is recommended for patients with cyanotic heart disease for decisions about prophylaxis.	• Clinicians may administer palivizumab prophylaxis in the **first year of life** to certain infants with hemodynamically significant heart disease.
Number of Monthly Doses	• Previously, fewer than 5 monthly doses were recommended for some infants.	• Clinicians may administer up to a maximum of 5 monthly doses of palivizumab during the RSV season to infants who qualify for prophylaxis in the first year of life. • Qualifying infants born during the RSV season will require fewer doses. For example, infants born in January would receive their last dose in March.

Risk Group/Topic	Previous Guidance	Updated Guidance
Prophylaxis in Second Year of Life	• Previously, two seasons of prophylaxis were recommended.	• Palivizumab prophylaxis is **not recommended in the second year of life** except for children who require at least 28 days of supplemental oxygen after birth and who continue to require medical intervention (supplemental oxygen, chronic corticosteroid, or diuretic therapy).
RSV Breakthrough Hospitalization & Prophylaxis	• Previously, prophylaxis was recommended to continue in a child who experiences a breakthrough RSV hospitalization.	• Monthly prophylaxis should be **discontinued** in any child who experiences a breakthrough RSV hospitalization.
Neuromuscular Disease & Prophylaxis	• Previous recommendation was for two years of prophylaxis.	• Children with pulmonary abnormality or neuromuscular disease that impairs the ability to clear secretions from the upper airways may be considered for prophylaxis in the **first year of life.**
Immunocompromised Children & Prophylaxis	• Previous recommendation was for two years of prophylaxis.	• Children less than 24 months of age who will be profoundly immunocompromised during the RSV season may be considered for prophylaxis.
Down Syndrome, Cystic Fibrosis (CF) & Prophylaxis	• Previously, the CF recommendation was for two years of prophylaxis. • Children with Down syndrome were not addressed previously.	• Insufficient data are available to routinely recommend palivizumab prophylaxis for children with cystic fibrosis or Down syndrome.
Alaska Natives & Prophylaxis	• Present recommendations allow for greater flexibility for Alaskan Native and Native American populations.	• The burden of RSV disease in certain remote areas may result in a broader use of palivizumab for RSV prevention in Alaskan Native populations and possibly in selected other Native American populations.

Additional Points:

- **Palivizumab pharmacokinetics:**
  - 5 monthly doses provides more than 6 months of protective serum concentration for most infants
- **Palivizumab prophylaxis and subsequent wheezing:**
  - Limited impact on subsequent wheezing episodes
- **Palivizumab prophylaxis is not recommended for prevention of nosocomial disease**
- **Palivizumab is not recommended for treatment of RSV disease**
  - Not licensed for and not recommended for this purpose

Guidance for Palivizumab Prophylaxis[1]

The AAP based their updated recommendations on several studies concluding that data consistently demonstrated the greatest increase in risk for hospitalization is in preterm infants born before 29 weeks' gestation. The AAP conclusions are based on the following studies:

Preterm Infants Without CLD:

- The New Vaccine Surveillance Network (NVSN) sponsored by the Center for Disease Control (CDC) was a prospective population-based surveillance program from 2000-2005 in three geographically diverse locations in the United States for young children hospitalized with laboratory-confirmed RSV respiratory illness (Table 2).
    - Data from NVSN revealed that for all preterm infants (<37 weeks' gestation), the RSV hospitalization rate was 4.6/1000 children, which was not significantly different from the hospitalization rate for term infants, which was 5.3/1000 children.
    - Infants born at <30 weeks' gestation experienced a higher RSV hospitalization rate (18.7/1000 children) than early preterm infants (30-33 weeks).

Table 2: Average RSV hospitalization Rates Among Children Younger Than 24 Months (2000-2005)

Children <24 Months	*N*	RSV Hospitalization Rate/1000
All infants regardless of gestational age	559	5.2
All term infants (≥ 37 wk gestation)	479	5.3
All preterm infants (<37 wk gestation)	56	4.6
≥35 wk gestation	494	5.1
32-34 wk gestation	23	6.9
29-31 wk gestation	6	6.3
<29 wk gestation	12	19.3
All very preterm (<30 wk gestation)	15	18.7

- A retrospective, cohort analysis of Tennessee Medicaid data for children younger than three years from 1989 to 1993 (included 248,652 child-years follow up) was conducted to determine RSV hospitalization rates among infants with different degrees of prematurity and other comorbidities.
    - Age groups were divided into three groups: (0 to <6 months, 6 to <12 months, and 12 to 24 months). Within each age group preterm infants had similar rates of RSV hospitalization regardless of the degree of prematurity.

- A historical cohort analysis from New York reported on RSV hospitalization rates among 1,029 consecutive preterm infants born before or at 32 weeks' gestation during a 5-year period.
    - The RSV hospitalization rate increased with decreasing gestational age with a breakpoint at ≤28 weeks' gestation.
    - Among infants born at or before 26 weeks' gestation, the risk of RSV-associated hospitalization was 13.9% vs 4.4% among children hospitalized at >30 to 32 weeks' gestation.

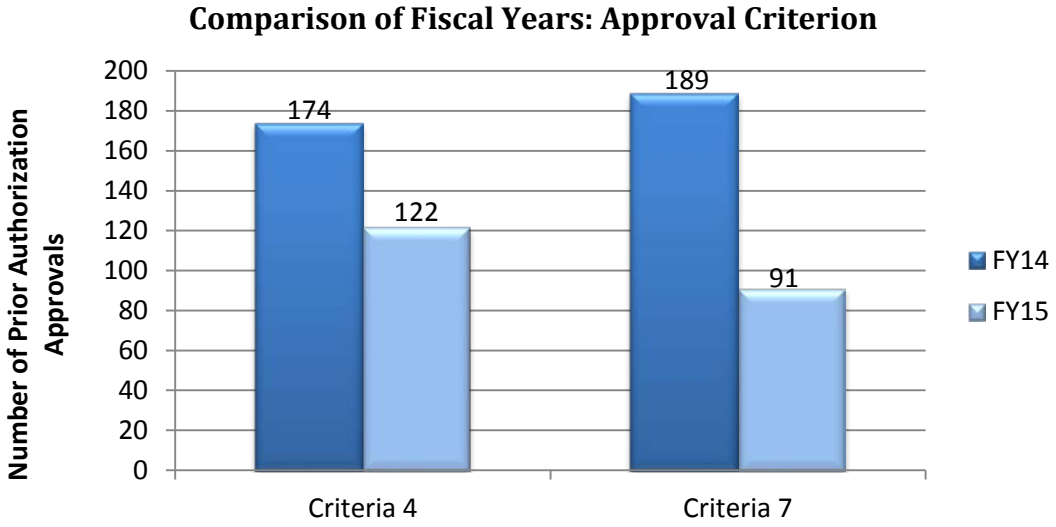
    - There was not a statistically significant difference in RSV hospitalization rates between infants with gestational ages of >28 to 30 weeks and infants with gestational ages of >30 to 32 weeks.
- A retrospective cohort study of infants enrolled in Medicaid in Texas and Florida between 1999 and 2004 examined RSV hospitalization rates in moderately preterm infants 32 to 34 weeks' gestation.
    - Palivizumab prophylaxis was associated with decreased hospitalization in moderately preterm infants in Texas but not in Florida.

Palivizumab Claims Analysis

If SoonerCare were to adopt the updated guidance for palivizumab prophylaxis the following member groups would no longer qualify for palivizumab prophylaxis (these include those meeting SoonerCare criteria number 4 and number 7 on the first page of this report):

- Criteria number 4: Infants less than 6 months of age, born at 29 to 31 weeks gestation
- Criteria number 7: Infants up to 3 months old at the start of RSV season, born at 32 to 34 weeks gestation, who have one of the following risk factors (up to three doses only):
    a. Child care attendance
    b. Siblings younger than 5 years of age

The following chart shows the number of prior authorizations approved based on criteria number 4 or 7 for fiscal years 2014 and 2015. Both of these patient groups would no longer qualify for palivizumab prophylaxis under the updated guidance. Many hospitals and physician groups adopted the updated guidance resulting in a lower number of prior authorization submissions and subsequently a lower number of approvals in fiscal year 2015. The projected cost of palivizumab for members that qualified for prophylaxis last season but would no longer qualify under the updated guidance is $1,914,185.06.



Recommendations

Based on the recommendations from the American Academy of Pediatrics, the College of Pharmacy recommends updating the prior authorization criteria of Synagis® (palivizumab) to the following criteria:

Synagis® (Palivizumab) Approval Criteria:

A. Member Selection:
   1. Infants less than 12 months old at the start of RSV season:
      a. Born before 29 weeks, 0 days gestation; or
      b. Born before 32 weeks, 0 days gestation and develop chronic lung disease (CLD) of prematurity (require >21% oxygen supplementation for at least 28 days after birth); or
      c. Have hemodynamically significant congenital heart disease (acyanotic heart disease and receiving medication to control Congestive Heart Failure (CHF) and will require surgical procedures, or moderate to severe pulmonary hypertension); or
      d. May be considered for:
         i. Infants with neuromuscular disease or congenital anomaly that impairs the ability to clear secretions from the upper airway because of ineffective cough
         ii. Infants who undergo cardiac transplantation during RSV season
         iii. Infants who are profoundly immunocompromised during RSV season
         iv. Infants with cystic fibrosis with clinical evidence of CLD and/or nutritionally compromised
   2. Infants 12 to 24 months old at the start of RSV season:
      a. Born before 32 weeks, 0 days gestation and have CLD of prematurity (required at least 28 days of oxygen after birth) and continue to require medical support (chronic corticosteroid therapy, bronchodilator therapy, or supplemental oxygen) during the 6 months before the start of the RSV season

B. Length of treatment: Palivizumab is approved for use only during RSV season. Approval dates will be November 1st through March 31st.

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

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

[1] Committee on Infectious Diseases and Bronchiolitis Guidelines Committee. "Updated Guidance for Palivizumab Prophylaxis Among Infants and Young Children at Increased Risk of Hospitalization for Respiratory Syncytial Virus Infection." *Pediatrics: Official Journal of the American Academy of Pediatrics* (2014): 415-20. Available online at: http://pediatrics.aappublications.org/content/early/2014/07/23/peds.2014-1665. Last accessed: August 26, 2015.

[2] Walpita P, Johns LM, Tandon R, Moore ML. Mammalian cell-derived respiratory syncytial virus-like particles protect the lower as well as the upper respiratory tract. *PLoS One*. 2015;10(7):e0130755.

[3] Novax Inc. "Novavax Announces Positive Top-Line Data from Phase 2 RSV F-Protein Vaccine Clinical Trial in Older Adults." Available online at: http://ir.novavax.com/phoenix.zhtml?c=71178&p=irol-newsArticle&ID=2078538. Last revised: August 10, 2015. Last accessed: August 21, 2015.

Appendix K

Fiscal Year 2015 Annual Review of Antihyperlipidemics and 30-Day Notice to Prior Authorize Epanova® (Omega-3-Carboxylic Acids), Praluent® (Alirocumab), and Repatha™ (Evolocumab)

Oklahoma Health Care Authority
September 2015

Current Prior Authorization Criteria

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

1. Member must have a documented 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. A documented adverse effect or contraindication to all available lower tiered products; or
3. A clinical exception will apply for Crestor® (rosuvastatin) 40mg for high risk members hospitalized for recent acute myocardial infarction or acute coronary syndrome.

Statin Medications and Zetia® (Ezetimibe) Special Prior Authorization (PA) Approval Criteria:

1. Use of any Special PA medication will require a patient-specific, clinically significant reason why lower tiered medications with similar or higher LDL reduction cannot be used; and
    a. 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
2. Clinical exceptions for Zetia® (ezetimibe) include the following:
    a. Documented active liver disease; or
    b. Documented unexplained, persistent elevations of serum transaminases; or
    c. Documented statin-related myopathy.

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

*Tier structure based on state maximum allowable cost (SMAC) and/or supplemental rebate participation.
+Crestor® 5mg and Crestor® 10mg require special reason for use.
CR = controlled-release

Lovaza® (Omega-3-Acid Ethyl Esters) and Vascepa® (Icosapent Ethyl) 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 HgA1C <7.5%); and
2. Previous failure with both nicotinic acid and fibric acid medications.

Juxtapid® (Lomitapide) and Kynamro® (Mipomersen) Approval Criteria:

1. An FDA approved diagnosis of homozygous familial hypercholesterolemia defined by the presence of at least one of the following criteria:
    a. A documented functional mutation(s) in both LDL receptor alleles or alleles known to affect LDL receptor functionality via genetic testing; or
    b. An untreated total cholesterol >500mg/dL and triglycerides <300mg/dL and at least one of the following:
        i. Documentation that both parents have untreated total cholesterol >250mg/dL; or
        ii. Presence of tendinous/cutaneous xanthoma prior to age 10 years; and
2. Documented failure of high dose statin therapy (LDL reduction capability equivalent to atorvastatin 80mg or higher); and
3. Prescriber must be certified with Juxtapid® or Kynamro® REMS program.

Utilization of Antihyperlipidemics: Fiscal Year 2015

Comparison of Fiscal Years: Statins and Zetia® (Ezetimibe)

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	17,662	72,967	$1,736,839.73	$23.80	$0.55	3,167,291	3,166,777
2015	15,798	66,508	$1,436,960.02	$21.61	$0.49	2,950,090	2,945,786
% Change	**-10.60%**	**-8.90%**	**-17.30%**	**-9.20%**	**-10.90%**	**-6.90%**	**-7.00%**
Change	**-1,864**	**-6,459**	**-$299,879.71**	**-$2.19**	**-$0.06**	**-217,201**	**-220,991**

*Total number of unduplicated members.

Comparison of Fiscal Years: Lovaza® (Omega-3-Acid Ethyl Esters) and Vascepa® (Icosapent Ethyl)

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	77	581	$113,117.99	$194.70	$6.59	62,282	17,165
2015	49	367	$67,038.00	$182.66	$6.08	38,548	11,020
% Change	**-36.40%**	**-36.80%**	**-40.70%**	**-6.20%**	**-7.70%**	**-38.10%**	**-35.80%**
Change	**-28**	**-214**	**-$46,079.99**	**-$12.04**	**-$0.51**	**-23,734**	**-6,145**

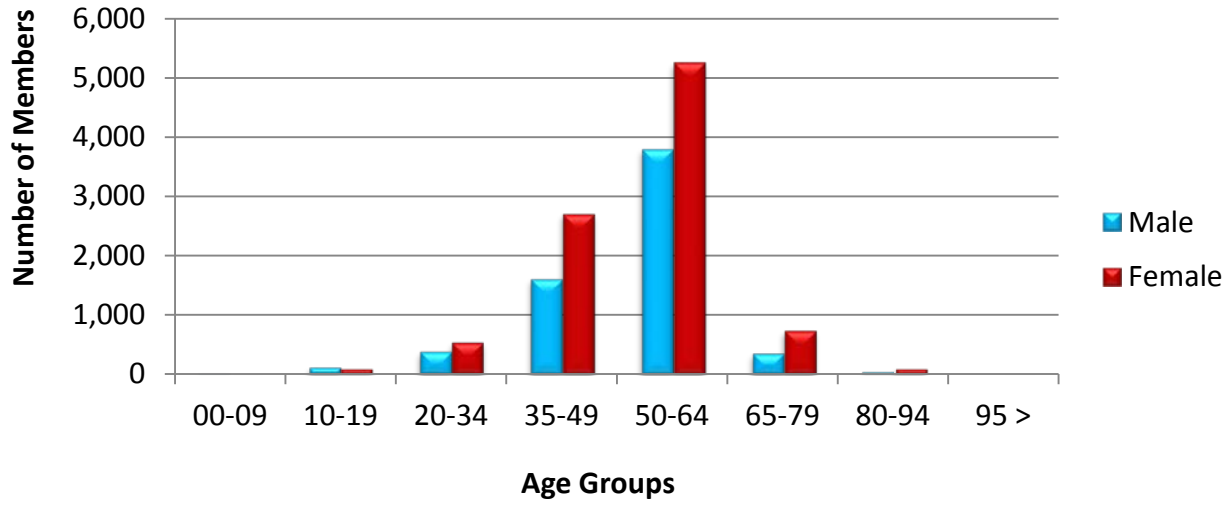
*Total number of unduplicated members.

Comparison of Fiscal Years: Juxtapid® (Lomitapide) and Kynamro® (Mipomersen)

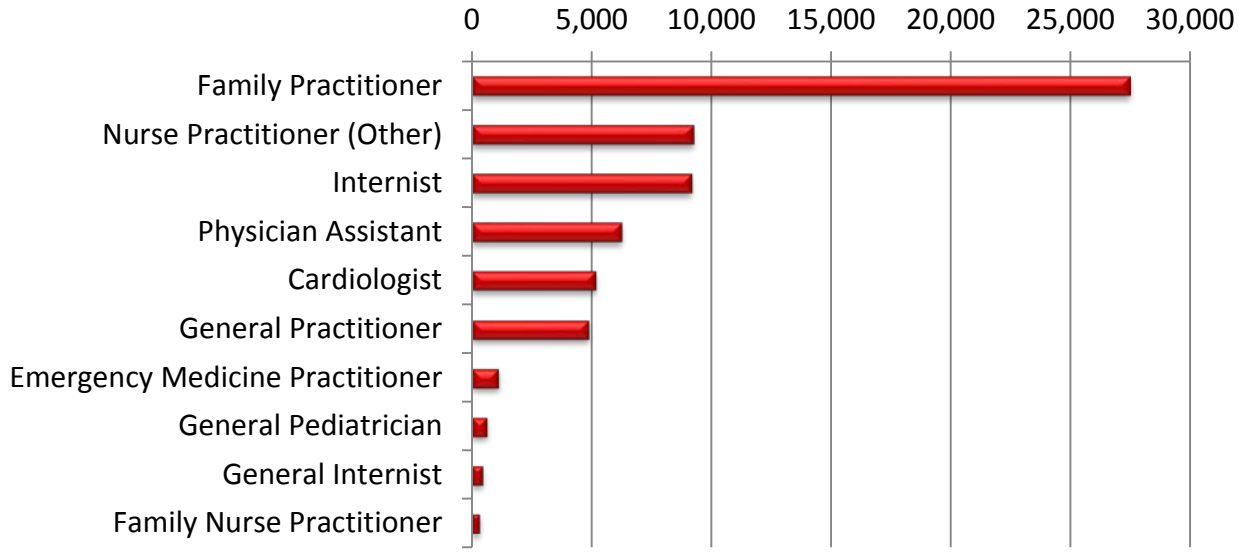
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	1	13	$371,375.82	$28,567.37	$952.25	420	390
2015	1	14	$822,451.30	$58,746.52	$1,958.22	810	420
% Change	**0.00%**	**7.70%**	**121.50%**	**105.60%**	**105.60%**	**92.90%**	**7.70%**
Change	**0**	**1**	**$451,075.48**	**$30,179.15**	**$1,005.97**	**390**	**30**

*Total number of unduplicated members.

Demographics of Members Utilizing Antihyperlipidemics

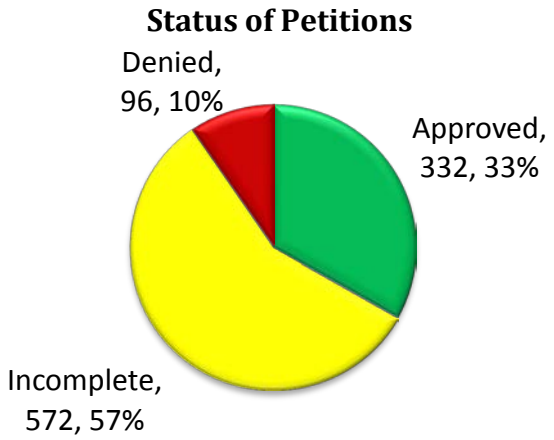


Top Prescriber Specialties of Antihyperlipidemics by Number of Claims



Prior Authorization of Antihyperlipidemics

There were 1,000 petitions submitted for the antihyperlipidemic medication category during fiscal year 2015. Computer edits are in place to detect Tier-1 statin medications in the member's recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions.



Market News and Updates[1,2,3,4,5,6,7]

Anticipated Patent Expirations:

- Vytorin® (simvastatin/ezetimibe): April 2017
- Altoprev® (lovastatin): March 2018
- Simcor® (simvastatin/niacin CR): March 2018
- Advicor® (lovastatin/niacin CR): March 2018
- Lescol XL® (fluvastatin ER): October 2020
- Crestor® (rosuvastatin): June 2022
- Livalo® (pitavastatin): February 2024
- Kynamro® (mipomersen): December 2025
- Zetia® (ezetimibe): April 2026
- Juxtapid® (lomitapide): August 2027
- Vascepa® (icosapent ethyl): April 2030

Discontinued Medications:

- Liptruzet™ (atorvastatin/ezetimibe) was discontinued from the market in June 2015 as a business decision and not based on safety or efficacy findings.

New FDA Approvals:

- In May 2014, the FDA approved Epanova® (omega-3-carboxylic acids), the first FDA approved prescription omega-3 in free fatty acid form, which may be dosed in as few as two capsules once daily. Epanova® is not yet available on the market.
- In July 2015, the FDA approved Praluent® (alirocumab), the first FDA approved medication in a new class of medications with a novel mechanism of action, Proprotein Convertase Subtilisin Kexin Type 9 (PCSK9) inhibitors. Normally, PCSK9 binds to the LDL receptors (LDLR) on the surface of hepatocytes to promote LDLR degradation within the

liver. LDLR is the primary receptor that clears circulating LDL; therefore, the decrease in LDLR levels by PCSK9 results in higher blood levels of LDL-C. By inhibiting the binding of PCSK9 to LDLR, alirocumab increases the number of LDLRs available to clear LDL, thereby lowering LDL-C levels. The market impact of PCSK9 inhibitors is expected to be significant, as patients needing PCSK9 inhibitors will likely be on the medications lifelong, with the yearly expense being roughly $15,000. Praluent® is currently available on the market.

- In late August 2015, the FDA approved Repatha™ (evolocumab), another PCSK9 inhibitor.

Medications in the Pipeline:

- **PCSK9 Inhibitors:** Other PCSK9 inhibitors are currently in development, including Pfizer's bococizumab as well as products from Roche, Eli Lilly, and Alnylam. An oral PCSK9 inhibitor, as well as an annual PCSK9 vaccine designed to induce the body to produce its own PCSK9 antibodies are also in the beginning stages of development.
- **Cholesterol Ester Transfer Protein (CETP) Inhibitors:** A new class of antihyperlipidemic medications, CETP inhibitors, is in development and includes Eli Lilly's evacetrapib and Merck's anacetrapib, both of which are currently in Phase III clinical trials, and another product from Dezima that is currently in Phase II clinical trials. These medications inhibit CETP, which normally transfers cholesterol from HDL cholesterol to VLDL or LDL cholesterol. Inhibition of this process results in higher HDL level and reduces LDL levels. New research suggests CETP inhibitors may provide a safe and effective option for modifying lipids in adults with dyslipidemia.

Epanova® (Omega-3-Carboxylic Acids) Product Summary[8,9]

Indications: Epanova® (omega-3-carboxylic acids) is indicated as an adjunct to diet to reduce triglyceride levels in adult patients with severe (≥ 500mg/dL) hypertriglyceridemia.

Dosing:

- Epanova® is available as soft gelatin capsules containing 1 gram of fish oil-derived free fatty acids, designated "omega-3-carboxylic acids", with at least 850mg of polyunsaturated fatty acids, including multiple omega-3 fatty acids (eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA] being the most abundant).
- The recommended dosing of omega-3-carboxylic acids is 2 grams or 4 grams once daily.
- Patients should be placed on an appropriate lipid-lowering diet before receiving omega-3-carboxylic acids and should continue this diet during treatment with omega-3-carboxylic acids.
- Laboratory studies should be done to ascertain that the triglyceride levels are consistently abnormal before instituting omega-3-carboxylic acids therapy. Attempts should be made to control serum lipids with appropriate diet, exercise, weight loss in obese patients, and control of any medical problems such as diabetes mellitus and hypothyroidism that are contributing to the lipid abnormalities.
- The dosage of omega-3-carboxylic acids should be individualized according to the patient's response and tolerability.

- Omega-3-carboxylic acids capsules may be taken without regard to meals, and capsules should be swallowed whole.

Mechanism of Action: The mechanism of action of omega-3-carboxylic acids is not completely understood. Potential mechanisms of action include inhibition of acyl-CoA: 1,2-diacylglycerol acyltransferase, increased mitochondrial and peroxisomal β-oxidation in the liver, decreased lipogenesis in the liver, and increased plasma lipoprotein lipase activity. Omega-3-carboxylic acids may reduce the synthesis of triglycerides in the liver because EPA and DHA are poor substrates for the enzymes responsible for triglyceride synthesis, and EPA and DHA inhibit esterification of other fatty acids.

Contraindications: Omega-3-carboxylic acids are contraindicated in patients with known hypersensitivity (e.g., anaphylactic reaction) to omega-3-carboxylic acids or to any of the components of Epanova®.

Safety:

- Laboratory Monitoring: In some patients, omega-3-carboxylic acids increase LDL-C levels. LDL-C levels should be monitored periodically during therapy with omega-3-carboxylic acids. In patients with hepatic impairment, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels should be monitored periodically during therapy with omega-3-carboxylic acids.
- Fish Allergy: Omega-3-carboxylic acids contain polyunsaturated free fatty acids derived from fish oils. It is not known whether patients with allergies to fish and/or shellfish are at an increased risk of an allergic reaction to omega-3-carboxylic acids. Omega-3-carboxylic acids should be used with caution in patients with known hypersensitivity to fish and/or shellfish.
- Pediatric Use: The safety and effectiveness of omega-3-carboxylic acids in pediatric patients have not been studied.

Adverse Reactions: The most common adverse reactions to omega-3-carboxylic acids reported in clinical trials, occurring at an incidence of at least 3% and with a higher incidence than placebo, include diarrhea, nausea, abdominal pain or discomfort, and eructation.

Efficacy:

- The effectiveness of omega-3-carboxylic acids as a treatment for severe hypertriglyceridemia was assessed in a 12-week randomized, placebo (olive oil)-controlled, double-blind, parallel-group trial.
- After a wash-out period of lipid-altering medications other than statins and ezetimibe, patients whose triglyceride levels were between 500 and 2,000mg/dL were randomly assigned to placebo or omega-3-carboxylic acids 2, 3, or 4 grams per day. Overall, the median baseline triglyceride level was 694mg/dL.
- Treatment with omega-3-carboxylic acids led to statistically significant reductions in fasting triglyceride levels. Treatment with omega-3-carboxylic acids also resulted in statistically significant reductions in non-HDL-C levels compared to placebo, but increased LDL-C levels.

- The effect of omega-3-carboxylic acids on cardiovascular mortality and morbidity has not been determined.

Estimated Acquisition Cost: The estimated acquisition cost of Epanova® is not yet available.

Praluent® (Alirocumab) Product Summary[10,1112,13,14,15,16,17]

Indications: Praluent® (alirocumab) is indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease, who require additional lowering of low-density lipoprotein cholesterol (LDL-C).

Dosing:

- Alirocumab is available as a 75mg/mL and 150mg/mL solution for subcutaneous injection in single-dose pre-filled pens and syringes.
- The recommended starting dose of alirocumab is 75mg administered subcutaneously every two weeks, since the majority of patients achieve sufficient LDL-C reduction with this dosage.
- LDL-C levels should be measured within four to eight weeks of initiating or titrating alirocumab to assess response and adjust the dose, if needed.
- If the LDL-C response to the 75mg dose is inadequate, the dosage may be increased to the maximum dosage of 150mg administered subcutaneously every two weeks.
- Patients and/or caregivers should be trained on the appropriate storage, preparation, and administration of alirocumab prior to use.
- Alirocumab must be stored in the refrigerator in the outer carton in order to protect it from light. Alirocumab should be allowed to warm to room temperature for 30-40 minutes prior to use and should be used as soon as possible after it has warmed to room temperature.
- Alirocumab should be administered by subcutaneous injection into the thigh, abdomen, or upper arm using a single-dose pre-filled pen or syringe.

Mechanism of Action: Alirocumab is a human monoclonal antibody (IgG1 isotype) that binds to and inhibits PCSK9. PCSK9 binds to the LDL receptors (LDLR) on the surface of hepatocytes to promote LDLR degradation within the liver. LDLR is the primary receptor that clears circulating LDL; therefore, the decrease in LDLR levels by PCSK9 results in higher blood levels of LDL-C. By inhibiting the binding of PCSK9 to LDLR, alirocumab increases the number of LDLRs available to clear LDL, thereby lowering LDL-C levels.

Contraindications: Alirocumab is contraindicated in patients with a history of a serious hypersensitivity reaction to alirocumab.

Safety:

- Allergic Reactions: Hypersensitivity reactions (e.g., pruritus, rash, urticarial), including some serious events (e.g., hypersensitivity vasculitis and hypersensitivity reactions requiring hospitalization), have been reported with alirocumab treatment. If signs or symptoms of serious allergic reactions occur, treatment with alirocumab should be

discontinued, and patients should be treated according to standard of care and monitored until signs and symptoms resolve.

- Immunogenicity: As with all therapeutic proteins, there is a potential for immunogenicity with alirocumab that could potentially impact efficacy as well as safety. In a pool of ten placebo- and active-controlled clinical trials, 4.8% of patients treated with alirocumab had anti-drug antibodies (ADA) newly detected after initiating treatment. Patients who developed ADA had a higher incidence of injection site reactions compared to patients who did not develop ADA. A total of 1.2% of patients treated with alirocumab developed neutralizing antibodies (NAb) on at least one occasion, and 0.3% of patients both tested positive for NAb and exhibited transient or prolonged loss of efficacy. The long-term consequences of continuing alirocumab treatment in the presence of persistent NAb are unknown.
- Low LDL-C Values: In clinical trials, approximately 20% and 40% of alirocumab-treated patients had at least one calculated LDL-C value less than 15mg/dL and less than 25mg/dL, respectively. The majority of patients were receiving 150mg of alirocumab every two weeks at the time of these LDL-C values. The long-term effects of very low levels of LDL-C induced by alirocumab are unknown.
- Pediatric Use: The safety and efficacy of alirocumab in pediatric patients have not been established. Alirocumab has not been studied in pediatric patients.

Adverse Reactions: The most common adverse reactions to alirocumab reported in clinical trials, occurring at an incidence of at least 2% and more frequently than in placebo-treated patients, include nasopharyngitis, injection site reactions, influenza, urinary tract infection, diarrhea, bronchitis, myalgia, muscle spasms, sinusitis, liver enzyme abnormalities, cough, contusion, and musculoskeletal pain. The most common adverse reactions leading to discontinuation of alirocumab were allergic reactions and elevated liver enzymes.

Efficacy:

- The FDA approval of alirocumab evaluated its efficacy in five double-blind, placebo-controlled trials that enrolled 3,499 patients; 36% were patients with HeFH and 54% were non-HeFH patients who had clinical atherosclerotic cardiovascular disease. All patients were receiving a maximally tolerated dose of a statin, with or without other lipid-modifying therapies.
- In trials that enrolled patients with HeFH, the diagnosis of HeFH was made either by genotyping or clinical criteria ("definite HeFH" using either the Simon Broome or Dutch Lipid Network criteria; *see Attachment A*).
- The diagnosis of clinical atherosclerotic cardiovascular disease was made by either a documented history of coronary heart disease (CHD), CHD risk equivalent(s) (as per European guidelines), or calculated 10-year fatal cardiovascular disease risk assessed with SCORE (Systemic Coronary Risk Estimation, as per European guidelines).
- All trials were at least 52 weeks in duration with the primary efficacy endpoint (mean percent change in LDL-C from baseline) measured at week 24.
- Maximal LDL-C lowering efficacy was observed at week 4 and persisted for the duration of the trials.

- Treatment with alirocumab led to statistically significant reductions in mean percent change in LDL-C from baseline in all five studies (*see following table*).

Study Number	Average Baseline LDL-C	Treatment Difference Between Alirocumab & Placebo in Mean Percent Change in LDL-C from Baseline
Study 1	122mg/dL	-58% (week 24)
Study 2	102mg/dL	-43% (week 24)
Study 3 & 4 (HeFH)	141mg/dL	-54% (week 24)
Study 5	198mg/dL	-36% (week 24)

- The effect of alirocumab on cardiovascular morbidity and mortality has not been determined.

Estimated Acquisition Cost: The estimated acquisition cost of Praluent® is $1,182.72 per 28 days (based on the FDA approved dosing regimen of one injection every two weeks).

Repatha™ (Evolocumab) Product Summary[18,19]

Indications: Repatha™ (evolocumab) is indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease, who require additional lowering of low-density lipoprotein cholesterol (LDL-C). Evolocumab is also indicated as an adjunct to diet and other LDL-lowering therapies (e.g. statins, ezetimibe, LDL apheresis) in patients with homozygous familial hypercholesterolemia (HoFH) who require additional lowering of LDL-C.

Dosing:

- Evolocumab is available as a 140mg/mL solution for subcutaneous injection in single-dose pre-filled autoinjectors and syringes.
- The recommended subcutaneous dosage of evolocumab in patients with HeFH or patients with primary hyperlipidemia with established clinical atherosclerotic CVD is either 140mg every two weeks or 420mg once monthly.
- The recommended subcutaneous dosage of evolocumab in patients with HoFH is 420mg once monthly. In patients with HoFH, measure LDL-C levels 4 to 8 weeks after starting evolocumab, since response to therapy will depend on the degree of LDL-receptor function.
- The 420mg dose should be administered by giving three evolocumab injections consecutively within 30 minutes.
- Patients and/or caregivers should be trained on the appropriate storage, preparation, and administration of evolocumab prior to use.
- Evolocumab must be stored in the refrigerator. Evolocumab should be allowed to warm to room temperature for 30 minutes prior to use. Evolocumab can be kept at room temperature in the original carton. However, under these conditions, Evolocumab must be used within 30 days.
- Evolocumab should be administered by subcutaneous injection into the thigh, abdomen, or upper arm using a single-dose autoinjector or syringe.

Mechanism of Action: Evolocumab is a human monoclonal antibody (IgG1 isotype) that binds to and inhibits PCSK9. PCSK9 binds to the LDL receptors (LDLR) on the surface of hepatocytes to promote LDLR degradation within the liver. LDLR is the primary receptor that clears circulating LDL; therefore, the decrease in LDLR levels by PCSK9 results in higher blood levels of LDL-C. By inhibiting the binding of PCSK9 to LDLR, evolocumab increases the number of LDLRs available to clear LDL, thereby lowering LDL-C levels.

Contraindications: Evolocumab is contraindicated in patients with a history of a serious hypersensitivity reaction to evolocumab.

Safety:

- Allergic Reactions: Hypersensitivity reactions (e.g., rash, urticaria) have been reported with evolocumab treatment. If signs or symptoms of serious allergic reactions occur, treatment with evolocumab should be discontinued, and patients should be treated according to standard of care and monitored until signs and symptoms resolve.
- Immunogenicity: As with all therapeutic proteins, there is a potential for immunogenicity with evolocumab. In a pool of placebo- and active-controlled clinical trials, 0.1% of patients treated with evolocumab tested positive for binding antibody development. Patients whose sera tested positive for binding antibodies were further evaluated for neutralizing antibodies; none of the patients tested positive for neutralizing antibodies. There was no evidence that the presence of anti-drug binding antibodies impacted the pharmacokinetic profile, clinical response, or safety of evolocumab, but the long-term consequences of continuing evolocumab treatment in the presence of anti-drug binding antibodies are unknown.
- Low LDL-C Values: In clinical trials, a total of 1,609 patients treated with evolocumab had at least one calculated LDL-C value less than 25mg/dL. Changes to background lipid-altering therapy were not made in response to low LDL-C values, and evolocumab dosing was not modified or interrupted on this basis. Although adverse consequences of very low LDL-C were not identified in these trials, the long-term effects of very low levels of LDL-C induced by evolocumab are unknown.
- Pediatric Use: The safety and effectiveness of evolocumab in adolescents with HoFH who require additional lowering of LDL-C were established based on data from a 12-week, placebo-controlled trial that included ten adolescents ages 13 to 17 years old with HoFH. The effect of evolocumab on LDL-C was generally similar to that observed among adult patients with HoFH. The safety and effectiveness of evolocumab have not been established in pediatric patients with HoFH who are younger than 13 years of age. The safety and effectiveness of evolocumab have not been established in pediatric patients with primary hyperlipidemia or HeFH.

Adverse Reactions: The most common adverse reactions to evolocumab reported in clinical trials, occurring at an incidence of at least 5% and more frequently than in placebo-treated patients, include nasopharyngitis, upper respiratory tract infection, back pain, injection site reactions, and influenza.

Efficacy:

- The FDA approval of evolocumab evaluated its efficacy in four double-blind, randomized, placebo controlled trials that enrolled a total of 813 patients; 40% were patients with HeFH, 54% were non-HeFH patients who had clinical atherosclerotic cardiovascular disease, and 6% were patients with HoFH. All patients were receiving concomitant statin therapy or other lipid-modifying therapies.
- In the trial that enrolled patients with HeFH, the diagnosis of HeFH was made by the Simon Broome criteria (*See Attachment A*).
- In the trial that enrolled patients with HoFH, the diagnosis was made by genetic confirmation or a clinical diagnosis based on a history of an untreated LDL-C concentration greater than 500mg/dL together with either xanthoma before 10 years of age or evidence of HeFH in both parents.
- The diagnosis of clinical atherosclerotic cardiovascular disease was made by either a documented history of coronary heart disease (CHD), CHD risk equivalent(s) (as per National Cholesterol Education Program (NCEP) Adult Treatment Panel-III (ATP-III) guidelines), or high 10-year cardiovascular risk as per Framingham Risk Score (*See Attachment B*).
- Patients in Study 1 and Study 3 were randomized to receive subcutaneous injections of either evolocumab 140mg every 2 weeks, evolocumab 420mg once monthly, or placebo. The two different dosing regimens were designed to cater to the patient's preference of receiving an injection every 2 weeks versus once monthly, and were not designed to allow titration based on the magnitude of LDL-C reduction.
- Patients in Study 2 and Study 4 were randomized to receive subcutaneous injections of either evolocumab 420mg once monthly or placebo, and did not include the dosing regimen of 140mg every 2 weeks.
- The primary efficacy endpoint in all four of the trials was the mean percent change in LDL-C from baseline measured at week 12 in three studies and week 52 in one study.
- Treatment with evolocumab led to statistically significant reductions in mean percent change in LDL-C from baseline in all four studies (*see following table*).

Study Number	Average Baseline LDL-C	Treatment Difference Between Evolocumab & Placebo in Mean Percent Change in LDL-C from Baseline
Study 1	108mg/dL	-71%$^{\alpha}$ and -63%$^{\beta}$ (week 12)
Study 2	105mg/dL	-54%$^{\beta}$ (week 52)
Study 3 (HeFH)	156mg/dL	-61%$^{\alpha}$ and -60%$^{\beta}$ (week 12)
Study 4 (HoFH)	349mg/dL	-31%$^{\beta}$ (week 12)

α Based on the dosing regimen of evolocumab 140mg every 2 weeks.
β Based on the dosing regimen of evolocumab 420mg once monthly.

- The effect of evolocumab on cardiovascular morbidity and mortality has not been determined.

Wholesale Acquisition Cost: The wholesale acquisition cost (WAC) of Repatha™ is reported to be $14,100 annually (based on the FDA approved dosing regimen of one 140mg injection every two weeks). The estimated acquisition cost (EAC) of Repatha™ is not yet available.

Place in Therapy: PCSK9 Inhibitors[20,21,22,23,24,25,26]

In 2013, the National Heart, Lung, and Blood Institute (NHLBI) initiated collaboration with the American College of Cardiology (ACC) and the American Heart Association (AHA) to work with other organizations to complete and publish new clinical practice guidelines for assessment of cardiovascular risk, lifestyle modifications to reduce cardiovascular risk, and management of blood cholesterol, overweight, and obesity in adults. The joint ACC/AHA Task Force on Practice Guidelines published new guidelines on the treatment of cholesterol to reduce atherosclerotic cardiovascular risk in adults in 2013. Recommendations from the joint ACC/AHA Task Force were derived from randomized trials, meta-analyses, and observational studies evaluated for quality, and were not formulated when sufficient evidence was not available. The new ACC/AHA guidelines do not contain recommendations for specific LDL and non-HDL cholesterol targets as were previously the centerpiece of the ATP-III guidelines last updated in 2004, but instead, focus on four groups of primary- and secondary-prevention patients in whom physicians should focus their efforts to reduce cardiovascular disease events. In these four patient groups, recommendations are provided regarding the appropriate intensity of statin therapy in order to achieve relative reductions in LDL-C. Both the ATP-III guidelines and the ACC/AHA guidelines emphasize the value of lifestyle interventions. The current guidelines for the treatment of cholesterol to reduce atherosclerotic cardiovascular risk do not address the new PCSK9 inhibitors; PCSK9 inhibitors were first FDA approved in July 2015.

Statins have achieved significant reductions in cardiovascular morbidity and mortality in both primary- and secondary-prevention settings. Despite these significant reductions and the current guidelines' recommendations for statin use, statins continue to be underused because of perceived or actual intolerances due to myopathy. Although muscle symptoms may occur, true statin intolerance is uncommon. Given the benefits of statins in atherosclerotic cardiovascular disease risk reduction, clinicians should partner with the patient to gain a thorough symptom history and determine if the patient is truly statin intolerant. The ACC recently launched an interactive tool (ACC Statin Intolerance App) for clinicians to evaluate patients who report muscle pain while taking statins; this tool is available as a free application for a smart phone or can be downloaded as a web application. The information and recommendations in the ACC Statin Intolerance App are derived from the 2013 ACC/AHA Guidelines on the Treatment of Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults and from the prescribing information for each statin. Strategies for patients who have previously experienced statin-induced myopathy include intermittent nondaily dosing, dose reduction, or switching to a different statin. These strategies may be useful to capitalize on the benefits of statin therapy without statin-induced myopathy.

The clinical trials of PCSK9 inhibitors that were the basis for FDA approval targeted specific populations: patients on maximally tolerated statin therapy with the diagnosis of HeFH or clinical atherosclerotic cardiovascular disease. FDA approved indications for PCSK9 inhibitors are specific for these patient populations, and are approved as an adjunct to diet and maximally tolerated statin therapy. Therefore, in treatment of cholesterol to reduce atherosclerotic cardiovascular risk, PCSK9 inhibitors have a place in therapy in severe cases: for patients on

maximally tolerated statin therapy, with the diagnosis of HeFH or clinical atherosclerotic cardiovascular disease, and who require additional lowering of LDL-C.

Cost Comparison: High-Intensity Statins and PCSK9 Inhibitors

Medication Name	Strength	Cost/Unit*	Cost/Month	Cost/Year
atorvastatin	80mg	$0.23[+]	$6.90	$82.80
Crestor® (rosuvastatin)	20mg	$7.61[∞]	$228.30	$2,739.60
Crestor® (rosuvastatin)	40mg	$7.61[∞]	$228.30	$2,739.60
Praluent® (alirocumab)	75mg/mL	$591.36[∞]	$1,182.72[α]	$15,375.36
Praluent® (alirocumab)	150mg/mL	$591.36[∞]	$1,182.72[α]	$15,375.36

*Costs listed in the table above do not take into account federal or supplemental rebate participation; therefore, do not reflect net costs.

[+]Cost/unit based on state maximum allowable cost (SMAC).

[∞]Cost/unit based on estimated acquisition cost (EAC).

[α]Cost/month for Praluent® is based on a 28-day dosing regimen (one injection every two weeks).

Recommendations

The College of Pharmacy recommends the prior authorization of Epanova® (omega-3-carboxylic acids) with the following criteria:

Lovaza® (Omega-3-Acid Ethyl Esters) , Vascepa® (Icosapent Ethyl), and Epanova® (Omega-3-Carboxylic Acids) 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 HgA1C < 7.5%); and
2. Previous failure with both nicotinic acid and fibric acid medications; and
3. Use of Vascepa® or Epanova® requires a patient specific, clinically significant reason why the member cannot use omega-3-acid ethyl esters (generic Lovaza®).

Additionally, the College of Pharmacy recommends the prior authorization of PCSK9 inhibitors, Praluent® (alirocumab) and Repatha™ (evolocumab), with the following criteria:

PCSK9 Inhibitors Approval Criteria:

1. An FDA approved diagnosis of heterozygous familial hypercholesterolemia (HeFH) defined by the presence of one of the following criteria:
    a. A documented functional mutation(s) in the LDL receptor (LDLR) gene or other HeFH-related genes via genetic testing; or
    b. Definite HeFH using either the Simon Broome Register criteria or the Dutch Lipid Network criteria (*See Attachment A)*; or
2. An FDA approved diagnosis of homozygous familial hypercholesterolemia (HoFH) defined by the presence of at least one of the following:
    a. A documented functional mutation(s) in both LDL receptor alleles or alleles known to affect LDL receptor functionality via genetic testing; or

   b. An untreated total cholesterol greater than 500mg/dL and at least one of the following:
      i. Documented evidence of definite HeFH in both parents; or
      ii. Presence of tendinous/cutaneous xanthoma prior to age 10 years; or
3. An FDA approved diagnosis of clinical atherosclerotic cardiovascular disease defined by the presence of one of the following criteria:
   a. High cardiovascular risk confirmed by Framingham risk score (*See Attachment B)*; and
      i. Supporting diagnoses/conditions signifying this risk level; or
   b. Documented history of Coronary Heart Disease (CHD); and
      i. Supporting diagnoses/conditions and dates of occurrence signifying history of CHD; and
4. Member must be 18 years of age or older for the diagnosis of HeFH or clinical atherosclerotic cardiovascular disease, or must be 13 years of age or older for the diagnosis of HoFH; and
5. Member must be on high dose statin therapy (LDL reduction capability equivalent to rosuvastatin 40mg) or on maximally tolerated statin therapy; and
   a. Statin trials must be at least 12 weeks in duration (dosing, dates, duration of treatment, and reason for discontinuation must be provided); and
   b. LDL-cholesterol (LDL-C) levels should be included following at least 12 weeks of treatment with each statin medication; and
   c. For statin intolerance due to myalgia, creatine kinase (CK) labs verifying rhabdomyolysis must be provided; and
   d. Tier structure rules still apply; and
6. Member requires additional lowering of LDL-C (baseline, current, and goal LDL-C levels must be provided); and
7. Prescriber must verify that member has been counseled on appropriate use, storage of the medication, and administration technique; and
8. Repatha™ requests for the dosing regimen of 420mg once monthly require a diagnosis of HoFH or require a patient-specific, clinically significant reason why member cannot use Repatha™ at the dosing regimen of 140mg every 2 weeks; and
9. A quantity limit of 2 syringes or pens per 28 days will apply for Praluent® and a quantity limit of 2 syringes or autoinjectors per 28 days will apply for Repatha™. Patients with the diagnosis of HoFH needing 3 Repatha™ syringes or autoinjectors per 30 days (for the dosing regimen of 420mg once monthly) will be approved for a quantity limit override upon meeting PCSK9 inhibitors approval criteria.
10. Initial approvals will be for the duration of 3 months. Continued authorization at that time will require the prescriber to provide recent LDL-C levels to demonstrate the effectiveness of this medication, and compliance will be checked at that time and every six months thereafter for continued approval.

Utilization Details of Statins and Zetia®: Fiscal Year 2015

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
SIMVASTATIN PRODUCTS						
SIMVASTATIN TAB 20MG	9,411	2,311	$40,121.08	$0.10	$4.26	2.79%
SIMVASTATIN TAB 40MG	6,727	1,787	$32,138.98	$0.10	$4.78	2.24%
SIMVASTATIN TAB 10MG	2,721	693	$12,213.50	$0.11	$4.49	0.85%
SIMVASTATIN TAB 80MG	643	184	$4,023.05	$0.12	$6.26	0.28%
SIMVASTATIN TAB 5MG	117	31	$580.32	$0.13	$4.96	0.04%
SUBTOTAL	**19,619**	**5,006**	**$89,076.93**	**$0.10**	**$4.54**	**6.20%**
ATORVASTATIN PRODUCTS						
ATORVASTATIN TAB 40MG	9,171	2,546	$100,203.66	$0.25	$10.93	6.97%
ATORVASTATIN TAB 20MG	7,696	2,203	$77,652.16	$0.24	$10.09	5.40%
ATORVASTATIN TAB 10MG	4,935	1,280	$43,837.75	$0.23	$8.88	3.05%
ATORVASTATIN TAB 80MG	3,897	1,056	$46,660.86	$0.27	$11.97	3.25%
SUBTOTAL	**25,699**	**7,085**	**$268,354.43**	**$0.25**	**$10.44**	**18.68%**
PRAVASTATIN PRODUCTS						
PRAVASTATIN TAB 40MG	8,168	2,113	$199,843.85	$0.53	$24.47	13.91%
PRAVASTATIN TAB 20MG	4,889	1,358	$95,320.55	$0.43	$19.50	6.63%
PRAVASTATIN TAB 80MG	1,302	349	$42,180.63	$0.67	$32.40	2.94%
PRAVASTATIN TAB 10MG	1,205	316	$22,289.34	$0.44	$18.50	1.55%
SUBTOTAL	**15,564**	**4,136**	**$359,634.37**	**$0.51**	**$23.11**	**25.03%**
LOVASTATIN PRODUCTS						
LOVASTATIN TAB 20MG	1,980	628	$11,524.87	$0.12	$5.82	0.80%
LOVASTATIN TAB 40MG	1,332	360	$9,946.85	$0.16	$7.47	0.69%
SUBTOTAL	**3,312**	**988**	**$21,471.72**	**$0.14**	**$6.48**	**1.49%**
TIER-1 SUBTOTAL	**64,194**	**15,475***	**$738,537.45**	**$0.26**	**$11.50**	**51.40%**
ROSUVASTATIN PRODUCTS						
CRESTOR TAB 20MG	807	184	$259,006.21	$6.78	$320.95	18.02%
CRESTOR TAB 40MG	601	137	$174,804.25	$6.61	$290.86	12.16%
CRESTOR TAB 10MG	229	42	$58,585.86	$7.17	$255.83	4.08%
CRESTOR TAB 5MG	28	7	$8,661.35	$6.01	$309.33	0.60%
SUBTOTAL	**1,665**	**370**	**$501,057.67**	**$6.75**	**$300.94**	**34.87%**
TIER-2 SUBTOTAL	**1,665**	**359***	**$501,057.67**	**$6.75**	**$300.94**	**34.87%**
EZETIMIBE PRODUCTS						
ZETIA TAB 10MG	415	74	$119,401.40	$7.08	$287.71	8.31%
SUBTOTAL	**415**	**74**	**$119,401.40**	**$7.08**	**$287.71**	**8.31%**
EZETIMIBE/SIMVASTATIN PRODUCTS						
VYTORIN TAB 10-40MG	135	23	$42,549.11	$6.82	$315.18	2.96%
VYTORIN TAB 10-20MG	25	6	$9,229.46	$6.84	$369.18	0.64%
VYTORIN TAB 10-80MG	16	5	$9,708.19	$6.74	$606.76	0.68%
SUBTOTAL	**176**	**34**	**$61,486.76**	**$6.81**	**$349.36**	**4.28%**
PITAVASTATIN PRODUCTS						
LIVALO TAB 2MG	31	7	$8,444.66	$5.98	$272.41	0.59%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
LIVALO TAB 4MG	17	4	$5,648.42	$6.07	$332.26	0.39%
SUBTOTAL	**48**	**11**	**$14,093.08**	**$6.02**	**$293.61**	**0.98%**
NIACIN/SIMVASTATIN PRODUCTS						
SIMCOR TAB 1000-40	10	1	$2,383.66	$7.95	$238.37	0.17%
SUBTOTAL	**10**	**1**	**$2,383.66**	**$7.95**	**$238.37**	**0.17%**
SPECIAL PA SUBTOTAL	**649**	**117***	**$197,364.90**	**$6.92**	**$304.11**	**13.73%**
TOTAL	**66,508**	**15,798***	**$1,436,960.02**	**$0.49**	**$21.61**	**100.00%**

*Total number of unduplicated members.

Utilization Details of Lovaza® and Vascepa®: Fiscal Year 2015

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
OMEGA-3-ACID ETHYL ESTERS PRODUCTS						
OMEGA-3-ACID CAP 1GM	282	46	$47,183.84	$5.54	$167.32	70.38%
LOVAZA CAP 1GM	84	19	$19,644.49	$7.96	$233.86	29.30%
SUBTOTAL	**366**	**65**	**$66,828.33**	**$6.08**	**$182.59**	**99.69%**
ICOSAPENT ETHYL PRODUCTS						
VASCEPA CAP 1GM	1	1	$209.67	$6.99	$209.67	0.31%
SUBTOTAL	**1**	**1**	**$209.67**	**$6.99**	**$209.67**	**0.31%**
TOTAL	**367**	**49***	**$67,038.00**	**$6.08**	**$182.66**	**100.00%**

*Total number of unduplicated members.

Utilization Details of Juxtapid® and Kynamro®: Fiscal Year 2015

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
LOMITAPIDE PRODUCTS						
JUXTAPID 20MG CAPS	14	1	$822,451.30	$1,958.22	$58,746.52	100.00%
TOTAL	**14**	**1***	**$822,451.30**	**$1,958.22**	**$58,746.52**	**100.00%**

*Total number of unduplicated members.
Kynamro® had no utilization in fiscal year 2015.

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[2] FDA Drug Shortages: Ezetimibe/Atorvastatin (Liptruzet™) Status: Discontinued. Available online at: http://www.accessdata.fda.gov/scripts/drugshortages/dsp_ActiveIngredientDetails.cfm?AI=Ezetimibe/Atorvastatin%20(LIPTRUZET)&st=d&tab=tabs-2. Last revised 6/2/15. Last accessed 8/18/15.

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[9] Epanova® Package Insert. Medlibrary.org. Available online at: http://medlibrary.org/lib/rx/meds/epanova/. Last revised 9/8/14. Last accessed 8/18/15.
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Attachment A: Diagnosis of Heterozygous Familial Hypercholesterolemia (HeFH)[1]

Simon Broome Register Criteria

A. A plasma cholesterol measurement of either:
   a. Total cholesterol >290mg/dL (adult patient) or >259mg/dL (age < 16 years); or
   b. Low-density lipoprotein cholesterol (LDL-C) > 189mg/dL (adult patient) or >155mg/dL (age <16 years)
B. Tendon xanthomas in the patient or any of the patient's first- or second-degree relatives
C. DNA-based evidence in the patient of mutation in LDLR or any other HeFH-related gene
D. Family history of myocardial infarction before the age of:
   a. 50 years in any first- or second-degree relative; or
   b. 60 years in any first-degree relative
E. Family history of plasma total cholesterol measurements >290mg/dL in any first- or second-degree relatives

Diagnosis	Criteria Required
Definite HeFH	A + B *or* C
Probable HeFH	A + D *or* A + E

Dutch Lipid Network Criteria

	Points
1. Family history: a first-degree relative with known:	
a. Premature* coronary and vascular disease	**1**
b. Plasma LDL-C concentration >95th percentile for age and sex	
i. In an adult relative	**1**
ii. In a relative <18 years of age	**2**
c. Tendon xanthomas or arcus cornealis	**2**
2. Clinical history: patient has premature*:	
a. Coronary artery disease	**2**
b. Cerebral or peripheral vascular disease	**1**
3. Physical examination of the patient:	
a. Tendon xanthomas	**6**
b. Arcus cornealis in a patient <45 years of age	**4**
4. LDL-C levels in patient's blood (mg/dL):	
a. ≥329	**8**
b. 251 – 328	**5**
c. 193 – 250	**3**
d. 155 – 192	**1**
5. DNA analysis showing a functional mutation in the LDLR or other HeFH-related gene	**8**

Diagnosis	Total Points
Definite HeFH	> 8
Probable HeFH	6 – 8
Possible HeFH	3 – 5

*Premature is defined as males <55 years of age or females <60 years of age.

[1] *CMAJ:* Heterozygous familial hypercholesterolemia: an under-recognized cause of early cardiovascular disease. Available online at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1421462/. Last revised 4/11/06. Last accessed 8/18/15.

Attachment B: Framingham Heart Study and Framingham Risk Score[1,2]

Background Information

The Framingham Heart Study is a long-term, ongoing cardiovascular study on the residents of Framingham, Massachusetts. The study began in 1948 and is now on its third generation of participants. The Framingham Heart Study is a project of the National Heart, Lung, and Blood Institute (NHLBI) in collaboration with Boston University. The objective of the study was to identify the common factors or characteristics that contribute to CVD by following its development over a long period of time in a large group of participants who had not yet developed overt symptoms of CVD or suffered a heart attack or stroke. Over the years, careful monitoring of the study population has led to the identification of major CVD risk factors (high blood pressure, high cholesterol, smoking, obesity, diabetes, and physical inactivity) as well as a great deal of valuable information on the effects of related factors such as triglyceride and HDL-C levels, age, gender, and psychosocial issues. Although the Framingham cohort is primarily Caucasian, the importance of the major CVD risk factors identified in this group have been shown in other studies to apply almost universally among racial and ethnic groups, even though the patterns of distribution may vary from group to group. The concept of CVD risk factors has become an integral part of the modern medical curriculum and has led to the development of effective treatment and preventative strategies in clinical practice.

An individual's 10-year risk of CVD, coronary heart disease (CHD), or atrial fibrillation can be estimated with the Framingham Risk Score (FRS). The FRS is based on findings of the Framingham Heart Study and uses various predictors (e.g. age, cholesterol levels, smoking) to estimate an individual's 10-year risk.

Framingham Risk Score (FRS): 10-Year Risk for Coronary Heart Disease (CHD)

Predictors for Estimating Risk of CHD in Men*	Points	Relative Risk
1. Age:		
a. 30-34 years	-1	n/a
b. 35-39 years	0	n/a
c. 40-44 years	1	n/a
d. 45-49 years	2	n/a
e. 50-54 years	3	n/a
f. 55-59 years	4	n/a
g. 60-64 years	5	n/a
h. 65-69 years	6	n/a
i. 70-74 years	7	n/a
2. LDL-C^{+}:		
a. < 100mg/dL	-3	very low risk
b. 100-129mg/dL	0	low risk
c. 130-159mg/dL	0	moderate risk
d. 160-190mg/dL	1	high risk
e. > 190mg/dL	2	very high risk
3. HDL-C:		
a. < 35mg/dL	2	very high risk
b. 35-44mg/dL	1	high risk
c. 45-49mg/dL	0	moderate risk
d. 50-59mg/dL	0	low risk

e. ≥ 60mg/dL	-1	very low risk
4. Blood Pressure[α]:		
a. < 120/80mmHg	0	very low risk
b. 120-129/80-84mmHg	0	low risk
c. 130-139/85-89mmHg	1	moderate risk
d. 140-159/90-99mmHg	2	high risk
e. ≥ 160/100mmHg	3	very high risk
5. Diabetes:		
a. Yes	2	high risk
b. No	0	low risk
6. Smoking:		
a. Yes	2	high risk
b. No	0	low risk

Total Points	FRS: 10-Year CHD Risk
≤ -3	1%
-2 to -1	2%
0	3%
1 to 2	4%
3	6%
4	7%
5	9%
6	11%
7	14%
8	18%
9	22%
10	27%
11	33%
12	40%
13	47%
≥ 14	≥ 56%

FRS	Relative Risk
< 10%	Low risk
10% - 19%	Moderate risk
≥ 20%	High risk

*Points for estimating risk of CHD vary based on sex; therefore, total points and risk score may be different for a female patient with the same predictor values and characteristics as a male patient.
[+]FRS may also be calculated using total cholesterol instead of LDL-C.
[α]When systolic and diastolic pressures provide different estimates for point scores, use the higher number.

[1] Framingham Heart Study: Coronary Heart Disease (10-year risk). Available online at: https://www.framinghamheartstudy.org/risk-functions/coronary-heart-disease/10-year-risk.php. Last accessed 8/18/15.
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State of Oklahoma: Oklahoma Health Care Authority
PCSK9 Inhibitor Prior Authorization Form

Pharmacy Section

Member Name: _____ ***Date of Birth:***_____ ***Member ID#:***_____

Pharmacy NPI:_____ ***Pharmacy Phone:*** _____ ***Pharmacy Fax:***_____

Pharmacy Name:_____ ***Pharmacist Name:***_____

Prescriber NPI: _____ ***Prescriber Name:*** _____ ***Specialty:*** _____

Prescriber Phone:_____ ***Prescriber Fax:*** _____ ***Drug Name/Strength:*** _____

NDC:_____ ***Regimen:***_____ ***Fill Quantity:***_____ ***Day Supply:***_____

Has member been trained on proper administration and storage of this medication? ___Yes ___ No

Pharmacist Signature: _____ **Date:** _____

Prescriber Section

1. Please indicate member's diagnosis:
   - ❑ Heterozygous familial hypercholesterolemia (HeFH) confirmed by one of the following:
     - ❑ Definite HeFH confirmed using the Simon Broome or the Dutch Lipid Network diagnostic criteria
       a) Please list factors leading to definite diagnosis of HeFH via Simon Broome Register criteria:
       _____ or
       b) Dutch Lipid Network criteria score: _____
     - ❑ Documented functional mutation(s) in the LDL receptor gene or other HeFH genes via genetic testing**
   - ❑ Homozygous familial hypercholesterolemia (HoFH) confirmed by one of the following:
     - ❑ Untreated total cholesterol >500mg/dL and at least one of the following:
       - ❑ Documented evidence of definite HeFH in both parents; or
       - ❑ Presence of tendinous/cutaneous xanthoma prior to age 10 years
     - ❑ Documented functional mutation(s) in both LDL receptor alleles via genetic testing**
       *(**Please note if this option is selected genetic testing results must be submitted with the prior authorization request)*
   - ❑ Clinical atherosclerotic cardiovascular disease defined by the presence of one of the following criteria:
     - ❑ High cardiovascular risk confirmed by Framingham risk score. Please provide both the Framingham risk score and supporting diagnoses/conditions signifying this risk level: _____
       _____ or
     - ❑ Documented history of Coronary Heart Disease (CHD). Please provide supporting diagnoses/conditions and dates of occurrence signifying history of CHD: _____
       _____

2. Please specify the member's current statin therapy:
   a) Drug Name: _____ Dose:_____ Duration of Treatment:_____
   b) Has member been adherent to high-dose statin therapy for at least 12 continuous weeks? Yes___ No___
   SoonerCare claims analysis will be conducted to verify adherence compliance.
   a) If member is statin intolerant due to myalgia, provide creatine kinase (CK) labs verifying rhabdomyolysis.
   Members with myalgia not confirmed by CK labs must have at least 2 trials of lower dose statin therapy or failure of intermittent dosing.
3. Member's baseline LDL-C: _____ Current LDL-C: _____ Goal LDL-C: _____
4. How will this medication be used? _____ Monotherapy _____ Adjunct to statin therapy, diet, and exercise

Initial approvals will be for the duration of 3 months. Continued authorization will require recent LDL-C levels to demonstrate effectiveness and compliance will be checked at that time and every 6 months thereafter.

Prescriber Signature: _____ **Date:** _____

Has the member been counseled on proper administration and storage of PCSK9 therapy? Yes___ No___

Please do not send in chart notes. Specific information will be requested if necessary. Failure to complete this form in full will result in processing delays

Member (Patient) Section

Please have the member initial after each line, fill in all blanks, and sign at the bottom.

1. I understand this medicine must be injected. **Initials:**_____
2. I understand I must give myself a shot every _____ week(s). **Initials:** _____
3. I understand this medication must be kept in the refrigerator. **Initials:** _____
4. I will not leave this medication in the car or anywhere it would get hot. **Initials:** _____
5. I understand this medication will not be replaced if I leave it out of the refrigerator. **Initials:** _____

Member Signature: _____ **Date:** _____

PLEASE PROVIDE THE INFORMATION REQUESTED AND RETURN TO:

University of Oklahoma College of Pharmacy
Pharmacy Management Consultants
Product Based Prior Authorization Unit
Fax: 1-800-224-4014

Appendix L

Fiscal Year 2015 Annual Review of Anticoagulants and Platelet Aggregation Inhibitors and 30-Day Notice to Prior Authorize Savaysa™ (Edoxaban)

Oklahoma Health Care Authority
September 2015

Current Prior Authorization Criteria

Effient® (Prasugrel) Approval Criteria:

1. The first 90 days of therapy do not require prior authorization; and
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); and
3. 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
4. Members greater than 75 years of age will generally not be approved without supporting information; and
5. Approvals will be for the duration of one year; and
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.

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.

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.

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® (rivaroxaban) 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® (rivaroxaban) 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 in patients following hip or knee replacement surgery.

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; or
    c. Treatment of DVT and PE and for the reduction in the risk of recurrent DVT or PE.

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
2014	2,316	11,952	$711,651.21	$59.54	$1.75	468,515	405,867
2015	2,213	12,132	$1,057,338.16	$87.15	$2.65	465,566	399,469
% Change	**-4.40%**	**1.50%**	**48.60%**	**46.40%**	**51.40%**	**-0.60%**	**-1.60%**
Change	**-103**	**180**	**$345,686.95**	**$27.61**	**$0.90**	**-2,949**	**-6,398**

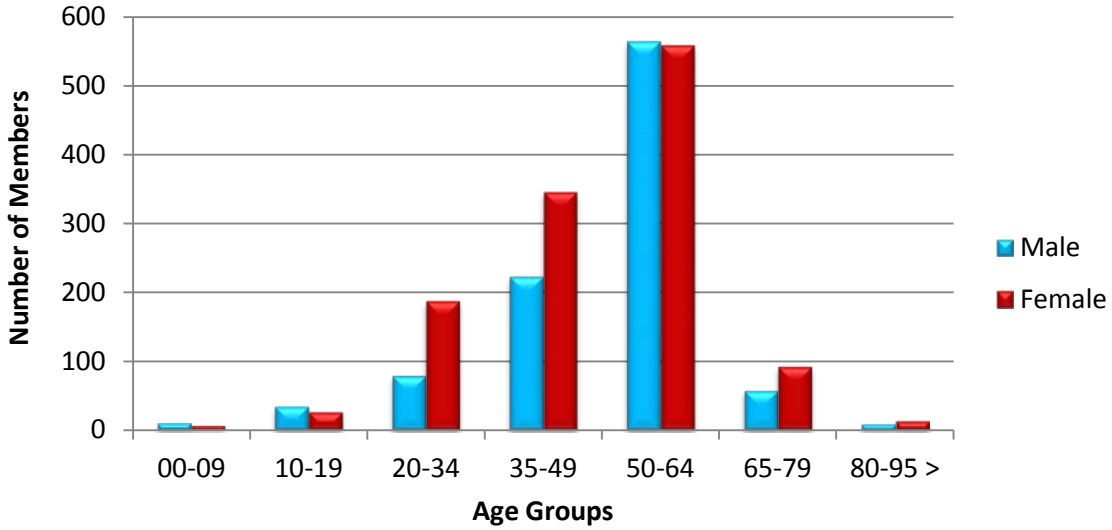
*Total number of unduplicated members.

Comparison of Fiscal Years: Platelet Aggregation Inhibitors

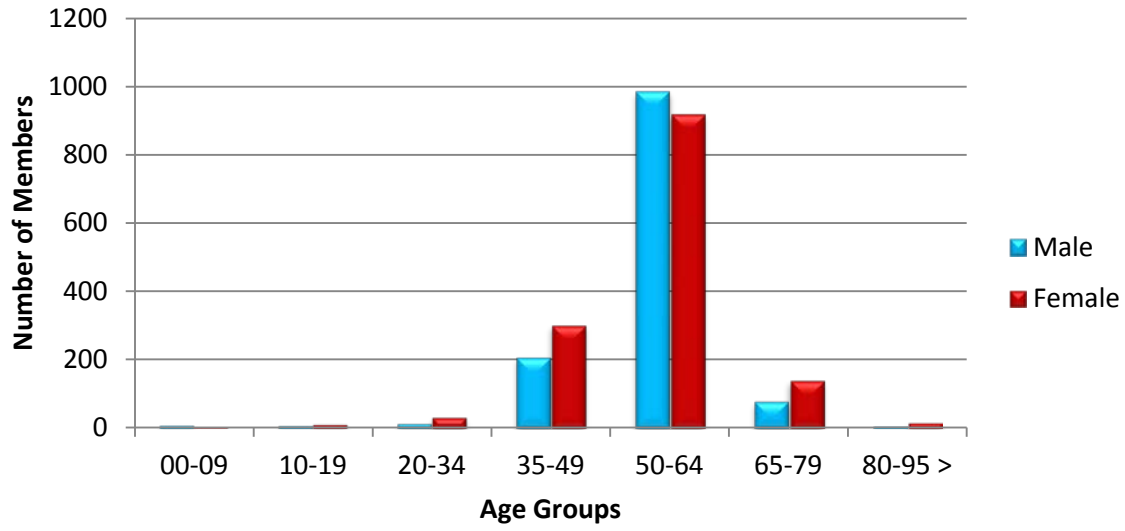
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	2,894	12,881	$407,434.24	$31.63	$0.78	531,624	525,040
2015	2,737	12,468	$420,370.82	$33.72	$0.81	529,713	520,543
% Change	**-5.40%**	**-3.20%**	**3.20%**	**6.60%**	**3.80%**	**-0.40%**	**-0.90%**
Change	**-157**	**-413**	**$12,936.58**	**$2.09**	**$0.03**	**-1,911**	**-4,497**

*Total number of unduplicated members.

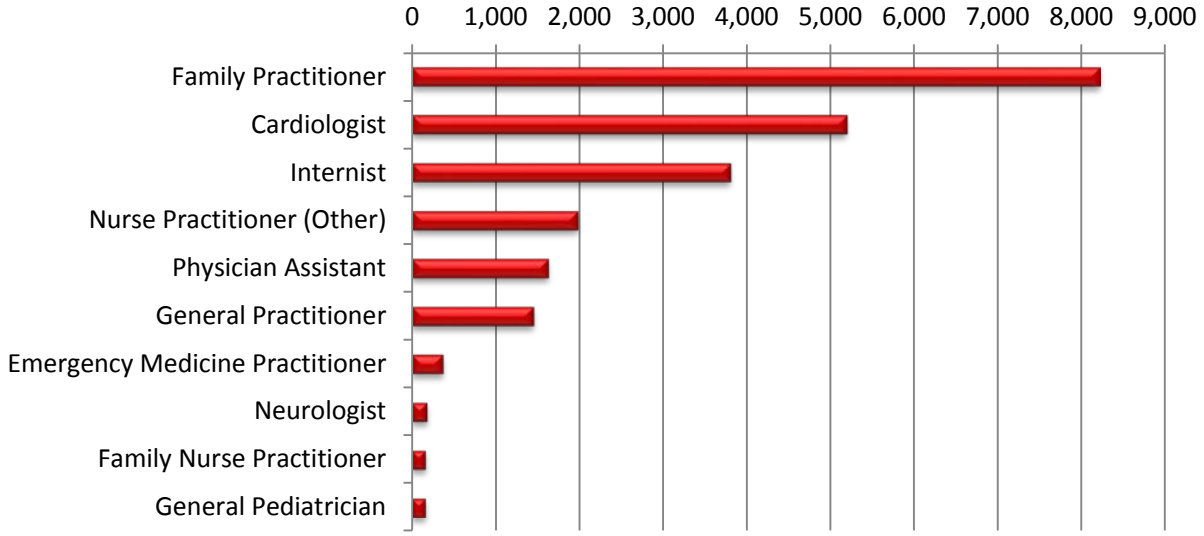
Demographics of Members Utilizing Anticoagulants



Demographics of Members Utilizing Platelet Aggregation Inhibitors



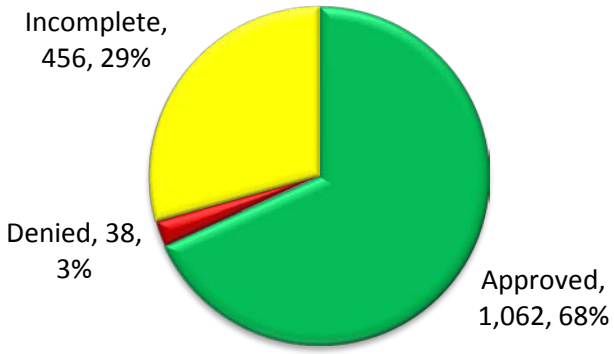
Top Prescriber Specialties of Anticoagulants and Platelet Aggregation Inhibitors by Number of Claims



Prior Authorization of Anticoagulants and Platelet Aggregation Inhibitors

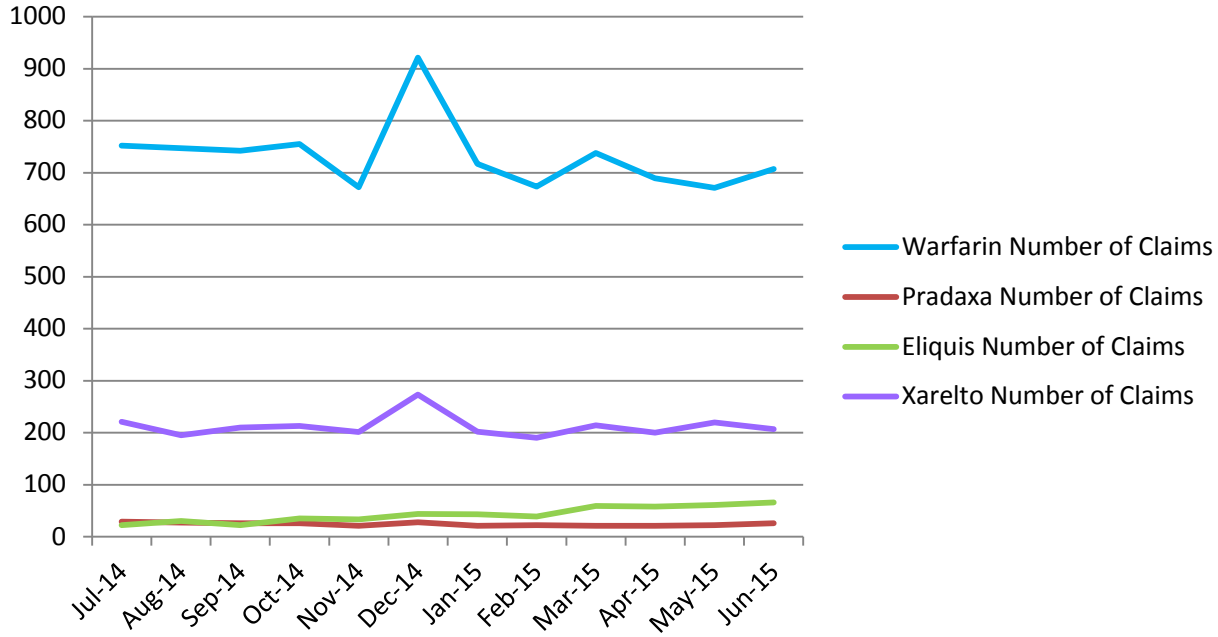
There were 1,556 prior authorizations submitted for anticoagulants and platelet aggregation inhibitors during fiscal year 2015. The following chart shows the status of the submitted petitions.

Status of Petitions

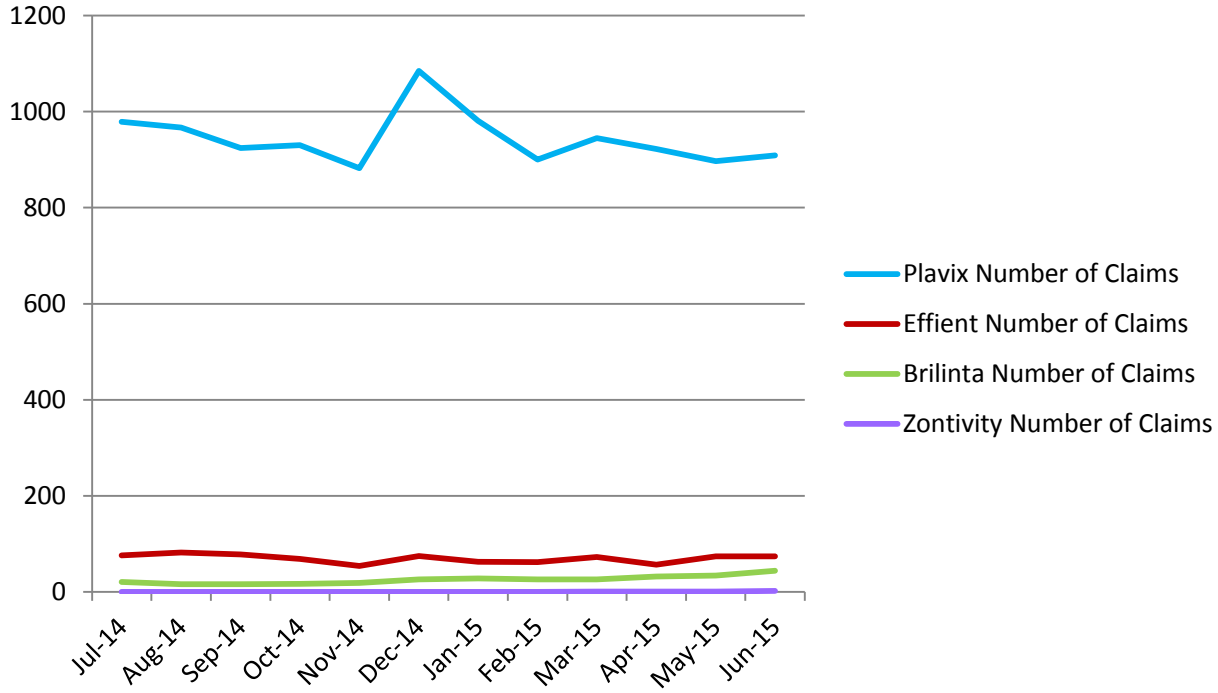


Oral Anticoagulants and Platelet Aggregation Inhibitors: Utilization Trends

Number of Claims for Oral Anticoagulants per Month: July 2014-June 2015



Number of Claims for Platelet Aggregation Inhibitors per Month: July 2014-June 2015



Market News and Updates[1, 2, 3]

Anticipated Patent Expirations:

- Xarelto® (rivaroxaban): February 2021
- Effient® (prasugrel): July 2021
- Brilinta® (ticagrelor): July 2021
- Eliquis® (apixaban): February 2023
- Zontivity® (vorapaxar): April 2024
- Pradaxa® (dabigatran): August 2027

FDA Safety Updates:

- **July 2015**: The FDA released a safety announcement warning healthcare professionals about reports of prescribing and dispensing errors with Brintellix® (vortioxetine) and Brilinta® (ticagrelor).

FDA Approvals and New Indications:

- **April 2015**: The FDA accepted a supplemental new drug application (sNDA) and granted Priority Review for Brilinta® (ticagrelor) for a potential new indication of chronic secondary prevention of atherothrombotic events in patients with a prior myocardial infarction.

Savaysa™ (Edoxaban) Product Summary[4]

FDA Approved: January 2015

Indications: Savaysa™ (edoxaban) is indicated to reduce the risk of stroke and systemic embolism (SE) in patients with non-valvular atrial fibrillation (NVAF). Edoxaban is also indicated for the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) following 5 to 10 days of initial therapy with a parenteral anticoagulant.

Dosing:

- Edoxaban is available as 15mg, 30mg, and 60mg oral tablets.
- For the treatment of NVAF, the recommended dosing of edoxaban is 60mg once daily in patients with CrCl 50 to 95 mL/min and 30mg once daily in patients with CrCl 15-50 mL/min.
- For the treatment of DVT and PE, the recommended dosing of edoxaban is 60mg once daily. The dose is reduced to 30mg once daily in patients with CrCl 15-50 mL/min or body weight less than or equal to 60kg or who use certain P-glycoprotein inhibitors (examples include itraconazole, ketoconazole, verapamil, and clarithromycin).

Mechanism of Action: Edoxaban inhibits platelet aggregation by selectively inhibiting Factor Xa.

Contraindication: Edoxaban is contraindicated in patients with active pathological bleeding.

Warnings and Precautions:

- Reduced efficacy in non-valvular atrial fibrillation patients with CrCl greater than 95mL/min
- Increased risk of stroke with premature discontinuation of edoxaban in non-valvular atrial fibrillation patients
- Serious and potentially fatal bleeding
- Not recommended in patients with mechanical heart valves or moderate-to-severe mitral stenosis

Adverse Reactions: The most common adverse reactions (≥5%) during clinical trials for non-valvular atrial fibrillation were bleeding and anemia. The most common adverse reactions (≥1%) during clinical trials for DVT and PE were bleeding, rash, abnormal liver function tests, and anemia.

Special Populations:

- Pregnancy: Edoxaban is Pregnancy Category C. There are no adequate and well-controlled studies in pregnant women. Edoxaban should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
- Pediatric Use: The safety and effectiveness of edoxaban in pediatric patients have not been established.
- Geriatric Use: In clinical trials the efficacy and safety of edoxaban in elderly (65 years or older) and younger patients were similar.
- Renal Impairment: Edoxaban blood levels are increased in patients with poor renal function compared to those with higher renal function. The dose of edoxaban should be reduced to 30mg once daily in renally impaired patients with CrCl 15-50mL/min. Edoxaban is not recommended in patients with CrCl less than 15mL/min.
- Hepatic Impairment: The use of edoxaban in patients with moderate or severe hepatic impairment (Child-Pugh B and C) is not recommended.
- Low Body Weight Consideration for Patients treated for DVT and/or PE: The dose of edoxaban should be reduced to 30mg in patients with body weight less than or equal to 60kg.

Efficacy: The efficacy of edoxaban for the reduction of risk of stroke and systemic embolic events in patients with NVAF is supported by the ENGAGE AF-TIMI 48 Study. This study was a multi-national, double-blind, non-inferiority study comparing two edoxaban treatment arms (60mg and 30mg) to warfarin. The study included 21,105 patients with a prior stroke, transient ischemic attack, or non-CNS systemic embolism. Patients were also included if they had two or more risk factors for stroke such as age ≥75 years, hypertension, heart failure, or diabetes mellitus. Patients were followed for a median of 2.8 years and treated for a median of 2.5 years. Both treatment arms of edoxaban were non-inferior to warfarin for the primary efficacy endpoint of stroke or systemic embolism (SE). In patients with CrCl ≤95 mL/min, the edoxaban 60mg treatment arm reduced the risk of stroke or SE when compared to warfarin [HR (95% CI: 0.82 (0.72, 0.93)].

The efficacy of edoxaban for the treatment of DVT and PE in patients is supported by the Hokusai VTE Study. This study was a multi-national, double-blind study comparing edoxaban 60mg to warfarin. The study included 8,292 patients with DVT or PE. Patients were treated from three months up to twelve months. The primary efficacy outcome of symptomatic VTE occurred in 3.2% in the group taking edoxaban compared with 3.5% in the warfarin group [HR (95% CI): 0.89 (0.70, 1.13)].

Utilization: There has been no utilization of edoxaban since it was FDA approved in January 2015.

Cost Comparison:

Medication Name	Cost Per Tablet or Capsule	Cost for 30 days of Therapy
Savaysa™ (edoxaban) 60mg Tablet	**$9.76[+]**	**$292.80**
Warfarin 5mg Tablet	$0.22[*]	$6.60
Xarelto® (rivaroxaban) 10mg, 15mg, 20mg Tablets	$11.08[+]	$332.40

+EAC= estimated acquisition cost
[*]State Maximum Allowable Cost (SMAC)

Recommendations

The College of Pharmacy recommends the prior authorization of Savaysa™ (edoxaban) with the following criteria:

Savaysa™ (Edoxaban) Approval Criteria:

1. An FDA approved diagnosis of one of the following:
    a. To reduce the risk of stroke and systemic embolism (SE) in patients with non-valvular atrial fibrillation; or
    b. For the treatment of deep vein thrombosis (DVT) or pulmonary embolism (PE) following 5 to 10 days of initial therapy with a parenteral anticoagulant; and
2. Requests for therapy for the treatment of DVT and PE must verify that the member has undergone 5 to 10 days of initial therapy with a parenteral anticoagulant; and
3. Member must not have a creatinine clearance (CrCl) greater than 95mL/min because of increased risk of ischemic stroke compared to warfarin at the highest dose studied (60mg); and
4. A quantity limit of 30 tablets per 30 days will apply.

Utilization Details of Anticoagulants: Fiscal Year 2015

Product Utilized	Total Claims	Total Members	Total Cost	Units/ Day	Claims/ Member	Cost/ Claim
Warfarin Products						
COUMADIN TAB 1MG	39	6	$925.78	0.95	6.5	$23.74
JANTOVEN TAB 1MG	56	17	$320.97	0.58	3.29	$5.73
WARFARIN TAB 1MG	770	238	$6,441.68	1.3	3.24	$8.37
COUMADIN TAB 2MG	27	6	$812.94	1.23	4.5	$30.11
JANTOVEN TAB 2MG	19	12	$112.41	0.91	1.58	$5.92
WARFARIN TAB 2MG	497	189	$3,563.37	1.23	2.63	$7.17
COUMADIN TAB 2.5MG	10	3	$57.00	0.67	3.33	$5.70
JANTOVEN TAB 2.5MG	34	13	$243.64	0.99	2.62	$7.17
WARFARIN TAB 2.5MG	398	144	$2,809.83	1.16	2.76	$7.06
COUMADIN TAB 3MG	33	7	$268.55	1.31	4.71	$8.14
JANTOVEN TAB 3MG	51	21	$368.94	0.95	2.43	$7.23
WARFARIN TAB 3MG	667	200	$5,048.06	1.07	3.34	$7.57
COUMADIN TAB 4MG	32	4	$744.66	1.24	8	$23.27
JANTOVEN TAB 4MG	95	30	$684.44	1.02	3.17	$7.20
WARFARIN TAB 4MG	719	231	$5,209.23	1.19	3.11	$7.25
COUMADIN TAB 5MG	82	11	$3,049.10	1.47	7.45	$37.18
JANTOVEN TAB 5MG	92	35	$1,056.47	1.12	2.63	$11.48
WARFARIN TAB 5MG	2,986	821	$31,196.72	1.19	3.64	$10.45
COUMADIN TAB 6MG	26	7	$835.53	0.9	3.71	$32.14
JANTOVEN TAB 6MG	29	11	$222.14	0.99	2.64	$7.66
WARFARIN TAB 6MG	656	172	$4,769.44	1.03	3.81	$7.27
COUMADIN TAB 7.5MG	5	3	$21.61	1	1.67	$4.32
JANTOVEN TAB 7.5MG	11	6	$86.63	1.07	1.83	$7.88
WARFARIN TAB 7.5MG	742	217	$4,589.13	0.96	3.42	$6.18
Subtotal	**8,784**	**1,540***	**$78,871.13**	**1.14**	**5.7**	**$8.98**
Dabigatran Products						
PRADAXA CAP 75MG	22	5	$6,373.85	2	4.4	$289.72
PRADAXA CAP 75MG	268	47	$81,707.22	1.99	5.7	$304.88
Subtotal	**290**	**51***	**$88,081.07**	**1.99**	**5.69**	**$303.73**
Rivaroxaban Products						
XARELTO TAB 10MG	294	185	$69,656.57	1	1.59	$236.93
XARELTO TAB 15MG	243	105	$82,769.01	1.25	2.31	$340.61
XARELTO TAB 20MG	2,004	394	$585,503.91	1	5.09	$292.17
Subtotal	**2,546**	**614***	**$740,757.29**	**1.02**	**4.15**	**$290.95**
Apixaban Products						
ELIQUIS TAB 2.5MG	99	34	$26,722.52	2	2.91	$269.92
ELIQUIS TAB 5MG	413	99	$122,906.15	1.98	4.17	$297.59
Subtotal	**512**	**131***	**$149,628.67**	**1.99**	**3.91**	**$292.24**
Total	**12,132**	**2,213***	**$1,057,338.16**	**1.17**	**5.48**	**$87.15**

*Total number of unduplicated members.

Utilization Details of Platelet Aggregation Inhibitors: Fiscal Year 2015

Product Utilized	Total Claims	Total Members	Total Cost	Units/ Day	Claims/ Member	Cost/ Claim
Clopidogrel Products						
CLOPIDOGREL TAB 75MG	11,311	2,513	$86,472.34	1	4.5	$7.64
PLAVIX TAB 75MG	10	5	$671.16	1	2	$67.12
Subtotal	**11,321**	**2517***	**$87,143.50**	**1**	**4.5**	**$7.70**
Prasugrel Products						
EFFIENT TAB 5MG	7	2	$2,152.84	1	3.5	$307.55
EFFIENT TAB 10MG	830	187	$247,570.21	1	4.44	$298.28
Subtotal	**837**	**189***	**$249,723.05**	**1**	**4.43**	**$298.35**
Ticagrelor Products						
BRILINTA TAB 90MG	305	90	$82,078.37	1.99	3.39	$269.11
Subtotal	**305**	**90**	**$82,078.37**	**1.99**	**3.39**	**$269.11**
Vorapaxar Products						
ZONTIVITY TAB 2.08MG	5	2	$1,425.90	1	2.5	$285.18
Subtotal	**5**	**2***	**$1,425.90**	**1**	**2.5**	**$285.18**
Total	**12,468**	**2,737***	**$420,370.82**	**1.02**	**4.56**	**$33.72**

*Total number of unduplicated members

[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 6/30/15. Last accessed 8/3/15.

[2]FDA Drug Safety Communication: FDA warns about prescribing and dispensing errors resulting from brand name confusion with antidepressant Brintellix (vortioxetine) and antiplatelet Brilinta (ticagrelor). Available online at: http://www.fda.gov/Drugs/DrugSafety/ucm456341.htm. Last revised 8/6/15. Last accessed 8/6/15.

[3]AstraZeneca Press Release: US FDA Grants Priority Review for Potential New Indication for Brilinta. Available online at: http://www.astrazeneca.com/Media/Press-releases/Article/2015029--us-fda-grants-priroity-review-for-brilinta. Last revised 4/29/2015. Last accessed 8/6/15.

[4]Savaysa™ Package Insert. Daiichi Sankyo, Inc. Available online at: http://medlibrary.org/lib/rx/meds/savaysa-1/. Last revised 5/6/2015. Last accessed 8/6/15.

Appendix M

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

FDA NEWS RELEASE

For Immediate Release: July 24th, 2015

FDA approves Technivie for treatment of chronic hepatitis C genotype 4

The U.S. Food and Drug Administration approved Technivie (ombitasvir, paritaprevir and ritonavir) for use in combination with ribavirin for the treatment of hepatitis C virus (HCV) genotype 4 infections in patients without scarring and poor liver function (cirrhosis).

Technivie in combination with ribavirin is the first drug that has demonstrated safety and efficacy to treat genotype 4 HCV infections without the need for co-administration of interferon, an FDA-approved drug also used to treat HCV infection.

Hepatitis C is a viral disease that causes inflammation of the liver that can lead to diminished liver function or liver failure. Most people infected with HCV have no symptoms of the disease until liver damage becomes apparent, which may take several years. Some people with chronic HCV infection develop cirrhosis over many years, which can lead to complications such as bleeding, jaundice, fluid accumulation in the abdomen, infections or liver cancer. According to the Centers for Disease Control and Prevention, approximately 2.7 million Americans are infected with HCV, of which genotype 4 is one of the least common.

The safety and efficacy of Technivie with ribavirin were evaluated in a clinical trial of 135 participants with chronic HCV genotype 4 infections without cirrhosis. Ninety-one participants received Technivie with ribavirin once daily for 12 weeks. Forty-four participants received Technivie once daily without ribavirin for 12 weeks. The studies were designed to measure whether a participant's hepatitis C virus was no longer detected in the blood 12 weeks after finishing treatment (sustained virologic response), suggesting a participant's infection had been cured.

Results showed that 100 percent of the participants who received Technivie with ribavirin achieved a sustained virologic response. Of those who received Technivie without ribavirin, 91 percent achieved sustained virologic response.

Safety information was available for 316 participants with HCV treated with the recommended dose of Technivie in combination with other anti-HCV drugs in clinical trials. The three drugs included in Technivie are also included in Viekira Pak, previously approved for the treatment of HCV genotype 1 infection. Additional safety information for those drugs was available from the Viekira Pak trials. The most common side effects of Technivie with ribavirin were fatigue, weakness (asthenia), nausea, insomnia, itching (pruritus) and other skin reactions.

Technivie carries a warning alerting patients and health care providers that elevations of liver enzymes to greater than five times the upper limit of normal occurred in approximately 1 percent of clinical trial participants. The elevations occurred more frequently in females taking contraceptives containing ethinyl estradiol. Contraceptives containing ethinyl estradiol must be discontinued prior to starting Technivie. Hepatic laboratory testing should be performed during the first four weeks of starting treatment, and as clinically indicated thereafter.

Technivie and Viekira Pak are marketed by AbbVie Inc. based in North Chicago, Illinois.

FDA NEWS RELEASE

For Immediate Release: July 24th, 2015

FDA approves Praluent to treat certain patients with high cholesterol

First in a new class of injectable cholesterol-lowering drugs

The U.S. Food and Drug Administration approved Praluent (alirocumab) injection, the first cholesterol-lowering treatment approved in a new class of drugs known as proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitors.

Praluent is approved for use in addition to diet and maximally tolerated statin therapy in adult patients with heterozygous familial hypercholesterolemia (HeFH) or patients with clinical atherosclerotic cardiovascular disease such as heart attacks or strokes, who require additional lowering of LDL cholesterol.

HeFH is an inherited condition that causes high levels of low-density lipoprotein (LDL) cholesterol. A high level of LDL cholesterol in the blood is linked to cardiovascular disease. Heart disease is the number one cause of death for Americans, both men and women. According to the Centers for Disease Control and Prevention, about 610,000 people die of heart disease in the United States every year– that equals one in every four deaths.
Praluent is an antibody that targets a specific protein, called PCSK9, which works by reducing the number of receptors on the liver that remove LDL cholesterol from the blood. By blocking PCSK9's ability to work, more receptors are available to get rid of LDL cholesterol from the blood and, as a result, lower LDL cholesterol levels.
The efficacy and safety of Praluent were evaluated in five placebo-controlled trials, involving 2,476 participants exposed to Praluent. All participants had HeFH or were otherwise at high risk for heart attack or stroke, and were taking maximally tolerated doses of a statin, with or without other lipid-modifying therapies. Participants taking Praluent had an average reduction in LDL cholesterol ranging from 36 to 59 percent, compared to placebo.
Multiple clinical trials have demonstrated that statins lower the risk of having a heart attack or stroke. A trial evaluating the effect of adding Praluent to statins on reducing cardiovascular risk is ongoing.
The most common side effects of Praluent include itching, swelling, pain, or bruising where injection is given, nasopharyngitis, and flu. Allergic reactions, such as hypersensitivity vasculitis (a skin rash usually appearing as purple-colored spots on the skin associated with inflammation of small blood vessels) and hypersensitivity reactions requiring hospitalization, have been reported with the use of Praluent. Patients should stop using Praluent and get medical help if they experience symptoms of a serious allergic reaction.
Praluent is marketed by Sanofi-Aventis U.S., based in Bridgewater, New Jersey, and Regeneron Pharmaceuticals Inc., based in Tarrytown, New York

FDA NEWS RELEASE

For Immediate Release: July 24th, 2015

FDA approves new treatment for most common form of advanced skin cancer

The U.S. Food and Drug Administration approved Odomzo (sonidegib) to treat patients with locally advanced basal cell carcinoma that has recurred following surgery or radiation therapy, or who are not candidates for surgery or radiation therapy.
Skin cancer is the most common cancer and basal cell carcinoma accounts for approximately 80 percent of non-melanoma skin cancers. Basal cell carcinoma starts in the top layer of the skin (called the epidermis) and usually develops in areas that have been regularly exposed to the sun and other forms of ultraviolet radiation. According to the National Cancer Institute, the number of new cases of non-melanoma skin cancer appears to be increasing every year. Locally advanced basal cell skin cancer refers to basal cancers that have not spread to other parts of the body, but cannot be curatively treated with local treatments, specifically surgery and radiation.
Odomzo is a pill taken once a day. It works by inhibiting a molecular pathway, called the Hedgehog pathway, which is active in basal cell cancers. By suppressing this pathway, Odomzo may stop or reduce the growth of cancerous lesions.
Odomzo carries a Boxed Warning alerting healthcare professionals that Odomzo may cause death or severe birth defects in a developing fetus when administered to a pregnant woman. Pregnancy status should be verified prior to the start of Odomzo treatment, and both male and female patients should be warned about these risks and advised to use effective contraception.
The efficacy of Odomzo was established in a multi-center, double-blind clinical trial, in which 66 patients with locally advanced basal cell carcinoma were randomly assigned to receive Odomzo 200 mg daily and 128 patients were assigned to receive Odomzo 800 mg daily. The study's primary endpoint was objective response rate, which is the percentage of patients who experienced partial shrinkage or complete disappearance of their tumor(s). Results showed that 58 percent of patients treated with Odomzo 200 mg had their tumors shrink or disappear. This effect lasted at least 1.9 to 18.6 months, and approximately half of the responding patients' tumor shrinkage lasted six months or longer. Response rates were similar in patients who received Odomzo 800 mg daily, however side effects were more common at this dose.
At a dose of 200 mg daily, the most common side effects of Odomzo were muscle spasms, alopecia (hair loss), dysgeusia (distortion in the sense of taste), fatigue, nausea, musculoskeletal pain, diarrhea, decreased weight, decreased appetite, myalgia (muscle pain), abdominal pain, headache, pain, vomiting

and pruritus (itching). Odomzo also has the potential to cause serious musculoskeletal-related side effects, including increased serum creatine kinase levels [with rare reports of muscle tissue breakdown (rhabdomyolysis)], muscle spasms, and myalgia.
Odomzo is marketed by East Hanover, New Jersey-based Novartis Pharmaceuticals Corporation. Erivedge is marketed by Genentech in San Francisco, California.

FDA NEWS RELEASE

For Immediate Release: August 18th, 2015

FDA approves first treatment for sexual desire disorder

The U.S. Food and Drug Administration approved Addyi (flibanserin) to treat acquired, generalized hypoactive sexual desire disorder (HSDD) in premenopausal women. Prior to Addyi's approval, there were no FDA-approved treatments for sexual desire disorders in men or women.
HSDD is characterized by low sexual desire that causes marked distress or interpersonal difficulty and is not due to a co-existing medical or psychiatric condition, problems within the relationship, or the effects of a medication or other drug substance. HSDD is acquired when it develops in a patient who previously had no problems with sexual desire. HSDD is generalized when it occurs regardless of the type of sexual activity, the situation or the sexual partner.
Addyi can cause severely low blood pressure (hypotension) and loss of consciousness (syncope). These risks are increased and more severe when patients drink alcohol or take Addyi with certain medicines (known as moderate or strong CYP3A4 inhibitors) that interfere with the breakdown of Addyi in the body. Because of the alcohol interaction, the use of alcohol is contraindicated while taking Addyi. Health care professionals must assess the likelihood of the patient reliably abstaining from alcohol before prescribing Addyi.
Addyi is being approved with a risk evaluation and mitigation strategy (REMS), which includes elements to assure safe use (ETASU). The FDA is requiring this REMS because of the increased risk of severe hypotension and syncope due to the interaction between Addyi and alcohol. The REMS requires that prescribers be certified with the REMS program by enrolling and completing training. Certified prescribers must counsel patients using a Patient-Provider Agreement Form about the increased risk of severe hypotension and syncope and about the importance of not drinking alcohol during treatment with Addyi. Additionally, pharmacies must be certified with the REMS program by enrolling and completing training. Certified pharmacies must only dispense Addyi to patients with a prescription from a certified prescriber. Additionally, pharmacists must counsel patients prior to dispensing not to drink alcohol during treatment with Addyi.
Addyi is also being approved with a Boxed Warning to highlight the risks of severe hypotension and syncope in patients who drink alcohol during treatment with Addyi, in those who also use moderate or strong CYP3A4 inhibitors, and in those who have liver impairment. Addyi is contraindicated in these patients. In addition, the FDA is requiring the company that owns Addyi to conduct three well-designed studies in women to better understand the known serious risks of the interaction between Addyi and alcohol.
Addyi is a serotonin 1A receptor agonist and a serotonin 2A receptor antagonist, but the mechanism by which the drug improves sexual desire and related distress is not known. Addyi is taken once daily. It is dosed at bedtime to help decrease the risk of adverse events occurring due to possible hypotension, syncope and central nervous system depression (such as sleepiness and sedation). Patients should discontinue treatment after eight weeks if they do not report an improvement in sexual desire and associated distress.
The effectiveness of the 100 mg bedtime dose of Addyi was evaluated in three 24-week randomized, double-blind, placebo-controlled trials in about 2,400 premenopausal women with acquired, generalized HSDD. The average age of the trial participants was 36 years, with an average duration of HSDD of approximately five years. In these trials, women counted the number of satisfying sexual events, reported sexual desire over the preceding four weeks (scored on a range of 1.2 to 6.0) and reported distress related to low sexual desire (on a range of 0 to 4). On average, treatment with Addyi increased the number of satisfying sexual events by 0.5 to one additional event per month over placebo increased the sexual desire score by 0.3 to 0.4 over placebo, and decreased the distress score related to sexual desire by 0.3 to 0.4 over placebo. Additional analyses explored whether the improvements with Addyi were meaningful to patients, taking into account the effects of treatment seen among those patients who reported feeling much

improved or very much improved overall. Across the three trials, about 10 percent more Addyi-treated patients than placebo-treated patients reported meaningful improvements in satisfying sexual events, sexual desire or distress. Addyi has not been shown to enhance sexual performance.
The 100 mg bedtime dose of Addyi has been administered to about 3,000 generally healthy premenopausal women with acquired, generalized HSDD in clinical trials, of whom about 1,700 received treatment for at least six months and 850 received treatment for at least one year.
The most common adverse reactions associated with the use of Addyi are dizziness, somnolence (sleepiness), nausea, fatigue, insomnia and dry mouth.
The FDA has recognized for some time the challenges involved in developing treatments for female sexual dysfunction. The FDA held a public Patient-Focused Drug Development meeting and scientific workshop on female sexual dysfunction on October 27 and October 28, 2014, to solicit perspectives directly from patients about their condition and its impact on daily life, and to discuss the scientific challenges related to developing drugs to treat these disorders. The FDA continues to encourage drug development in this area.
Consumers and health care professionals are encouraged to report adverse reactions from the use of Addyi to the FDA's MedWatch Adverse Event Reporting program at www.fda.gov/MedWatch or by calling 1-800-FDA-1088.
Addyi is marketed by Sprout Pharmaceuticals, based in Raleigh, North Carolina.

FDA NEWS RELEASE

For Immediate Release: August 24th, 2015

FDA extends use of Promacta in young children with rare blood disorder

The U.S. Food and Drug Administration approved Promacta (eltrombopag) to treat low blood platelet count in pediatric patients – ages one year and older – with a rare blood disorder called chronic immune thrombocytopenic purpura (ITP). Promacta can be used in these children when they have not achieved an appropriate response using other ITP medicines or surgery to remove the spleen.
ITP is a disorder that results in an abnormally low number of platelets, the cells that help your blood clot. Without enough platelets, bleeding can occur under the skin, in mucous membranes or in other parts of the body.
Promacta helps increase blood platelet production and is available as a tablet taken once-daily or as a powder that is mixed with liquid for children ages one to five to take orally. It was first approved in 2008 to treat adult patients with the same condition as the new pediatric indication.
Promacta should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increase the risk for bleeding.
The efficacy and safety of Promacta in pediatric patients ages one to 17 years with chronic ITP was evaluated in two double-blind, placebo-controlled trials of 159 participants where the primary endpoint was an increase in platelet counts. In the first trial (n=67), patients were randomly assigned to receive either Promacta or placebo daily for seven weeks. Of those taking Promacta, 62 percent had an improvement in platelet counts without rescue therapy between weeks one and six, compared to 32 percent in the placebo group. In the second trial (n=92), patients received either Promacta or placebo daily for 13 weeks and in those treated with Promacta, 41 percent experienced increased platelet counts for at least six out of eight weeks between weeks five to 12, compared to 3 percent of patients receiving placebo. In both trials, patients taking Promacta also had less need for other treatments to increase their platelet counts, such as corticosteroids or platelet transfusions. Among patients taking one or more ITP medications at the start of the trials, about half were able to reduce or discontinue their use of these medications, primarily corticosteroids.
The most common side effects of treatment with Promacta in children ages one and older were infections of the upper respiratory tract or nose and throat (symptoms including fever, cough, nasal congestion, runny nose and sore throat), diarrhea, abdominal pain, rash and increase in liver enzymes.
The safety and efficacy of Promacta in pediatric patients younger than one year with ITP, or in pediatric patients with thrombocytopenia associated with chronic hepatitis C and severe aplastic anemia, have not been established.
The FDA granted Promacta orphan drug designation because it treats a rare disease. Orphan drug designation provides financial incentives – like tax credits, user fee waivers, and eligibility for market exclusivity – to promote rare disease drug development.
Promacta is manufactured by Novartis in East Hanover, New Jersey.

Safety Announcements

FDA Drug Safety Communication: FDA warns about prescribing and dispensing errors resulting from brand name confusion with antidepressant Brintellix (vortioxetine) and antiplatelet Brilinta (ticagrelor)

[7-30-15] The U.S. Food and Drug Administration is warning health care professionals and patients that reports of confusion between the antidepressant Brintellix and anti-blood clotting medication Brilinta have resulted in the wrong medication being prescribed or dispensed. We have determined that the main reason for the confusion between these two medications is the similarity of their brand (proprietary) names. None of the reports indicates that a patient ingested the wrong medication; however, reports of prescribing and dispensing errors continue. As a result, we are alerting the public about this safety issue.

Health care professionals can reduce the risk of name confusion by including the generic (established) name of the medication, in addition to the brand name, and the indication for use when prescribing these medications. Patients should check their prescriptions to ensure that the correct medication was dispensed.

Brintellix (vortioxetine) is used to treat a certain type of depression called major depressive disorder (MDD) in adults. It is in a class of antidepressants called selective serotonin reuptake inhibitors (SSRIs) that work by affecting chemicals in the brain that may become unbalanced. Brintellix is a tear-shaped tablet stamped with “TL” on one side of the tablet and a number that indicates the tablet strength on the other side. It varies in color depending upon the strength prescribed.

Brilinta (ticagrelor) is an antiplatelet, anti-blood clotting medication used to lower the risk of having another heart attack, or dying from a heart problem after a heart attack or severe chest pain. It works by keeping the platelets in the blood from sticking together, thereby preventing blood clots that can occur with certain heart conditions. Brilinta is a round, yellow tablet with a “90” above a “T” stamped on one side.

As of June 2015, FDA has received 50 reports of medication error cases describing brand name confusion with Brintellix and Brilinta. Most of the cases reported concerns that similarities in the sound, look, or both sound and look of the two brand names could cause confusion for prescribers and pharmacists. Some cases resulted in the wrong medication being dispensed to a patient. In one case, a pharmacist misinterpreted Brintellix as Brilinta and did not dispense any medication because the patient had a contraindication to blood thinners.

We urge patients and health care professionals to report name confusion and medication errors involving Brintellix and Brilinta to the FDA MedWatch program.

Safety Announcements

FDA Drug Safety Communication: FDA warns about cases of rare brain infection with MS drug Gilenya (fingolimod) in two patients with no prior exposure to immunosuppressant drugs

[8-4-15] The U.S. Food and Drug Administration is warning that a case of definite progressive multifocal leukoencephalopathy (PML) and a case of probable PML have been reported in patients taking Gilenya (fingolimod) for multiple sclerosis (MS). These are the first cases of PML reported in patients taking Gilenya who had not been previously treated with an immunosuppressant drug for MS or any other medical condition. As a result, information about these recent cases is being added to the drug label.

Patients taking Gilenya should contact their health care professionals right away if they experience symptoms such as new or worsening weakness; increased trouble using their arms or legs; or changes in thinking, eyesight, strength, or balance. Patients should not stop taking Gilenya without first discussing it with their health care professionals. Health care professionals should stop Gilenya and perform a diagnostic evaluation if PML is suspected.

Gilenya is an immunomodulator shown to benefit patients with relapsing forms of MS. This type of MS causes attacks or relapses, which are periods of time when symptoms get worse. Immunomodulators alter the immune system to reduce inflammation.

PML is a rare and serious brain infection caused by the John Cunningham (JC) virus. The JC virus is a common virus that is harmless in most people but can cause PML in some patients who have weakened immune systems, including those taking immunosuppressant drugs. Symptoms of PML are diverse and may include progressive weakness on one side of the body; clumsiness; vision problems; confusion, and

changes in thinking, personality, memory and orientation. The progression of deficits can lead to severe disability or death. A magnetic resonance imaging (MRI) scan may find lesions in the brain before these symptoms develop.
In an August 2013 Drug Safety Communication, we reported that a patient developed PML after taking Gilenya. PML could not be conclusively linked to Gilenya in this case because prior to Gilenya treatment the patient had been treated with an immunosuppressant drug that can cause PML and during Gilenya treatment the patient had received multiple courses of intravenous corticosteroids, which can weaken the immune system.
Gilenya's manufacturer, Novartis, recently notified FDA about one patient with PML and one patient with probable PML that occurred during Gilenya treatment without prior or concurrent exposure to other immunosuppressant drugs. The patient with probable PML did not have clinical signs or symptoms suggestive of PML, and was diagnosed based on MRI findings compatible with PML and JC virus detected in the cerebrospinal fluid (CSF). The other patient was diagnosed with definite PML based on characteristic symptoms, MRI findings, and JC virus in the CSF. Gilenya treatment was stopped in both patients.
Information describing these two cases has been added to the *Warnings and Precautions* and *Patient Counseling Information* sections of the drug label, as well as to the patient Medication Guide.
We urge health care professionals and patients to report side effects involving Gilenya to the FDA MedWatch program.

Safety Announcements

FDA Drug Safety Communication: FDA warns of severe adverse events with application of Picato (ingenol mebutate) gel for skin condition; requires label changes

[8-21-15] The U.S. Food and Drug Administration (FDA) is warning about reports of severe allergic reactions and herpes zoster (shingles) associated with the use of Picato gel (ingenol mebutate). Picato is used to treat actinic keratosis, a scaly, crusty lesion on the skin that may be red or yellow in color.
We have also received reports of cases involving severe eye injuries and skin reactions associated with the application of Picato gel. Some cases were associated with Picato gel not being used according to the instructions for use on the label. As a result, we are requiring changes to the label to warn about these new safety risks and to provide additional instructions on the safe and appropriate application of the product.
Patients should use Picato gel as prescribed by their health care professionals, and should not use it on an area of skin larger or for a longer period than instructed in the drug label. Also patients should avoid applying the gel in, near, and around the mouth, lips and eye area. Accidental transfer of Picato gel from the hands even after washing has occurred, including through application of make-up and insertion of contact lenses. Applying Picato gel in a manner other than recommended in the product label has been associated with severe skin reactions and eye injuries.
Patients who experience a severe allergic reaction should stop using Picato gel and seek immediate medical attention. The allergic reaction may include throat tightness, difficulty breathing, feeling faint, or swelling of the lips or tongue. Patients should also stop using the product and contact their health care professionals if they develop hives, itching, or severe skin rash. If accidental eye exposure occurs, flush the eyes thoroughly with water and seek medical care.
Actinic keratosis, which is treated with Picato gel, is a scaly, crusty lesion on the skin that may be red or yellow in color. The lesions are typically located on areas exposed to the sun such as the face, scalp, back of the hands, and chest. The majority of these lesions are not harmful. However, actinic keratosis may occasionally develop into skin cancer.
We reviewed postmarketing cases submitted to the FDA Adverse Event Reporting System (FAERS) for Picato gel. In some cases, severe eye injuries and skin reactions occurred when the application of the product was not according to the instructions found in the labeling. Other cases described severe allergic reactions, including anaphylaxis. Herpes zoster was also reported.
We urge patients and health care professionals to report side effects or medication errors involving Picato gel to the FDA MedWatch program.

Safety Announcements

FDA Drug Safety Communication: FDA warns that DPP-4 inhibitors for type 2 diabetes may cause severe joint pain

[8-28-15] The U.S. Food and Drug Administration (FDA) is warning that the type 2 diabetes medicines sitagliptin, saxagliptin, linagliptin, and alogliptin may cause joint pain that can be severe and disabling. We have added a new Warning and Precaution about this risk to the labels of all medicines in this drug class, called dipeptidyl peptidase-4 (DPP-4) inhibitors.
Patients should not stop taking their DPP-4 inhibitor medicine, but should contact their health care professional right away if they experience severe and persistent joint pain. Health care professionals should consider DPP-4 inhibitors as a possible cause of severe joint pain and discontinue the drug if appropriate.
DPP-4 inhibitors are used along with diet and exercise to lower blood sugar in adults with type 2 diabetes. When untreated, type 2 diabetes can lead to serious problems, including blindness, nerve and kidney damage, and heart disease. These medicines are available as single-ingredient products and in combination with other diabetes medicines such as metformin.
In a search of the FDA Adverse Event Reporting System (FAERS) database and the medical literature, we identified cases of severe joint pain associated with the use of DPP-4 inhibitors. Patients started having symptoms from 1 day to years after they started taking a DPP-4 inhibitor. After the patients discontinued the DPP-4 inhibitor medicine, their symptoms were relieved, usually in less than a month. Some patients developed severe joint pain again when they restarted the same medicine or another DPP-4 inhibitor.
We urge health care professionals and patients to report side effects involving DPP-4 inhibitors to the FDA MedWatch program.

Current Drug Shortages Index (as of August 28th, 2015):

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

Acetohydroxamic Acid (Lithostat) Tablets	***Currently in Shortage***
Ammonium Chloride Injection	***Currently in Shortage***
Aprepitant (Emend) Capsules	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Azathioprine Tablet	***Currently in Shortage***
Caffeine Anhydrous (125mg/mL); Sodium Benzoate (125mg/mL) Injection	***Currently in Shortage***
Calcium Chloride Injection, USP	***Currently in Shortage***
Calcium Gluconate Injection	***Currently in Shortage***
Cefazolin Injection	***Currently in Shortage***
Cefepime Injection	***Currently in Shortage***
Cefotaxime Sodium (Claforan) Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***
Chloramphenicol Sodium Succinate Injection	***Currently in Shortage***
Chloroquine Phosphate Tablets	***Currently in Shortage***
Dexamethasone Sodium Phosphate Injection	***Currently in Shortage***
Dextrose 5% Injection Bags	***Currently in Shortage***
Dextrose Injection USP, 70%	***Currently in Shortage***
Disopyramide Phosphate (Norpace) Capsules	***Currently in Shortage***
Doxorubicin (Adriamycin) Injection	***Currently in Shortage***
Epinephrine 1mg/mL (Preservative Free)	***Currently in Shortage***
Epinephrine Injection	***Currently in Shortage***
Ethiodized Oil (Lipiodol) Injection	***Currently in Shortage***
Fentanyl Citrate (Sublimaze) Injection	***Currently in Shortage***
Fluoxymesterone (Androxy) Tablets, USP	***Currently in Shortage***
Fomepizole Injection	***Currently in Shortage***
Gemifloxacin Mesylate (Factive) Tablets	***Currently in Shortage***

Haloperidol Lactate Injection	***Currently in Shortage***
Imipenem and Cilastatin for Injection, USP	***Currently in Shortage***
Indigo Carmine Injection	***Currently in Shortage***
Ketorolac Tromethamine Injection	***Currently in Shortage***
L-Cysteine Hydrochloride Injection	***Currently in Shortage***
Leucovorin Calcium Lyophilized Powder for Injection	***Currently in Shortage***
Leuprolide Acetate Injection	***Currently in Shortage***
Levetiracetam (Keppra) Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection	***Currently in Shortage***
Liotrix (Thyrolar) Tablets	***Currently in Shortage***
Magnesium Sulfate Injection	***Currently in Shortage***
Mecasermin [rDNA origin] (Increlex) Injection	***Currently in Shortage***
Memantine Hydrochloride (Namenda) XR Capsules	***Currently in Shortage***
Meropenem for Injection, USP	***Currently in Shortage***
Methyldopate Hydrochloride Injection	***Currently in Shortage***
Methylin Chewable Tablets	***Currently in Shortage***
Methylphenidate Hydrochloride ER Capsules/Tablets	***Currently in Shortage***
Multi-Vitamin Infusion (Adult and Pediatric)	***Currently in Shortage***
Nebivolol (BYSTOLIC) Tablets	***Currently in Shortage***
Nimodipine (Nymalize) Oral Solution	***Currently in Shortage***
Pancuronium Bromide Injection	***Currently in Shortage***
Peritoneal Dialysis Solutions	***Currently in Shortage***
Phentolamine Mesylate Injection	***Currently in Shortage***
Phosphate (Glycophos) Injection	***Currently in Shortage***
Piperacillin and Tazobactam (Zosyn) Injection	***Currently in Shortage***
Potassium Chloride Injection	***Currently in Shortage***
Reserpine Tablets	***Currently in Shortage***
Sacrosidase (Sucraid) Oral Solution	***Currently in Shortage***
Sincalide (Kinevac) Lyophilized Powder for Injection	***Currently in Shortage***
Sodium Chloride 0.9% Injection Bags	***Currently in Shortage***
Sodium Chloride 23.4% Injection	***Currently in Shortage***
Sufentanil Citrate (Sufenta) Injection	***Currently in Shortage***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***
Thiotepa (Thioplex) for Injection	***Currently in Shortage***
Tiopronin (Thiola)	***Currently in Shortage***
Tobramycin Injection	***Currently in Shortage***
Trace Elements	***Currently in Shortage***
Triamcinolone Hexacetonide Injectable Suspension (Aristospan)	***Currently in Shortage***
Trimipramine Maleate (SURMONTIL) Capsules	***Currently in Shortage***
Vancomycin Hydrochloride for Injection, USP	***Currently in Shortage***