Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
May 9, 2018

No live May meeting. May is a packet only meeting.

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 (DUR) Board Members

FROM: Bethany Holderread, Pharm.D.

SUBJECT: Packet Contents for Board Packet – May 9th, 2018

DATE: April 30, 2018

Enclosed are the following items related to the May meeting.
Material is arranged in order of the agenda.

DUR Board Meeting Minutes – Appendix A

Update on Medication Coverage Authorization Unit/2018 Spring Pipeline Update – Appendix B

Annual Review of Anti-Parasitic Medications and 30-Day Notice to Prior Authorize Benznidazole – Appendix C

Annual Review of Bowel Preparation Medications and 30-Day Notice to Prior Authorize Clenpiq™ (Sodium Picosulfate/Magnesium Oxide/Anhydrous Citric Acid) – Appendix D

Annual Review of Otic Anti-Infective Medications and 30-Day Notice to Prior Authorize Otiprio® (Ciprofloxacin Otic Suspension) – Appendix E

Annual Review of Granulocyte Colony-Stimulating Factors (G-CSFs) – Appendix F

Annual Review of Elaprase® (Idursulfase) – Appendix G

Annual Review of Kuvan® (Sapropterin) – Appendix H

Annual Review of Ophthalmic Anti-Inflammatories – Appendix I

Annual Review of Topical Acne Products – Appendix J

Industry News and Updates – Appendix K

U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates – Appendix L

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
May 9, 2018

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

AGENDA

Discussion on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

1. DUR Board Meeting Minutes – See Appendix A

A. April 11, 2018 DUR Minutes
B. April 11, 2018 DUR Recommendations Memorandum

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

2. Update on Medication Coverage Authorization Unit/2018 Spring Pipeline Update – See Appendix B

A. Medication Coverage Activity for April 2018
B. Pharmacy Help Desk Activity for April 2018
C. 2018 Spring Pipeline Update

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

3. Annual Review of Anti-Parasitic Medications and 30-Day Notice to Prior Authorize Benznidazole – See Appendix C

A. Current Prior Authorization Criteria
B. Utilization of Anti-Parasitic Medications
C. Prior Authorization of Anti-Parasitic Medications
D. Chagas Disease Background Information
E. Benznidazole Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Anti-Parasitic Medications

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

4. Annual Review of Bowel Preparation Medications and 30-Day Notice to Prior Authorize Clenpiq™ (Sodium Picosulfate/Magnesium Oxide/Anhydrous Citric Acid) – See Appendix D

A. Current Prior Authorization Criteria
B. Utilization of Bowel Preparation Medications
C. Prior Authorization of Bowel Preparation Medications
D. Market News and Updates
E. Clenpiq™ (Sodium Picosulfate/Magnesium Oxide/Anhydrous Citric Acid) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Bowel Preparation Medications

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

5. Annual Review of Otic Anti-Infective Medications and 30-Day Notice to Prior Authorize Otiprio® (Ciprofloxacin Otic Suspension) – See Appendix E

A. Current Prior Authorization Criteria
B. Utilization of Otic Anti-Infective Medications
C. Prior Authorization of Otic Anti-Infective Medications
D. Market News and Updates
E. Otiprio® (Ciprofloxacin Otic Suspension) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Otic Anti-Infective Medications

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

6. Annual Review of Granulocyte Colony-Stimulating Factors (G-CSFs) – See Appendix F

A. Current Prior Authorization Criteria
B. Utilization of G-CSFs
C. Prior Authorization of G-CSFs
D. Market News and Updates
E. College of Pharmacy Recommendations
F. Utilization Details of G-CSFs

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

7. Annual Review of Elaprase® (Idursulfase) – See Appendix G

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Elaprase® (Idursulfase)
D. Prior Authorization of Elaprase® (Idursulfase)
E. Market News and Updates
F. College of Pharmacy Recommendations

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

8. Annual Review of Kuvan® (Sapropterin) – See Appendix H

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Kuvan® (Sapropterin)
D. Prior Authorization of Kuvan® (Sapropterin)
E. Market News and Updates
F. College of Pharmacy Recommendations
G. Utilization Details of Kuvan® (Sapropterin)

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

9. Annual Review of Ophthalmic Anti-Inflammatories – See Appendix I

A. Current Prior Authorization Criteria
B. Utilization of Ophthalmic Anti-Inflammatories
C. Prior Authorization of Ophthalmic Anti-Inflammatories
D. Market News and Updates
E. College of Pharmacy Recommendations
F. Utilization Details of Ophthalmic Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)
G. Utilization Details of Ophthalmic Corticosteroids

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

10. Annual Review of Topical Acne Products – See Appendix J

A. Current Prior Authorization Criteria
B. Utilization of Topical Acne Products
C. Prior Authorization of Topical Acne Products
D. Market News and Updates
E. College of Pharmacy Recommendations
F. Utilization Details of Topical Acne Products

Non-Presentation; Questions Only:

11. Industry News and Updates – See Appendix K

A. Introduction
B. News and Updates

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

12. U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates – See Appendix L

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

13. Future Business* (Upcoming Product and Class Reviews)

A. ADHD and Narcolepsy Medications
B. Atypical Antipsychotic Medications
C. Various Special Formulations
D. Vesicular Monoamine Transporter-2 (VMAT-2) Inhibitors
E. Lung Cancer Medications
F. Prostate Cancer Medications
G. Crysvita® (Burosumab-twza)

**Future business subject to change.*

14. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF APRIL 11, 2018

BOARD MEMBERS:	PRESENT	ABSENT
Stephen Anderson, Pharm.D.		x
Theresa Garton, M.D.	x	
Carla Hardzog-Britt, M.D.		x
Anetta Harrell, Pharm.D.		x
Ashley Huddleston, Pharm.D., BCOP	x	
John Muchmore, M.D., Ph.D.; Chairman	x	
Lee Munoz, Pharm.D.		x
James Osborne, Pharm.D.	x	
Paul Louis Preslar, D.O., MBA; Vice Chairman	x	
Bruna Varalli-Claypool, MHS, PA-C	x	

COLLEGE OF PHARMACY STAFF:	PRESENT	ABSENT
Terry Cothran, D.Ph.; Pharmacy Director	x	
Melissa Abbott, Pharm.D.; Clinical Pharmacist	x	
Michyla Adams, Pharm.D.; Clinical Pharmacist	x	
Wendi Chandler, Pharm.D.; Clinical Pharmacist	x	
Karen Egesdal, D.Ph.; SMAC-ProDUR Coordinator/OHCA Liaison	x	
Erin Ford, Pharm.D.; Clinical Pharmacist		x
Thomas Ha, 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
Timothy Pham, Ph.D.; Postdoctoral Research Fellow	x	
Leslie Robinson, D.Ph.; PA Coordinator		x
Sarah Schmidt, Pharm.D., BCPS, BCOP; Clinical Assistant Professor	x	
Ashley Teel, Pharm.D.; Clinical Pharmacist	x	
Jacquelyn Travers, Pharm.D.; Practice Facilitating Pharmacist		x
Graduate Students: Christina Bulkley, Pharm.D.		x
Laura Tidmore, Pharm.D.	x	
Corby Thompson, Pharm.D.		x
Visiting Pharmacy Student(s): N/A		

OKLAHOMA HEALTH CARE AUTHORITY STAFF:	PRESENT	ABSENT
Melody Anthony, Deputy State Medicaid Director		x
Marlene Asmussen, R.N.; Population Care Management Director	x	
Burl Beasley, D.Ph.; M.P.H.; M.S. Pharm.; Assistant Pharmacy Director	x	
Kelli Brodersen, Marketing Coordinator		x
Robert Evans, M.D.; Sr. Medical Director		x
Michael Herndon, D.O.; Chief Medical Officer		x
Nancy Nesser, Pharm.D.; J.D.; Pharmacy Director	x	
Thomas Nunn, D.O.; Medical Director	x	
Rebecca Pasternik-Ikard, J.D.; M.S.; R.N.; State Medicaid Director; CEO		x
Jill Ratterman, D.Ph.; Clinical Pharmacist	x	
Garth Splinter, M.D.; M.B.A.; Deputy Chief Executive Officer		x
Joseph Young, J.D.; Deputy General Counsel IV	x	
Kerri Wade, Pharmacy Operations Manager	x	

OTHERS PRESENT:		
Jon Maguire, GSK	Jeff Knappen, Spark Therapeutics	Rei Nakamura, Spark Therapeutics
Trebla Grant, Kite	Nima Nabavi, Novo Nordisk	Matt Forney, Merck
Jim Chapman, AbbVie	Quynh Doan, AbbVie	Marc Parker, Sunovion
Jim Dunlap, PhRma	Cris Valladares, Celgene	Scott Poole, Intersect ENT
Brent Hildebrand, Gilead	Aaron Shaw, BI	Brian Maves, Pfizer
Bob Atkins, Biogen	Amber Schrantz, Lilly	Terry McCurren, Otsuka America
Melvin Nwamadi, Abbott	Erica Brumleve, GSK	

PRESENT FOR PUBLIC COMMENT:	
Rei Nakamura	Spark Therapeutics

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 ITEM NO. 6 SPEAKER: REI NAKAMURA

ACTION: NONE REQUIRED

AGENDA ITEM NO. 3: APPROVAL OF DUR BOARD MEETING MINUTES

3A: MARCH 14, 2018 DUR MINUTES – VOTE

3B: MARCH 14, 2018 DUR RECOMMENDATIONS MEMORANDUM

3C: CORRESPONDENCE

Materials included in agenda packet; presented by Dr. Cothran

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/METOCLOPRAMIDE (REGLAN®) INDUCED TARDIVE DYSKINESIA SAFETY MAILING UPDATE

4A: MEDICATION COVERAGE ACTIVITY FOR MARCH 2018

4B: PHARMACY HELP DESK ACTIVITY FOR MARCH 2018

4C: METOCLOPRAMIDE (REGLAN®) INDUCED TARDIVE DYSKINESIA SAFETY MAILING UPDATE

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: VOTE TO PRIOR AUTHORIZE OCREVUS™ (OCRELIZUMAB)

5A: INTRODUCTION

5B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Holderread

Dr. Garton moved to approve; seconded by Dr. Huddleston

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: VOTE TO PRIOR AUTHORIZE LUXTURNA™ (VORETIGENE NEPARVOVEC-RZYL)

6A: INTRODUCTION

6B: OTHER AAV2 CLINICAL STUDIES

6C: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Adams

The board recommended the addition of the following to the criteria: A prior authorization request with patient-specific information may be submitted for consideration of Luxturna™ for members not meeting all of the current prior authorization criteria requirements.

Dr. Preslar moved to approve; seconded by Dr. Garton
ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: VOTE TO PRIOR AUTHORIZE PROLASTIN®-C LIQUID [ALPHA$_1$-PROTEINASE INHIBITOR (HUMAN)]
7A: INTRODUCTION
7B: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Chandler
Dr. Garton moved to approve; seconded by Ms. Varalli-Claypool
ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: VOTE TO PRIOR AUTHORIZE ARZERRA® (OFATUMUMAB), GAZYVA® (OBINUTUZUMAB), IMBRUVICA® (IBRUTINIB), VENCLEXTA™ (VENETOCLAX), AND ZYDELIG® (IDELALISIB)
8A: INTRODUCTION
8B: RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Schmidt
Dr. Huddleston moved to approve; seconded by Ms. Varalli-Claypool
ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: ANNUAL REVIEW OF THE SOONERCARE PHARMACY BENEFIT
9A: SUMMARY
9B: MEDICAID DRUG REBATE PROGRAM
9C: ALTERNATIVE PAYMENT MODELS
9D: DRUG APPROVAL TRENDS
9E: TRADITIONAL VERSUS SPECIALTY PHARMACY PRODUCTS
9F: TOP 10 THERAPEUTIC CLASSES BY REIMBURSEMENT
9G: TOP 10 MEDICATIONS BY REIMBURSEMENT
9H: COST PER CLAIM
9I: CONCLUSION
9J: TOP 100 REIMBURSED DRUGS BY FISCAL YEAR
9K: TOP 50 MEDICATIONS BY TOTAL NUMBER OF CLAIMS
9L: TOP 10 TRADITIONAL AND SPECIALTY THERAPEUTIC CLASSES BY FISCAL YEAR
Materials included in agenda packet; presented by Dr. Holderread
ACTION: NONE REQUIRED

AGENDA ITEM NO. 10: HEPATITIS C MEDICATION CRITERIA UPDATE
10A: INTRODUCTION
10B: UTILIZATION OF HEPATITIS C MEDICATIONS
10C: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Holderread
Dr. Preslar moved to approve; seconded by Ms. Varalli-Claypool
ACTION: MOTION CARRIED

AGENDA ITEM NO. 11: ANNUAL REVIEW OF BENLYSTA® (BELIMUMAB)
11A: CURRENT PRIOR AUTHORIZATION CRITERIA
11B: UTILIZATION OF BENLYSTA® (BELIMUMAB)
11C: PRIOR AUTHORIZATION OF BENLYSTA® (BELIMUMAB)
11D: MARKET NEWS AND UPDATES
11E: COLLEGE OF PHARMACY RECOMMENDATIONS
11F: UTILIZATION DETAILS OF BENLYSTA® (BELIMUMAB)
Materials included in agenda packet; presented by Dr. Adams
Dr. Huddleston moved to approve; seconded by Ms. Varalli-Claypool
ACTION: MOTION CARRIED

AGENDA ITEM NO. 12: **ANNUAL REVIEW OF DIABETES MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ADMELOG® (INSULIN LISPRO), FIASP® (INSULIN ASPART), HUMULIN® R U-500 VIALS (INSULIN HUMAN 500 UNITS/ML), OZEMPIC® (SEMAGLUTIDE), STEGLATRO™ (ERTUGLIFLOZIN), SEGLUROMET™ (ERTUGLIFLOZIN/METFORMIN), AND STEGLUJAN™ (ERTUGLIFLOZIN/SITAGLIPTIN)**

12A: CURRENT PRIOR AUTHORIZATION CRITERIA
12B: UTILIZATION OF DIABETES MEDICATIONS
12C: PRIOR AUTHORIZATION OF DIABETES MEDICATIONS
12D: MARKET NEWS AND UPDATES
12E: ADMELOG® (INSULIN LISPRO) PRODUCT SUMMARY
12F: FIASP® (INSULIN ASPART) PRODUCT SUMMARY
12G: OZEMPIC® (SEMAGLUTIDE) PRODUCT SUMMARY
12H: STEGLATRO™ (ERTUGLIFLOZIN) PRODUCT SUMMARY
12I: SEGLUROMET™ (ERTUGLIFLOZIN/METFORMIN) PRODUCT SUMMARY
12J: STEGLUJAN™ (ERTUGLIFLOZIN/SITAGLIPTIN) PRODUCT SUMMARY
12K: COLLEGE OF PHARMACY RECOMMENDATIONS
12L: UTILIZATION DETAILS OF NON-INSULIN DIABETES MEDICATIONS
12M: UTILIZATION DETAILS OF INSULIN MEDICATIONS

Materials included in agenda packet; presented by Dr. Chandler
ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: **ANNUAL REVIEW OF ANTIHYPERTENSIVE MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE PREXXARTAN® (VALSARTAN ORAL SOLUTION), TEKTURNA® (ALISKIREN ORAL PELLETS), AND CAROSPIR® (SPIRONOLACTONE ORAL SUSPENSION)**

13A: CURRENT PRIOR AUTHORIZATION CRITERIA
13B: UTILIZATION OF ANTIHYPERTENSIVE MEDICATIONS
13C: PRIOR AUTHORIZATION OF ANTIHYPERTENSIVE MEDICATIONS
13D: MARKET NEWS AND UPDATES
13E: PREXXARTAN® (VALSARTAN ORAL SOLUTION) PRODUCT SUMMARY
13F: TEKTURNA® (ALISKIREN ORAL PELLETS) PRODUCT SUMMARY
13G: CAROSPIR® (SPIRONOLACTONE ORAL SUSPENSION) PRODUCT SUMMARY
13H: COLLEGE OF PHARMACY RECOMMENDATIONS
13I: UTILIZATION DETAILS OF ANTIHYPERTENSIVE MEDICATIONS

Materials included in agenda packet; presented by Dr. Abbott
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: **INDUSTRY NEWS AND UPDATES**

14A: INTRODUCTION
14B: NEWS AND UPDATES

Materials included in agenda packet; Non-presentation; Questions only
ACTION: NONE REQUIRED

AGENDA ITEM NO. 15: **U.S. FOOD AND DRUG ADMINISTRATION (FDA) AND DRUG ENFORCEMENT ADMINISTRATION (DEA) UPDATES**

Materials included in agenda packet; presented by Dr. Cothran
ACTION: NONE REQUIRED

AGENDA ITEM NO. 16: **FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)**
NO LIVE MEETING SCHEDULED FOR MAY. MAY WILL BE PACKET ONLY MEETING.

16A: OTIC ANTI-INFECTIVE MEDICATIONS
16B: ELAPRASE® (IDURSULFASE)
16C: KUVAN® (SAPROPTERIN)
16D: GRANULOCYTE COLONY STIMULATING FACTORS (G-CSFs)
16E: OPHTHALMIC ANTI-INFLAMMATORIES
16F: ANTI-PARASITIC MEDICATIONS

16G: BOWEL PREPARATION MEDICATIONS

FUTURE BUSINESS SUBJECT TO CHANGE

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 17: ADJOURNMENT

The meeting was adjourned at 5:17 PM

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

Memorandum

Date: April 12, 2018

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

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

Subject: Drug Utilization Review (DUR) Board Recommendations from Meeting of April 11, 2018

Recommendation 1: Metoclopramide (Reglan®) Induced Tardive Dyskinesia Safety Mailing Update

NO ACTION REQUIRED.

Recommendation 2: Vote to Prior Authorize Ocrevus™ (Ocrelizumab)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Ocrevus™ (ocrelizumab) with the following criteria:

Ocrevus™ (Ocrelizumab) Approval Criteria:

1. An FDA approved diagnosis of relapsing or primary progressive forms of Multiple Sclerosis (MS); and
2. Approvals will not be granted for concurrent use with other disease modifying therapies; and
3. Ocrevus™ must be administered in a setting with appropriate equipment and personnel to manage anaphylaxis or serious infusion reactions. The prescriber must agree that the member will be monitored for one hour after each infusion; and

4. Prescriber must verify hepatitis B virus (HBV) testing has been performed prior to initiating Ocrevus™ therapy and member does not have active HBV; and
5. Verification from the prescriber that member has no active infection(s); and
6. Verification from the prescriber that female members are not currently pregnant and will use contraception while receiving Ocrevus™ therapy and for six months after the last infusion of Ocrevus™; and
7. Compliance will be checked for continued approval.

Recommendation 3: Vote to Prior Authorize Luxturna™ (Voretigene Neparvovec-rzyl)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Luxturna™ (voretigene neparvovec-rzyl) with the following criteria with changes noted in red based on recommendations by the DUR Board:

Luxturna™ (Voretigene Neparvovec-rzyl) Approval Criteria:

1. An FDA approved diagnosis of biallelic *RPE65* mutation-associated retinal dystrophy; and
    a. Diagnosis must be confirmed by genetic testing; and
2. Member must have sufficient viable retinal cells in both eyes as determined by the treating physician(s); and
3. Member must have best corrected visual acuity of 20/60 or worse in both eyes and/or visual field less than 20 degrees in any meridian in both eyes; and
4. Member must be four years of age or older; and
5. Member must not have participated in a previous *RPE65* gene therapy study or have previously received treatment with Luxturna™; and
6. ~~Member must not have used high-dose retinoid compounds (>7,500 retinal equivalent units or >3,300 IU per day of vitamin A) in the past 18 months; and~~
7. Member must not have had intraocular surgery in the past 6 months; and
8. Female members of child bearing age must not be pregnant and must have a negative pregnancy test immediately prior to administration of Luxturna™; and
9. Male and female members of child bearing age must be willing to use effective contraception during treatment with Luxturna™ and for at least 4 months after administration of Luxturna™; and
10. Member must take the recommended systemic oral corticosteroid regimen, starting 3 days prior to administration of Luxturna™ to each eye, and continuing after administration of Luxturna™, as per package labeling of Luxturna™; and
11. Luxturna™ must be prescribed and administered by a retinal surgeon with expertise in the treatment of biallelic *RPE65* mutation-associated retinal dystrophy and in the administration of Luxturna™ at an Ocular Gene Therapy Treatment Center; and
    a. Luxturna™ must be shipped via cold chain supply shipping and delivery to the Ocular Gene Therapy Treatment Center where the member is scheduled to receive treatment; and
    b. Luxturna™ must be stored frozen prior to preparation for administration (Luxturna™ should be administered within 4 hours of preparation); and

c. The receiving facility must have in place a mechanism to track patient-specific Luxturna™ from receipt to storage to administration; and

12. Luxturna™ must be administered subretinally to each eye on separate days within a close interval, but no fewer than 6 days apart; and
    a. The scheduled procedure date for each eye must be provided; and
13. Only one single-dose vial per eye will be approved per member per lifetime; and
    a. Each single-dose vial of Luxturna™ is to be dispensed immediately prior to the scheduled procedure for the specific eye.
14. A prior authorization request with patient-specific information may be submitted for consideration of Luxturna™ for members not meeting all of the current prior authorization criteria requirements.

Recommendation 4: Vote to Prior Authorize Prolastin®-C Liquid [Alpha$_1$-Proteinase Inhibitor (Human)]

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Prolastin®-C Liquid [alpha$_1$-proteinase inhibitor (human)] with the following criteria:

Prolastin®-C Liquid [Alpha$_1$-Proteinase Inhibitor (Human)] Approval Criteria:

1. An FDA approved indication for augmentation and maintenance therapy of patients 18 years of age or older with severe hereditary deficiency of alpha$_1$-antitrypsin (AAT) with clinical evidence of emphysema; and
2. Diagnosis confirmed by all of the following:
   a. Genetic confirmation of PiZZ, PiZ(null) or Pi(null, null) phenotype alpha$_1$-antitrypsin deficiency (AATD) or other alleles determined to increase risk of AATD; and
   b. Serum levels of AAT less than 11µmol/L; and
   c. Documented emphysema with airflow obstruction; and
3. Prescriber must document that member's forced expiratory volume in one second (FEV_1) is less than or equal to 65% predicted; and
4. Must be prescribed by a pulmonary disease specialist or advanced care practitioner specializing in pulmonary disease; and
5. The prescriber must verify the member is a non-smoker; and
6. The prescriber must verify the member does not have antibodies to IgA; and
7. A patient-specific, clinically significant reason why the member cannot use Prolastin®-C, Aralast NP™, Glassia®, and Zemaira®; and
8. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling.

The College of Pharmacy also recommends adding Zemaira® to the current Aralast NP™ and Glassia® criteria based on net cost after rebates.

Aralast NP™, ~~and~~ Glassia®, and Zemaira® [Alpha$_1$-Proteinase Inhibitor (Human)] Approval Criteria:

1. An FDA approved indication for augmentation and maintenance therapy of patients 18 years of age or older with severe hereditary deficiency of alpha$_1$-antitrypsin (AAT) with clinical evidence of emphysema; and
2. Diagnosis confirmed by all of the following:
   a. Genetic confirmation of PiZZ, PiZ(null) or Pi(null, null) phenotype alpha$_1$-antitrypsin deficiency (AATD) or other alleles determined to increase risk of AATD; and
   b. Serum levels of AAT less than 11µmol/L; and
   c. Documented emphysema with airflow obstruction; and
3. Prescriber must document that member's forced expiratory volume in one second (FEV_1) is less than or equal to 65% predicted; and
4. Must be prescribed by a pulmonary disease specialist or advanced care practitioner specializing in pulmonary disease; and
5. The prescriber must verify the member is a non-smoker; and
6. The prescriber must verify the member does not have antibodies to IgA; and
7. A patient-specific, clinically significant reason why the member cannot use Prolastin®-C; and
8. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling.

Recommendation 5: Vote to Prior Authorize Arzerra® (Ofatumumab), Gazyva® (Obinutuzumab), Imbruvica® (Ibrutinib), Venclexta™ (Venetoclax), and Zydelig® (Idelalisib)

MOTION CARRIED by unanimous approval.

Arzerra® (Ofatumumab) Approval Criteria [Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) Diagnosis]:

1. As first-line treatment of CLL in combination with chlorambucil or bendamustine; or
2. For relapsed or refractory disease as a single-agent or in combination with fludarabine and cyclophosphamide; or
3. As maintenance therapy as second-line extended dosing following complete or partial response to relapsed or refractory therapy (maximum 2 years).

Arzerra® (Ofatumumab) Approval Criteria [Waldenström's Macroglobulinemia (WM)/Lymphoplasmacytic Lymphoma Diagnosis]:

1. For previously treated disease that does not respond to primary therapy or for progressive or relapsed disease; and
2. As a single-agent or combination therapy; and
3. Member is rituximab-intolerant.

Gazyva® (Obinutuzumab) Approval Criteria [Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) Diagnosis]:

1. In combination with chlorambucil or bendamustine for first-line therapy; or
2. As a single-agent for relapsed or refractory disease.

Gazyva® (Obinutuzumab) Approval Criteria [Follicular Lymphoma (FL) Diagnosis]:

1. Grade 1 or 2 patients with Stage I (≥7cm), contiguous Stage II (≥7cm), noncontiguous Stage II, Stage III, or Stage IV patients (first, second, or subsequent therapy); and
2. In combination with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), CVP (cyclophosphamide, vincristine, and prednisone), or bendamustine; and
3. When used for maintenance therapy a total of 12 doses will be approved.

Gazyva® (Obinutuzumab) Approval Criteria [Gastric or Nongastric Mucosa-Associated Lymphoid Tissue (MALT) Lymphoma, Nodal or Splenic Marginal Zone Lymphoma (MZL) Diagnosis]:

1. As second-line or subsequent therapy in combination with bendamustine; or
2. Maintenance therapy as second-line consolidation or extended dosing in rituximab-refractory patients treated with obinutuzumab and bendamustine for a total of 12 doses.

Imbruvica® (Ibrutinib) Approval Criteria [Follicular Lymphoma (FL) Diagnosis]:

1. A diagnosis of Grade 1 or 2 FL; and
2. As subsequent therapy (third-line or greater) for histologic transformation to non-germinal center diffuse large B-cell lymphoma.

Imbruvica® (Ibrutinib) Approval Criteria [Gastric or Nongastric Mucosa-Associated Lymphoid Tissue (MALT) Lymphoma, Nodal or Splenic Marginal Zone Lymphoma (MZL) Diagnosis]:

1. As second-line or subsequent therapy for refractory or progressive disease.

Imbruvica® (Ibrutinib) Approval Criteria [Chronic Graft-Versus-Host Disease (cGVHD) Diagnosis]:

1. A diagnosis of cGVHD after failure of one or more lines of therapy.

Imbruvica® (Ibrutinib) Approval Criteria [Histologic Transformation of Marginal Zone Lymphoma (MZL) to Diffuse Large B-Cell Lymphoma Diagnosis]:

1. As third-line or greater therapy for patients who have transformed to non-germinal center diffuse large B-cell lymphoma.

Imbruvica® (Ibrutinib) Approval Criteria [Mantle Cell Lymphoma (MCL) Diagnosis]:

1. As second-line or subsequent therapy; and
2. Used as a single-agent or in combination with rituximab or lenalidomide/rituximab.

Imbruvica® (Ibrutinib) Approval Criteria [Diffuse Large B-Cell Lymphoma Diagnosis or Acquired Immunodeficiency Syndrome (AIDS)-Related B-Cell Lymphoma Diagnosis]:

1. A diagnosis of non-germinal center diffuse large B-cell lymphoma; and
2. As second-line or subsequent therapy; and
3. Member is not a candidate for high-dose therapy.

Imbruvica® (Ibrutinib) Approval Criteria [Post-Transplant Lymphoproliferative Disorders Diagnosis]:

1. As second-line and subsequent therapy in patients with partial response, persistent, or progressive disease; and

2. Non-germinal center B-cell type.

Imbruvica® (Ibrutinib) Approval Criteria [Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) Diagnosis]:

1. As first or subsequent therapy for CLL/SLL; and
2. As a single-agent or in combination with bendamustine/rituximab.

Imbruvica® (Ibrutinib) Approval Criteria [Hairy Cell Leukemia Diagnosis]:

1. As a single-agent in patients with indication for treatment for progression.

Imbruvica® (Ibrutinib) Approval Criteria [Waldenström's Macroglobulinemia (WM)/Lymphoplasmacytic Lymphoma Diagnosis]:

1. As first or subsequent therapy; and
2. As a single-agent.

Venclexta™ (Venetoclax) Approval Criteria [Mantle Cell Lymphoma (MCL) Diagnosis]:

1. As second-line or subsequent therapy; and
2. As a single-agent only.

Venclexta™ (Venetoclax) Approval Criteria [Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) Diagnosis]:

1. For relapsed/refractory disease; and
2. In combination with rituximab or as a single-agent.

Zydelig® (Idelalisib) Approval Criteria [Follicular Lymphoma (FL) Diagnosis]:

1. A diagnosis of Grade 1 to 2 FL; and
2. As second-line or subsequent therapy for refractory or progressive disease; and
3. Refractory to both alkylator and rituximab therapy.

Zydelig® (Idelalisib) Approval Criteria [Gastric or Nongastric Mucosa-Associated Lymphoid Tissue (MALT) Lymphoma, Nodal or Splenic Marginal Zone Lymphoma (MZL) Diagnosis]:

1. As second-line or subsequent therapy for refractory or progressive disease; and
2. Refractory to both alkylator and rituximab therapy.

Zydelig® (Idelalisib) Approval Criteria [Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) Diagnosis]:

1. For relapsed or refractory disease; and
2. In combination with rituximab or rituximab/bendamustine; or
3. As a single-agent.

Recommendation 6: Annual Review of the SoonerCare Pharmacy Benefit

NO ACTION REQUIRED.

Recommendation 7: Hepatitis C Medication Criteria Update

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends adding the following criteria to all prior authorized hepatitis C virus (HCV) medications regarding confirmation of chronic HCV infection:

1. Member has chronic HCV infection defined by:
    a. If the member has a liver fibrosis score ≥F1 (METAVIR equivalent) then only one detectable and quantifiable HCV RNA (>15 IU/mL) test within the last 12 months is required; or
    b. If the member has a liver fibrosis score <F1 (METAVIR equivalent) then the following must be met:
        i. Positive (i.e., reactive) HCV antibody test that is at least six months old and has a detectable and quantifiable HCV RNA (>15 IU/mL) test six months after date of positive HCV antibody test; or
        ii. Two detectable and quantifiable HCV RNA (>15 IU/mL) tests at least six months apart.

Recommendation 8: Annual Review of Benlysta® (Belimumab)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the changes shown in red based on the recent U.S. Food and Drug Administration (FDA) approval of the subcutaneous (subQ) formulation of Benlysta® (belimumab):

Benlysta® (Belimumab) Approval Criteria:

1. The intravenous (IV) formulation will be covered as a medical claim only benefit while the subcutaneous (subQ) formulation will be covered as a pharmacy only benefit; and
2. An FDA approved indication of the treatment of adults with active, autoantibody-positive, systemic lupus erythematosus (SLE) already receiving standard therapy; and
3. Documented inadequate response to at least two of the following medications:
    a. High-dose oral corticosteroids; or
    b. Methotrexate; or
    c. Azathioprine; or
    d. Mycophenolate; or
    e. Cyclophosphamide; and
4. Member must not have severe active lupus nephritis or severe active central nervous system lupus; and
5. Benlysta® will not be approved for combination use with biologic therapies or IV cyclophosphamide.

Recommendation 9: Annual Review of Diabetes Medications and 30-Day Notice to Prior Authorize Admelog® (Insulin Lispro), Fiasp® (Insulin Aspart), Humulin® R U-500 Vials (Insulin Human 500 Units/mL), Ozempic® (Semaglutide), Steglatro™ (Ertugliflozin), Segluromet™ (Ertugliflozin/Metformin), and Steglujan™ (Ertugliflozin/Sitagliptin)

NO ACTION REQUIRED.

Recommendation 10: Annual Review of Antihypertensive Medications and 30-Day Notice to Prior Authorize Prexxartan® (Valsartan Oral Solution), Tekturna® (Aliskiren Oral Pellets), and CaroSpir® (Spironolactone Oral Suspension)

NO ACTION REQUIRED.

Recommendation 11: Industry News and Updates

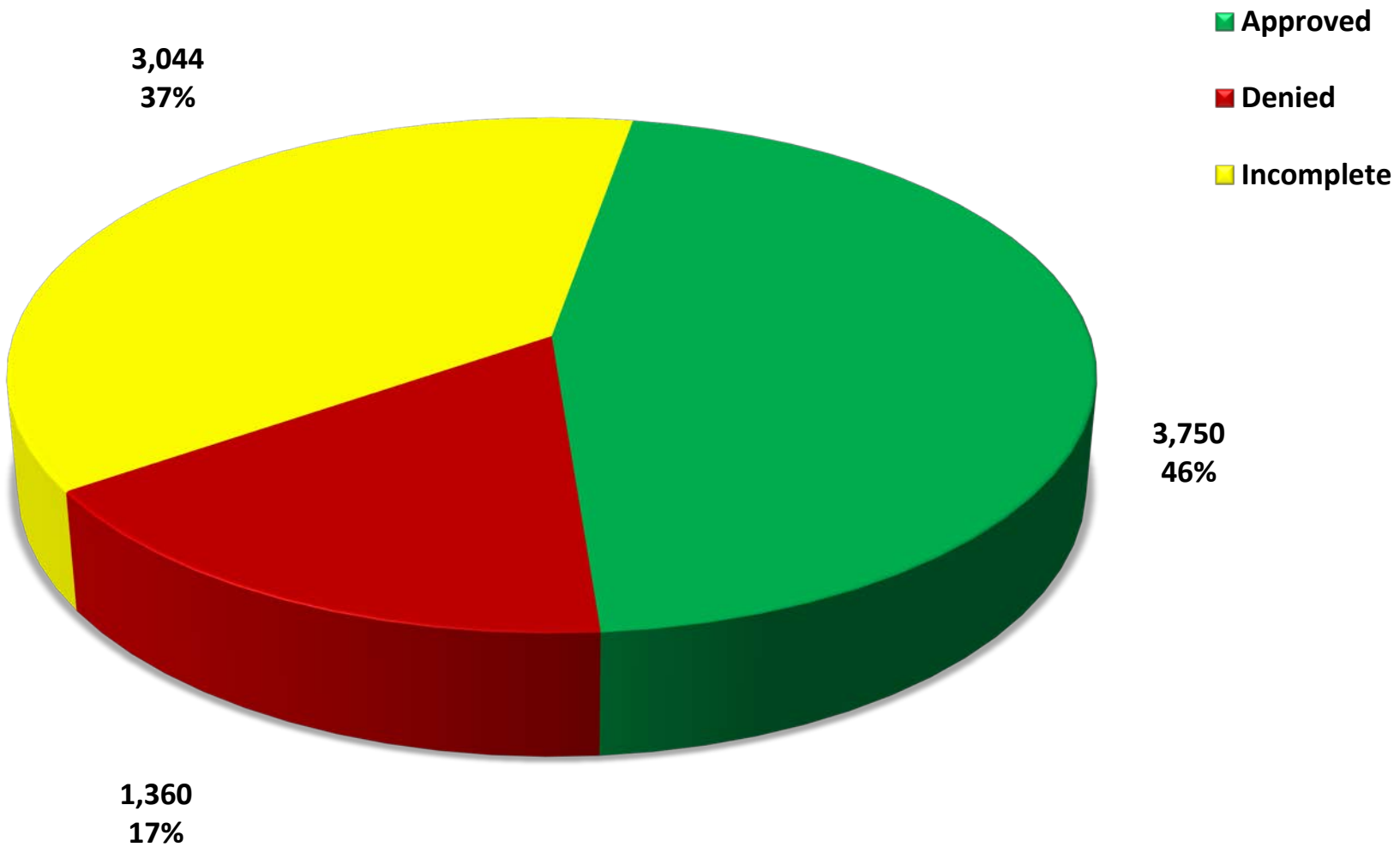
NO ACTION REQUIRED.

Recommendation 12: U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates

NO ACTION REQUIRED.

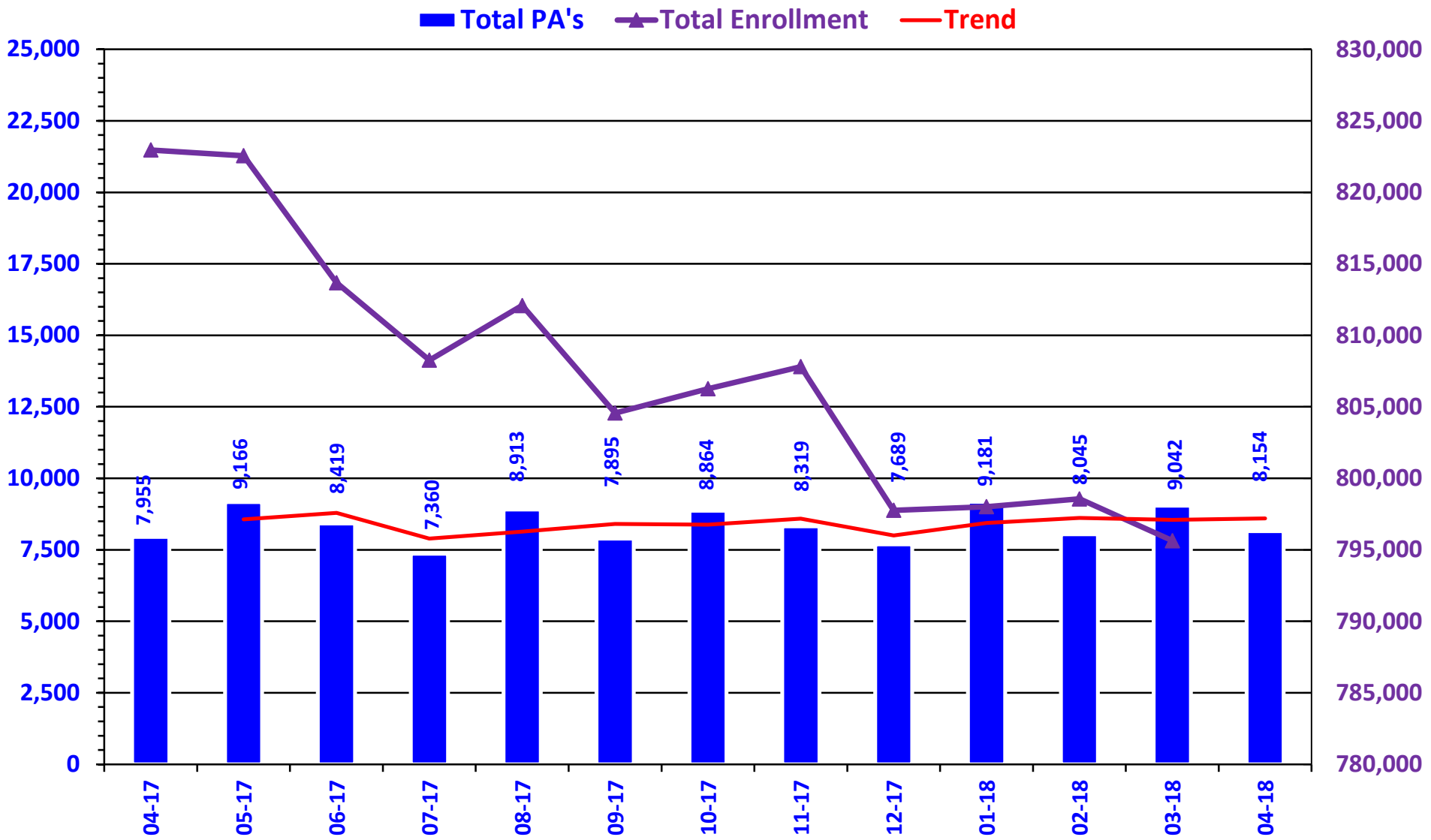
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: APRIL 2018



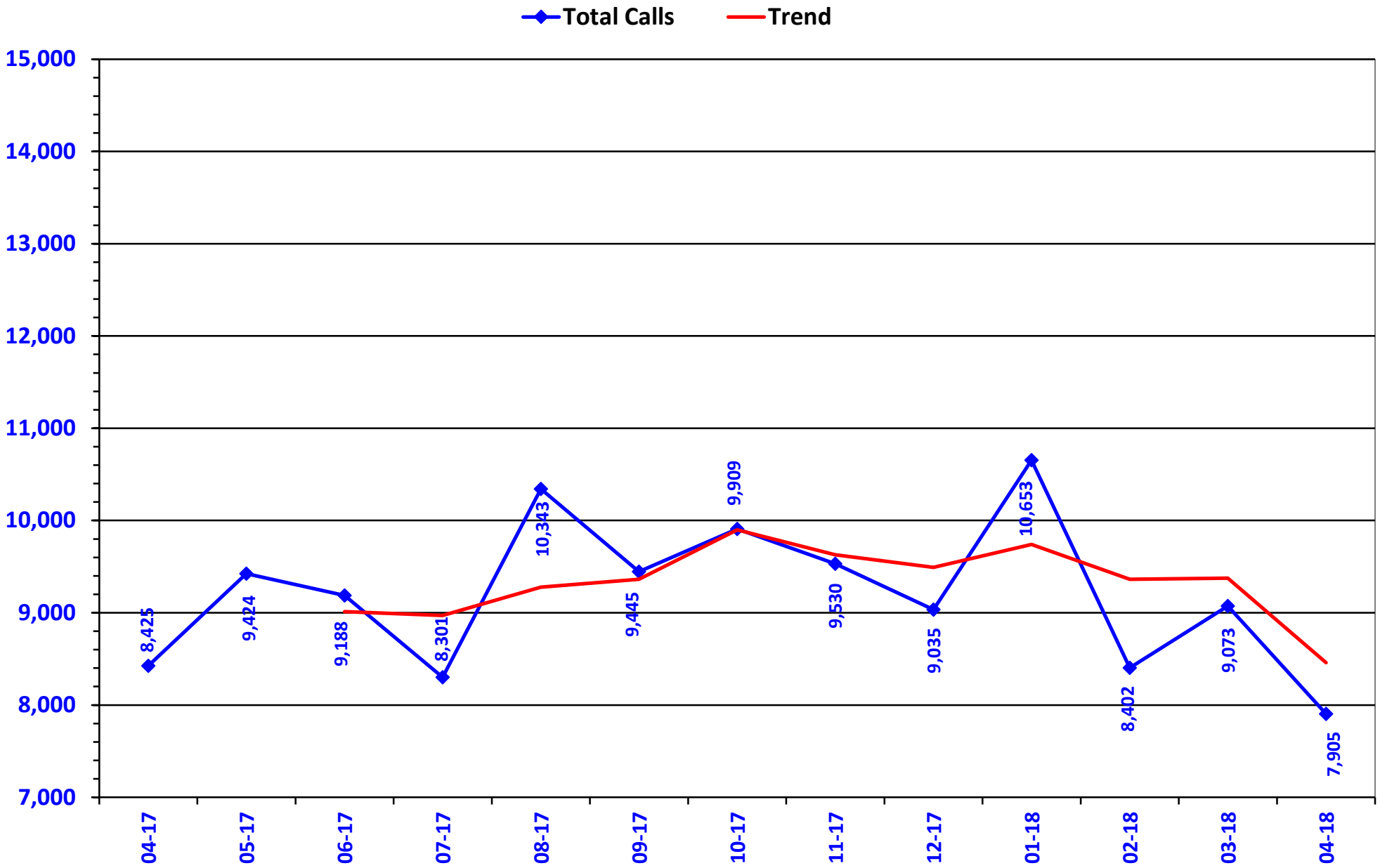
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: APRIL 2017 – APRIL 2018



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
APRIL 2017 – APRIL 2018



Prior Authorization Activity

4/1/2018 Through 4/30/2018

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	184	18	51	115	358
Analgesic - NonNarcotic	33	0	11	22	0
Analgesic - Narcotic	396	198	49	149	159
Angiotensin Receptor Antagonist	18	7	5	6	357
Antiasthma	62	12	20	30	275
Antibiotic	32	13	3	16	202
Anticonvulsant	127	43	19	65	323
Antidepressant	163	43	30	90	313
Antidiabetic	221	81	45	95	354
Antihistamine	29	6	11	12	267
Antimigraine	48	6	19	23	244
Antineoplastic	74	47	9	18	163
Antiparasitic	19	1	5	13	8
Antiulcers	129	37	45	47	151
Anxiolytic	61	35	6	20	294
Atypical Antipsychotics	208	106	33	69	343
Biologics	86	50	13	23	295
Bladder Control	42	14	12	16	357
Blood Thinners	223	139	13	71	339
Botox	49	28	13	8	353
Buprenorphine Medications	406	291	19	96	74
Cardiovascular	122	50	24	48	310
Chronic Obstructive Pulmonary Disease	155	32	40	83	307
Constipation/Diarrhea Medications	162	16	74	72	195
Contraceptive	22	12	2	8	294
Corticosteroid	11	4	1	6	188
Dermatological	300	103	86	111	301
Diabetic Supplies	454	256	20	178	197
Endocrine & Metabolic Drugs	94	71	2	21	131
Erythropoietin Stimulating Agents	17	8	4	5	99
Fibric Acid Derivatives	13	1	5	7	360
Fibromyalgia	218	28	108	82	324
Fish Oils	23	1	8	14	358
Gastrointestinal Agents	119	31	19	69	191
Genitourinary Agents	15	2	6	7	220
Growth Hormones	69	54	5	10	160
Hematopoietic Agents	11	6	1	4	118
Hepatitis C	176	134	8	34	8
HFA Rescue Inhalers	48	3	13	32	353
Insomnia	48	9	13	26	139
Insulin	143	43	22	78	286
Miscellaneous Antibiotics	10	1	2	7	8
Multiple Sclerosis	46	26	5	15	149
Muscle Relaxant	32	4	10	18	109
Nasal Allergy	79	13	29	37	148
Neurological Agents	112	30	36	46	173
Neuromuscular Agents	13	8	3	2	258
NSAIDs	170	17	45	108	218
Ocular Allergy	39	5	14	20	191
Ophthalmic Anti-infectives	15	1	4	10	5

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Osteoporosis	5	2	1	2	355
Other*	325	61	97	167	276
Otic Antibiotic	20	0	5	15	0
Respiratory Agents	39	18	4	17	164
Statins	18	8	6	4	336
Stimulant	705	349	56	300	346
Testosterone	62	18	16	28	357
Topical Antifungal	29	4	7	18	27
Topical Corticosteroids	77	1	32	44	86
Vitamin	78	14	34	30	149
Pharmacotherapy	35	27	0	8	213
Emergency PAs	0	0	0	0	
Total	**6,739**	**2,646**	**1,298**	**2,795**	
Overrides					
Brand	39	25	3	11	303
Compound	16	9	1	6	132
Cumulative Early Refill	3	3	0	0	121
Diabetic Supplies	22	17	0	5	83
Dosage Change	300	280	2	18	13
High Dose	2	2	0	0	113
Ingredient Duplication	13	12	0	1	37
Lost/Broken Rx	97	95	2	0	11
NDC vs Age	269	173	20	76	265
Nursing Home Issue	65	64	0	1	10
Opioid Quantity	25	17	3	5	174
Other	49	45	0	4	9
Quantity vs. Days Supply	532	368	30	134	259
STBS/STBSM	21	16	2	3	67
Stolen	6	5	1	0	12
Third Brand Request	22	19	2	1	40
Overrides Total	**1,415**	**1,104**	**62**	**249**	
Total Regular PAs + Overrides	**8,154**	**3,750**	**1,360**	**3,044**	

Denial Reasons	
Unable to verify required trials.	2,389
Does not meet established criteria.	1,392
Lack required information to process request.	621
Other PA Activity	
Duplicate Requests	567
Letters	9,566
No Process	10
Changes to existing PAs	630
Helpdesk Initiated Prior Authorizations	614
PAs Missing Information	14

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

2018 Spring Pipeline Update

Oklahoma Health Care Authority
May 2018

Introduction

The following report is a pipeline review compiled by the University of Oklahoma College of Pharmacy. Information in this report is focused on medications not yet approved by the U.S. Food and Drug Administration (FDA). The pipeline report is not an all-inclusive list, and medications expected to be highly utilized or have a particular impact in the SoonerCare population have been included for review. Pipeline data is collected from a variety of sources and is subject to change; dates listed are projections and all data presented are for informational purposes only. Costs listed in the following report do not reflect rebated prices or net costs.

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

Anticipated Indication(s): Orally administered gonadotropin-releasing hormone (GnRH) receptor antagonist for the treatment of pain associated with endometriosis and uterine fibroids.

Clinical Trial(s): Elagolix was evaluated in two randomized, double-blind, placebo-controlled Phase 3 clinical studies including a total of 1,700 women with moderate-to-severe endometriosis-associated pain. The data from the Phase 3 studies demonstrated that, at month three and month six, elagolix 150mg once daily and 200mg twice daily resulted in a statistically significant higher proportion of responders for menstrual pain (dysmenorrhea) [150mg: 46.4%; 200mg: 75.8%; placebo: 22.7% (P<0.001 for all comparisons)] and non-menstrual pelvic pain associated with endometriosis as measured by the Daily Endometriosis Pain Impact scale versus placebo [150mg: 50.4%; 200mg: 54.5%; placebo: 36.5% (P<0.001 for all comparisons)]. A reduction in the amount and frequency of rescue pain medication use, including nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids, compared to placebo was also seen in the elagolix higher dose at month three and six. Compared to placebo, women who received elagolix had higher rates of hot flushes, higher levels of serum lipids, and greater decreases from baseline in bone mineral density (BMD); no adverse endometrial findings were found.

Place in Therapy: Endometriosis affects up to 10% of women between 15 to 49 years of age. Current treatments for endometriosis include NSAIDs, progestins, and injectable GnRH agonists. Currently there are several GnRH agonists on the market indicated for the treatment of pain associated with endometriosis [e.g., Lupron Depot® (leuprolide), Lupaneta Pack™ (leuprolide depot/norethindrone tablets), Synarel® (nafarelin), Zoladex® (goserelin)]. Unlike GnRH agonists, elagolix does not suppress ovulation and may have less BMD loss.

Projected FDA Decision: 3rd quarter 2018

SoonerCare Impact: During calendar year 2017, a total of 84 female members 15 to 49 years of age had paid pharmacy claims for GnRH agonists, accounting for 190 claims totaling $415,616.34 in drug spending and an average cost per claim of $2,187.45. Additionally, 336 female members had two or more diagnosis claims for endometriosis during calendar year 2017.

Ulipristal Acetate[1,2,6,7,8,9]

Anticipated Indication(s): Orally administered selective progesterone receptor modulator (SPRM) for the treatment of abnormal uterine bleeding in women with uterine fibroids.

Clinical Trial(s): Ulipristal acetate was evaluated in two Phase 3 randomized, double-blind, placebo-controlled trials. The second Phase 3 trial, Venus II, included 432 United States patients randomized to ulipristal acetate 5mg, 10mg, or placebo. The co-primary efficacy endpoints were percentage of patients with absence of uterine bleeding and time to absence of uterine bleeding on treatment over 12 weeks. Significantly more patients in the 10mg group (54.8%) and the 5mg group (42.0%) achieved absence of bleeding compared to placebo (0%) ($P<0.001$ for all comparisons).

Place in Therapy: An estimated 26 million women between the ages of 15 to 50 years have uterine fibroids in the United States. Current treatments for uterine fibroids include hormonal therapies (e.g., combined hormonal contraceptives, progestins), and injectable GnRH agonists. Currently, Lupron Depot® (leuprolide), a GnRH agonist, is available for use prior to fibroid surgery to improve anemia due to vaginal bleeding from fibroids. Ulipristal acetate is approved outside the United States in Europe and Canada for preoperative therapy and short intermittent courses interrupted by menstruation.

Projected FDA Decision: August 2018

SoonerCare Impact: During calendar year 2017, a total of 84 female members 15 to 49 years of age had paid pharmacy claims for GnRH agonists, accounting for 190 claims totaling $415,616.34 in drug spending and an average cost per claim of $2,187.45. Additionally, 798 female members had two or more diagnosis claims for uterine fibroids during calendar year 2017.

Fremanezumab[1,2,10,11,12,13]

Anticipated Indication(s): Subcutaneously administered calcitonin gene-related peptide (CGRP) ligand antagonist for the prevention of migraines.

Clinical Trial(s): Fremanezumab was evaluated in a 16-week, multicenter, randomized, double-blind, placebo-controlled, parallel-group study with a total of 2,005 patients with episodic migraine (EM) and chronic migraine (CM). A total of 875 patients were assigned to the EM arm, while the CM arm had 1,130 patients. Participants in both studies were randomized into two treatment groups (monthly or quarterly dosing) or placebo. The primary endpoint for the EM study was the mean change from baseline in the average number of migraine days per month, 12 weeks after the first dose was given. The CM study had a similar primary endpoint, except

the average number of headache days was observed, not migraine days. Results of the EM group saw a reduction in monthly migraine days from baseline in both the monthly (-3.7 days, baseline 9.2 days) and quarterly (-3.4 days, baseline 9.1 days) dosing when compared to placebo (-2.2 days, baseline 9.1 days). For the CM group, a reduction in monthly headache days from baseline was also seen for both the monthly (-4.6 days, baseline 12.8 days) and quarterly (-4.3 days, 13.2 days) dosing when compared to placebo (-2.5 days, baseline 13.3 days). In both treatment groups of the trial, a reduction in the number of monthly headache or migraine days were seen when compared to placebo.

Place in Therapy: Migraine is the third most prevalent illness in the world and affects over 1 billion people worldwide. Fremanezumab is a monoclonal antibody that antagonizes the CGRP ligand, which is a target in migraine prevention. Current drug therapies in migraine prevention include beta-blockers, calcium channel blockers, tricyclic antidepressants, selective serotonin reuptake inhibitors, anti-convulsants, serotonin antagonists, and Botox® (onabotulinumtoxinA). Fremanezumab is being studied for once monthly and once quarterly dosing and is expected to be an option for patients who do not respond to conventional migraine prevention medications.

Projected FDA Decision: Mid-2018

SoonerCare Impact: During calendar year 2017, 5,602 members had paid pharmacy claims for triptan medications, accounting for $463,810.76 in drug spending with an average cost of $37.54 per claim.

Epidiolex® (Cannabidiol)[1,2,14,15,16,17,18]

Anticipated Indication(s): A pure plant-derived, orally administered cannabinoid receptor antagonist for adjunctive treatment of seizures associated with Lennox-Gastaut syndrome (LGS) and Dravet syndrome.

Clinical Trial(s): Cannabidiol was evaluated in a 14-week, randomized, double-blind, placebo-controlled, Phase 3 trial with 120 patients 2 to 18 years of age with uncontrolled Dravet syndrome. Patients were randomly assigned to add either cannabidiol or placebo to their current drug regimen. Results of the trial saw a decrease of monthly convulsive seizures by 38.9% (12.4 to 5.9 seizures) in the treatment group compared to 13.3% (14.9 to 14.1 seizures) in the placebo group. Common adverse events seen in this trial included somnolence, loss of appetite, and diarrhea. Cannabidiol was also evaluated in patients with LGS in a 14-week, randomized, double-blind, placebo-controlled Phase 3 trial. Patients 2 to 55 years of age were randomized to either receive 20mg/kg of cannabidiol or placebo with their current drug regimen. The primary efficacy endpoint was the percent change from baseline in the monthly number of drop seizures during the treatment period. Cannabidiol showed a greater median percent reduction in the number of monthly drop seizures when compared to placebo (43.9% vs. 21.8%). In this trial, cannabidiol was seen to be efficacious in reducing the number of drop seizures and was also well tolerated.

Place in Therapy: LGS is a rare seizure disorder that typically occurs in children 3 to 5 years of age and accounts for only 2 to 5% of childhood epilepsies. Dravet syndrome is a rare genetic dysfunction of the brain that causes seizures in the first year of life. While there are limited treatments for LGS, there are no FDA-approved treatments for Dravet syndrome. For LGS, valproic acid is usually considered first-line therapy and is commonly given as monotherapy initially. If valproic acid is ineffective, other anti-epileptic drugs such as clobazam, lamotrigine, and topiramate are given. In Dravet syndrome, valproic acid is also first-line therapy with the addition of clobazam if seizures are poorly controlled. For patients with Dravet syndrome, sodium-channel agents such as carbamazepine and phenytoin should be avoided due to potential exacerbation of seizures. The limited number of treatments available for these two rare diseases may make cannabidiol an effective option for use in conjunction with current therapies to help reduce the number of seizures.

Projected FDA Decision: June 27, 2018

SoonerCare Impact: During calendar year 2017, 108 unique members had a diagnosis claim for LGS. No specific diagnosis code is available for Dravet syndrome; during calendar year 2017, no members had diagnosis claims for related diagnosis codes commonly used for Dravet syndrome.

Pipeline Table[1,2,19]

Medication Name*	Manufacturer	Therapeutic Use	Route of Admin	Approval Status	Anticipated FDA Response
eptacog beta	LFB Group	hemophilia A or B	IV	Filed BLA	Pending
lofexidine	US WorldMeds	opioid dependence	PO	Filed NDA	Pending
Ryplazim™ (human plasminogen)	Prometic/Hematech	hypoplasmino-genemia	IV	Filed BLA	Pending
rizatriptan film	IntelGenx	acute migraines	SL	Filed NDA	2nd quarter 2018
solifenacin/mirabegron	Astellas	OAB	PO	Filed sNDA	04/28/2018
AndexXa® (andexanet)	Portola	anticoagulant reversal	IV	Filed NDA	05/04/2018
Aimovig™ (erenumab)	Amgen	migraine prevention	SC	Filed BLA	05/17/2018
avatrombopag	Astellas/Dova	thrombocytopenia	PO	Filed NDA	05/21/2018
Cimzia® (certolizumab)	UCB	PSO	SC	Filed sBLA	05/25/2018
meloxicam	Recro Pharma	postsurgical pain	IM, IV	Filed NDA	05/26/2018
pegvaliase	Biomarin	PKU	SC	Filed BLA	05/28/2018
Prolia® (denosumab)	Amgen	glucocorticoid-induced osteoporosis	SC	Filed sBLA	05/28/2018
Consensi™ (celecoxib/amlodipine)	Kitov	HTN/OA	PO	Filed NDA	05/31/2018
baricitinib	Eli Lilly	RA	PO	Filed NDA	Mid-2018
Tbria™ (salmon calcitonin)	Tarsa Therapeutics	osteoporosis	PO	Filed NDA	Mid-2018
moxidectin	Medicines Development for Global Health	parasitic infections	PO	Filed NDA	06/2018
Xeljanz® (tofacitinib)	Pfizer	UC	PO	Filed sNDA	06/2018
fremanezumab	Teva	migraine prevention	SC	Filed BLA	06/15/2018
halobetasol/tazarotene	Valeant	PSO	TOP	Filed NDA	06/18/2018

Medication Name*	Manufacturer	Therapeutic Use	Route of Admin	Approval Status	Anticipated FDA Response
furosemide pump	scPharmaceuticals	CHF	SC	Filed NDA	06/23/2018
plazomicin	Achaogen	complicated UTI	IV	Filed NDA	06/25/2018
Epidiolex® (cannabidiol)	GW Pharmaceuticals	LGS	PO	Filed NDA	06/27/2018
glycopyrronium	Dermira	hyperhidrosis	TOP	Filed NDA	06/30/2018
aripiprazole lauroxil ER	Alkermes	schizophrenia	IV	Filed NDA	06/30/2018
buprenorphine/ samidorphan	Alkermes	MDD	PO	Filed NDA	3rd quarter 2018
clobazam	Aquestive	seizures	PO	Filed NDA	3rd quarter 2018
darunavir/emtracitabine/ cobicstat/tenofovir	Janssen	HIV-1 infection	PO	Filed NDA	3rd quarter 2018
Dupixent® (dupilumab)	Regeneron	asthma	SC	Filed sBLA	3rd quarter 2018
elagolix	AbbVie/Neurocrine	endometriosis	PO	Filed NDA	3rd quarter 2018
galcanezumab	Eli Lilly/Arteaus	migraine prevention	SC	Filed BLA	3rd quarter 2018
inotersen	Ionis	familial amyloid polyneuropathy	SC	Filed NDA	07/06/2018
buprenorphine spray	Insys	acute pain	SL	Filed NDA	07/27/2018
risperidone depot	Indivior	schizophrenia	SC	Filed NDA	07/27/2018
tefenoquine	GlaxoSmithKline	malaria	PO	Filed NDA	07/27/2018
ulipristal acetate	Allergan	uterine fibroids	PO	Filed NDA	08/2018
cyclosporine	Sun	dry eye	IO	Filed NDA	08/01/2018
loteprednol etabonate	Kala	ocular inflammation	IO	Filed NDA	08/24/2018
volanersorsen	Ionis	FCS/lipodystrophy	SC	Filed NDA	08/30/2018
damoctocog alfa pegol	Bayer	hemophilia A	IV	Filed BLA	08/31/2018
dasotraline	Sumitomo Dainippon	ADHD	PO	Filed NDA	08/31/2018
ervacycline	Tetraphase	intra-abdominal infections	IV, PO	Filed NDA	08/31/2018
stannsoporfin	InfaCare	hyperbilirubinemia	IM	Filed NDA	09/04/2018
Nucala® (mepolizumab)	GlaxoSmithKline	COPD	IV, SC	Filed sBLA	09/07/2018
Ruconest® (C_1-esterase inhibitor)	Pharming	HAE prophylaxis	IV	Filed sNDA	09/21/2018
Symjepi® (epinephrine)	Adamis	anaphylaxis	SC	Filed sNDA	09/29/2018
alicaforsen	Atlantic Healthcare/ Ionis	UC	IV, REC	Filed NDA	4th quarter 2018
cyclosporine	Auven Therapeutics	dry eyes	IO	Filed NDA	4th quarter 2018
estradiol/progesterone	TherapeuticsMD	menopause	PO	Filed NDA	4th quarter 2018
halobetasol propionate	Valeant	PSO	TOP	Filed NDA	4th quarter 2018
nestorone/ethinyl estradiol 1 year ring	Allergan	contraception	VG	Filed NDA	4th quarter 2018
patisiran	Alnylam	familial amyloid polyneuropathy	IV	Filed NDA	4th quarter 2018
tecovirimat	SIGA	smallpox	IV, PO	Filed NDA	4th quarter 2018
amisulpride	Acacia	PONV	IV	Filed NDA	10/05/2018
levodopa	Acorda	PD	INH	Filed NDA	10/07/2018
tafenoquine	60 Degrees	malaria prevention	PO	Filed NDA	10/18/2018
doravirine/lamivudine/ tenofovir	Merck	HIV-1 infection	PO	Filed NDA	10/23/2018
oliceridine	Travena	acute pain	IV	Filed NDA	11/02/2018

Medication Name*	Manufacturer	Therapeutic Use	Route of Admin	Approval Status	Anticipated FDA Response
revefenacin	Theravance	COPD	INH	Filed NDA	11/13/2018
migalastat	Amicus	Fabry's disease	PO	Filed NDA	12/14/2018
solriamfetol	Jazz/Aerial	narcolepsy; sleep apnea	PO	Filed NDA	12/20/2018
afamelanotide	Clinuvel	EPP; PLE; vitiligo	SC implant	Filed NDA	Late 2018
lusutrombopag	Shionogi	thrombocytopenia	PO	Filed NDA	Late 2018
cengermin	Dompe	neurotrophic keratitis	IO	Filed BLA	Late 2018
astodrimer sodium	Starpharma	bacterial vaginosis	VG	Filed NDA	Late 2018
ozanimod	Celgene	MS; UC	PO	Filed NDA	Late 2018

NDA = New Drug Application; BLA = Biologic License Application; sBLA = supplemental Biologic License Application; sNDA = supplemental New Drug Application; IV = intravenous; PO = oral; SL = sublingual; SC = subcutaneous; IM = intramuscular; TOP = topical; IO = intraocular; REC = rectal; VG = vaginal; INH = inhaled; OAB = overactive bladder; PSO = psoriasis; PKU = phenylketonuria; HTN = hypertension; OA = osteoarthritis; RA = rheumatoid arthritis; UC = ulcerative colitis; CHF = congestive heart failure; UTI = urinary tract infection; LGS = Lennox-Gastaut syndrome; ER = extended-release; MDD = major depressive disorder; HIV = human immunodeficiency virus; FCS = familial chylomicronemia syndrome; ADHD = attention-deficit/ hyperactivity disorder; COPD = chronic obstructive pulmonary disease; HAE = hereditary angioedema; PONV = postoperative nausea and vomiting; PD = Parkinson's disease; EPP = erythropoietic protoporphyria; PLE = polymorphous light eruption; MS = multiple sclerosis

*Biosimilars and oncology medications excluded from table. Medications known to have received a Complete Response Letter from the FDA that have not resubmitted were excluded.

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Appendix C

Calendar Year 2017 Annual Review of Anti-Parasitic Medications and 30-Day Notice to Prior Authorize Benznidazole

Oklahoma Health Care Authority
May 2018

Current Prior Authorization Criteria

Albenza® (Albendazole) Approval Criteria:

1. A quantity of six tablets will process without prior authorization. For infections requiring additional doses, a prior authorization will need to be submitted and the following criteria will apply:
    a. An FDA approved diagnosis of one of the following:
        i. Treatment of parenchymal neurocysticercosis due to active lesions caused by larval forms of the pork tapeworm, *Taenia solium*; or
        ii. Treatment of cystic hydatid disease of the liver, lung, and peritoneum, caused by the larval form of the dog tapeworm, *Echinococcus granulosus*.

Emverm® (Mebendazole) Approval Criteria:

1. An FDA approved diagnosis of any of the following:
    a. Treatment of *Enterobius vermicularis* (pinworm); or
    b. Treatment of *Trichuris trichiura* (whipworm); or
    c. Treatment of *Ascaris lumbricoides* (roundworm); or
    d. Treatment of *Ancylostoma duodenale* (hookworm); or
    e. Treatment of *Necator americanus* (hookworm); and
2. For the treatment of *Enterobius vermicularis* (pinworm), *Ascaris lumbricoides* (roundworm), *Ancylostoma duodenale* (hookworm), or *Necator americanus* (hookworm), a patient-specific, clinically significant reason why a more cost-effective anthelmintic therapy, such as albendazole or pyrantel pamoate, cannot be used must be provided.
3. The following quantity limits will apply:
    a. *Enterobius vermicularis* (pinworm): 2 tablets per approval
    b. *Trichuris trichiura* (whipworm): 6 tablets per approval
    c. *Ascaris lumbricoides* (roundworm): 6 tablets per approval
    d. *Ancylostoma duodenale* (hookworm): 6 tablets per approval
    e. *Necator americanus* (hookworm): 6 tablets per approval

Impavido® (Miltefosine) Approval Criteria:

1. An FDA approved indication for treatment of:
    a. Visceral leishmaniasis due to *Leishmania donovani*; or
    b. Cutaneous leishmaniasis due to *Leishmania braziliensis*, *Leishmania guyanensis*, or *Leishmania panamensis*; or
    c. Mucosal leishmaniasis due to *Leishmania braziliensis*; and

2. Female members must not be pregnant and must have a negative pregnancy test prior to therapy initiation. Female members must be willing to use effective contraception while on therapy and for five months after completion of therapy; and
3. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling.
4. A quantity limit of 84 capsules per 28 days will apply.

Utilization of Anti-Parasitic Medications: Calendar Year 2017

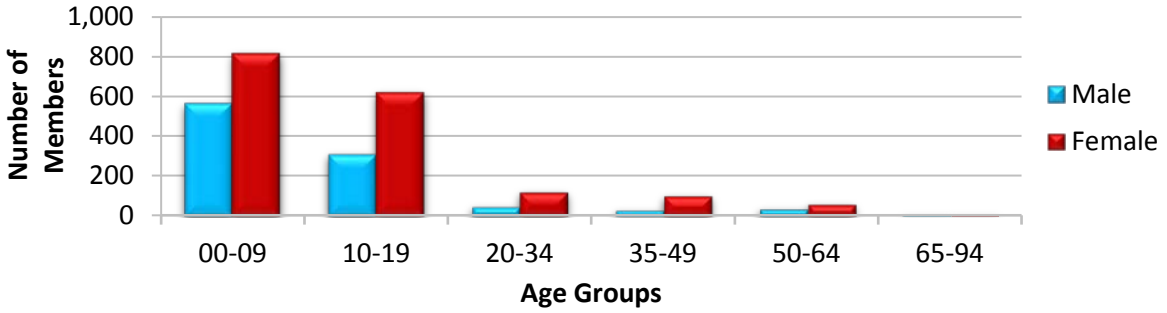
Comparison of Calendar Years

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	2,736	3,303	$1,091,266.69	$330.39	$39.71	15,314	27,484
2017	2,705	3,211	$953,973.65	$297.10	$36.93	12,588	25,830
% Change	**-1.10%**	**-2.80%**	**-12.60%**	**-10.10%**	**-7.00%**	**-17.80%**	**-6.00%**
Change	**-31**	**-92**	**-$137,293.04**	**-$33.29**	**-$2.78**	**-2,726**	**-1,654**

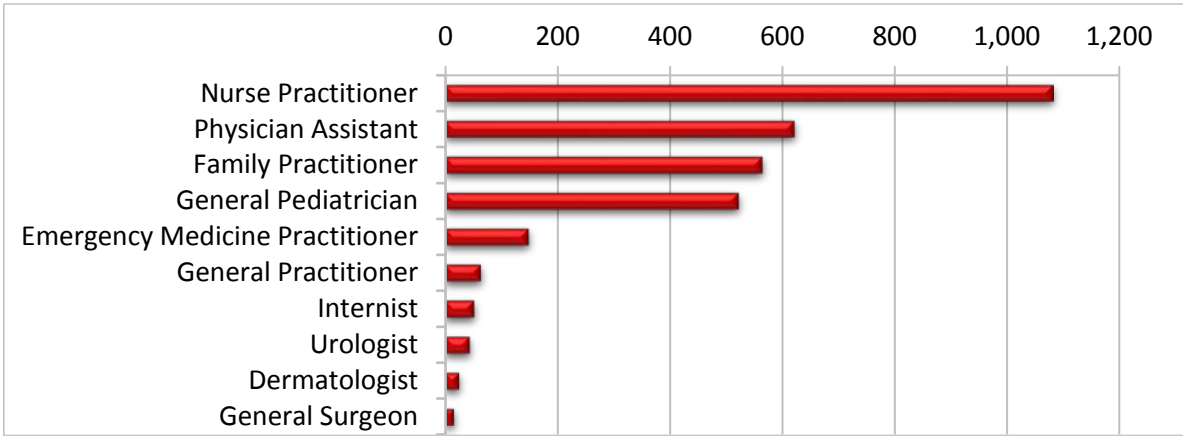
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

- Some of the anti-parasitic medications have significant federal rebates; therefore, costs shown do not reflect net costs.

Demographics of Members Utilizing Anti-Parasitic Medications

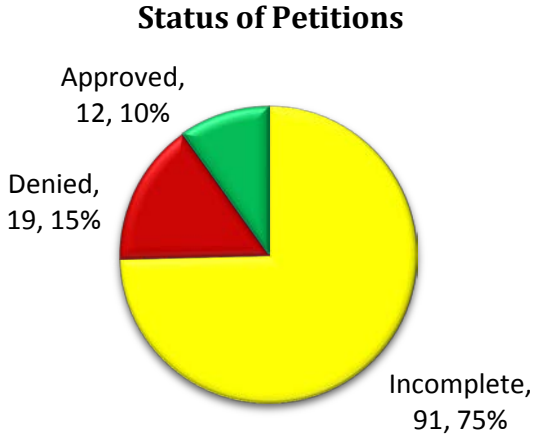


Top Prescriber Specialties of Anti-Parasitic Medications by Number of Claims



Prior Authorization of Anti-Parasitic Medications

There were 122 prior authorization requests submitted for anti-parasitic medications during calendar year 2017. The following chart shows the status of the submitted petitions for calendar year 2017.



Chagas Disease Background Information[1,2,3,4,5]

Chagas disease, also known as American trypanosomiasis, is caused by infection with *Trypanosoma cruzi* (*T. cruzi*), a protozoan parasite. According to the Centers for Disease Control and Prevention (CDC), an estimated 8 million people in Mexico, Central America, and South America have Chagas disease, and most do not know they are infected. The epidemiology of Chagas disease is changing due to migration of individuals within and outside of endemic areas as well as successful programs to reduce transmission in endemic areas. As a result, there are a large number of infected individuals living in Latin America and in the United States, Spain, and other European countries. It is estimated that 300,000 infected immigrants may be living in the United States. The major route of Chagas transmission is vector-borne transmission via infected triatomine bugs. Transmission can also occur from mother to fetus, via transfusion of infected blood components, via transplantation of an organ from an infected donor, via ingestion of contaminated food or drink, or via laboratory exposure.

There are two phases of Chagas disease: acute and chronic. Both phases may be symptom free or life threatening. The acute phase lasts for the first few weeks to months of infection. Typically, the acute phase occurs unnoticed as individuals are symptom free or have only mild signs and symptoms that are not specific to Chagas disease. Symptoms reported by patients include fever, fatigue, body aches, headache, and rash. The most recognized marker of acute Chagas disease is called Romaña's sign, which includes swelling of the eyelid on the side of the face near the bite wound or where the bug feces were accidentally rubbed into the eye or deposited. Even if patients display symptoms during the acute phase, they usually resolve on their own. However, even though the symptoms resolve, if the patient is left untreated the infection persists. Rarely, young children die from myocarditis or meningoencephalitis. The acute phase may also be severe in patients who are immunocompromised. During the chronic phase, the infection remains silent for decades or possibly even for life. However, some

individuals develop cardiac and intestinal complications. The average lifetime risk for developing one or more complications is approximately 30%.

Anti-parasitic treatment is indicated for all cases of acute or reactivated Chagas disease and for chronic *T. cruzi* infection in children up to 18 years of age. Congenital infections are considered acute disease and treatment is warranted in these cases. Treatment is also strongly recommended for adults up to 50 years of age with chronic infection who do not already have advanced Chagas cardiomyopathy. The decision to treat adults older than 50 years of age with chronic *T. cruzi* infection with anti-parasitic medications should be considered on an individual basis, weighing the potential benefits and risks for the patient. The two medications used to treat *T. cruzi* infection are nifurtimox and benznidazole. Benznidazole is approved by the U.S. Food and Drug Administration (FDA) for children 2 to 12 years of age. Nifurtimox is not currently FDA approved. According to the CDC, both medications are available under investigational protocols from the CDC. Benznidazole is expected to become commercially available in 2018, but until it is commercially available, the CDC will continue to provide benznidazole under its existing investigational protocol. Side effects are fairly common with both medications and tend to occur more frequently and are more severe in older patients. In general, benznidazole is better tolerated and is therefore favored as the first-line treatment for Chagas disease.

Benznidazole Product Summary[6,7,8]

FDA Approval: August 2017

Indication(s): Benznidazole is a nitroimidazole antimicrobial indicated in pediatric patients 2 to 12 years of age for the treatment of Chagas disease (American trypanosomiasis), caused by *T. cruzi*.

- This indication was approved under accelerated approval based on the number of treated patients who became Immunoglobulin G (IgG) antibody negative against the recombinant *T. cruzi*. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Dosing:

- Benznidazole is supplied as 100mg and 12.5mg tablets.
- Benznidazole tablets are dosed by body weight. The total daily dose for pediatric patients 2 to 12 years of age is 5mg/kg to 8mg/kg orally administered in two divided doses separated by approximately 12 hours for a duration of 60 days. Please refer to the prescribing information for detailed information on recommended dosage of benznidazole tablets.
- Benznidazole 100mg tablets are functionally scored and can be split into one-half (50mg) or one-quarter (25mg) at the scored lines to provide doses less than 100mg.
- Benznidazole 100mg and 12.5mg tablets can be made into a slurry as an alternative method of administration.

Contraindication(s):

- History of hypersensitivity reaction to benznidazole or other nitroimidazole derivatives

- Disulfiram usage within the last two weeks
- Alcoholic beverage consumption during and for at least three days after therapy

Warnings and Precautions:

- Potential for Genotoxicity and Carcinogenicity: Genotoxicity has been demonstrated in humans, in vitro in several bacterial species and mammalian cell systems, and in vivo in rodents. Carcinogenicity has been observed in mice and rats treated chronically with nitroimidazole agents which are structurally similar to benznidazole. Similar data have not been reported with benznidazole. It is not known whether benznidazole is associated with carcinogenicity in humans.
- Embryo-Fetal Toxicity: Based on findings from animal studies, benznidazole tablets can cause fetal harm when administered to pregnant women. Pregnant women should be advised of the potential risk to a fetus. Pregnancy testing is recommended for females of reproductive potential, and females of reproductive potential should be advised to use effective contraception during treatment with benznidazole tablets and for 5 days after the last dose.
- Hypersensitivity Skin Reactions: Serious skin and subcutaneous disorders including acute generalized exanthematous pustulosis (AGEP), toxic epidermal necrolysis (TEN), erythema multiforme, and eosinophilic drug reaction have been reported with benznidazole. Treatment should be discontinued at the first evidence of these serious cutaneous reactions. Extensive skin reactions, such as rash, have also been reported and most cases occurred after approximately 10 days of treatment with benznidazole. Most rashes resolved following treatment discontinuation. In cases of skin reactions presenting with additional symptoms or signs of systemic involvement such as lymphadenopathy, fever, and/or purpura, it is recommended to discontinue treatment.
- Central and Peripheral Nervous System Effects: Treatment with benznidazole tablets can cause paresthesia or symptoms of peripheral neuropathy that may take several months to resolve. Headache and dizziness have been reported. Immediate discontinuation of treatment is recommended in cases where neurological symptoms occur. In most cases, symptoms occur late in the course of treatment.
- Hematological Manifestations of Bone Marrow Depression: There have been reports of hematological manifestations of bone marrow depression, such as neutropenia, thrombocytopenia, anemia, and leukopenia, which resolved after discontinuation of treatment. Patients with hematological manifestations of bone marrow depression must take benznidazole tablets only under strict medical supervision. Complete blood counts should be monitored. Total and differential leukocyte counts are recommended before, during, and after therapy.

Adverse Reactions: The most common adverse reactions (at least 5% of patients) observed with benznidazole treatment include the following:

- Abdominal pain
- Rash
- Decreased weight
- Headache
- Nausea
- Vomiting
- Neutropenia
- Urticaria
- Pruritus
- Eosinophilia
- Decreased appetite

Use in Specific Populations:

- Pregnancy: Based on findings from animal studies, benznidazole tablets may cause fetal harm when administered to a pregnant woman. Published post-marketing reports on benznidazole use during pregnancy are insufficient to inform a drug-associated risk of adverse pregnancy-related outcomes. There are risks to the fetus associated with Chagas disease. Published data from case-control and observational studies on chronic Chagas disease during pregnancy are inconsistent in their findings. Since pregnancy findings are inconsistent, treatment of chronic Chagas disease during pregnancy is not recommended due to the risk of embryo-fetal toxicity from benznidazole tablets. Acute symptomatic Chagas disease is rare in pregnant women; however, symptoms may be serious or life-threatening. If a pregnant woman presents with acute symptomatic Chagas disease, the risk versus benefit of treatment with benznidazole tablets to the mother and fetus should be evaluated on a case-by-case basis.
- Lactation: Limited published literature, based on breast milk sampling, reports that benznidazole is present in human milk at infant doses of 5.5 to 17% of the maternal weight-adjusted dosage. Because of the potential for serious adverse reactions, and transmission of Chagas disease, patients should be advised that breastfeeding is not recommended during treatment with benznidazole.
- Females and Males of Reproductive Potential: Pregnancy testing is recommended for females of reproductive potential. Females of reproductive potential should be advised to use effective contraception during treatment with benznidazole and for 5 days after the final dose. Based on findings in rodents, benznidazole tablets may impair fertility in males of reproductive potential and it is not known whether these effects are reversible.
- Pediatric Use: The safety and effectiveness of benznidazole tablets have been established in pediatric patients 2 to 12 years of age for the treatment of Chagas disease. The safety and effectiveness in pediatric patients younger than 2 years of age and older than 12 years of age have not been established.
- Hepatic Impairment: Use of benznidazole tablets has not been evaluated in patients with hepatic impairment.
- Renal Impairment: Use of benznidazole tablets has not been evaluated in patients with renal impairment.

Efficacy: The safety and effectiveness of benznidazole for the treatment of Chagas disease were demonstrated in two placebo-controlled trials in pediatric patients with chronic Chagas disease.

- Trial 1: Patients between 6 to 12 years of age with chronic indeterminate Chagas disease (N=106) were randomized to receive either benznidazole (5mg/kg/day for 60 days) or placebo and followed for 4 years. The chronic indeterminate form of Chagas disease includes patients with serologic evidence of *T. cruzi* infection without symptoms of cardiac or gastrointestinal disease. Patients with at least two positive conventional serologic tests for antibodies to *T. cruzi* were included in the study.
- Trial 2: Patients between 7 to 12 years of age with chronic indeterminate Chagas disease (N=129) were randomized to receive either benznidazole (7.5mg/kg/day for 60 days) or placebo and followed for 3 years. Patients with three positive conventional serologic tests for antibodies to *T. cruzi* were included in the study.

- Both Trials 1 and 2 measured anti-*T. cruzi* IgG antibodies changing from positive to negative. In Trial 1, 60% of patients treated with benznidazole versus 13.5% treated with placebo were seronegative [difference = 46.5; 95% confidence interval (CI): 24.5, 64.4]. In Trial 2, 54.7% of benznidazole-treated patients versus 4.6% of placebo-treated patients were seronegative (difference = 50.1; 95% CI: 35.8, 63.4).
- Trial 3: An uncontrolled study of the safety and pharmacokinetics of benznidazole in pediatric patients 2 to 12 years of age with chronic indeterminate Chagas disease provided information for dosing recommendations down to 2 years of age.

Cost: The wholesale acquisition cost (WAC) of benznidazole 100mg tablets is $3.00 per tablet, resulting in an approximate cost of $720.00 for treatment of a 60kg patient for 60 days.

Specialist Recommendation: The College of Pharmacy received input from an infectious disease specialist regarding benznidazole. The specialist recommended prior authorization of benznidazole to ensure appropriate usage.

Recommendations

The College of Pharmacy recommends the prior authorization of benznidazole tablets with the following criteria:

Benznidazole Tablets Approval Criteria:

1. An FDA approved diagnosis of Chagas disease (American trypanosomiasis) caused by *Trypanosoma cruzi*; and
2. Benznidazole must be prescribed by or in consultation with an infectious disease specialist; and
3. Female members of reproductive potential must have a pregnancy test prior to treatment with benznidazole; and
4. Female members of reproductive potential must be willing to use effective contraception during treatment with benznidazole tablets and for 5 days after the last dose; and
5. Member must not have taken disulfiram within the last two weeks; and
6. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug. Doses (weight-based) must not exceed 400mg per day. The approval duration will be for 60 days of therapy.

Utilization Details of Anti-Parasitic Medications: Calendar Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ UNIT	COST/ CLAIM
ALBENZA TAB 200MG	1,700	1,492	$909,529.57	$168.24	$535.02
IVERMECTIN TAB 3MG	1,488	1,229	$38,931.90	$5.50	$26.16
BILTRICIDE TAB 600MG	15	11	$2,731.22	$88.10	$182.08
EMVERM CHW 100MG	6	5	$2,761.82	$306.87	$460.30
MEBENDAZOLE POWDER	2	1	$19.14	$0.32	$9.57
TOTAL	**3,211**	**2,705***	**$953,973.65**	**$75.78**	**$297.10**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

- Some of the anti-parasitic medications have significant federal rebates; therefore, costs shown do not reflect net costs.

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Appendix D

Calendar Year 2017 Annual Review of Bowel Preparation Medications and 30-Day Notice to Prior Authorize Clenpiq™ (Sodium Picosulfate/Magnesium Oxide/Anhydrous Citric Acid)

Oklahoma Health Care Authority
May 2018

Current Prior Authorization Criteria

ColPrep™ Kit, OsmoPrep®, Prepopik®, and SUPREP® Approval Criteria:

1. An FDA approved indication for use in cleansing of the colon as a preparation for colonoscopy; and
2. A patient-specific, clinically significant reason other than convenience why the member cannot use other bowel preparation medications available without prior authorization.
3. If the member requires a low volume polyethylene glycol electrolyte lavage solution, Moviprep® is available without prior authorization. Other medications currently available without a prior authorization include: Colyte®, Gavilyte®, Golytely®, and Trilyte®.

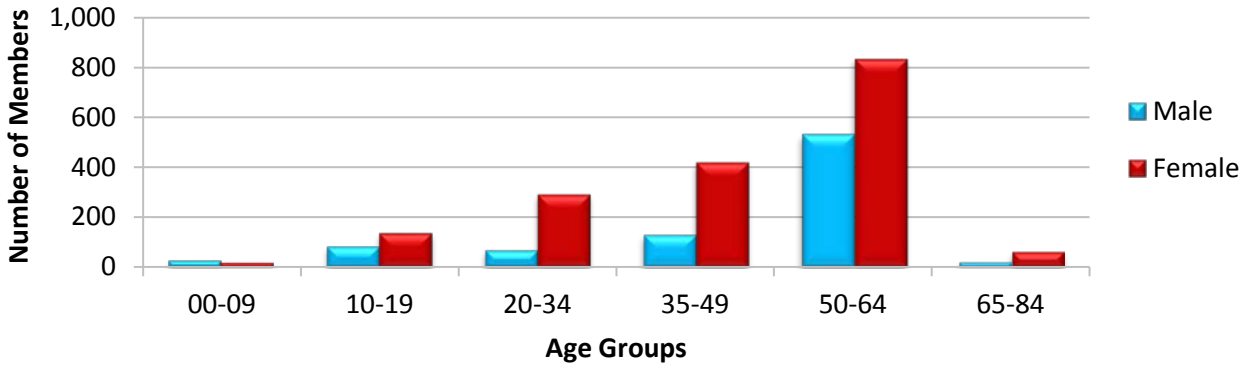
Utilization of Bowel Preparation Medications: Calendar Year 2017

Comparison of Calendar Years

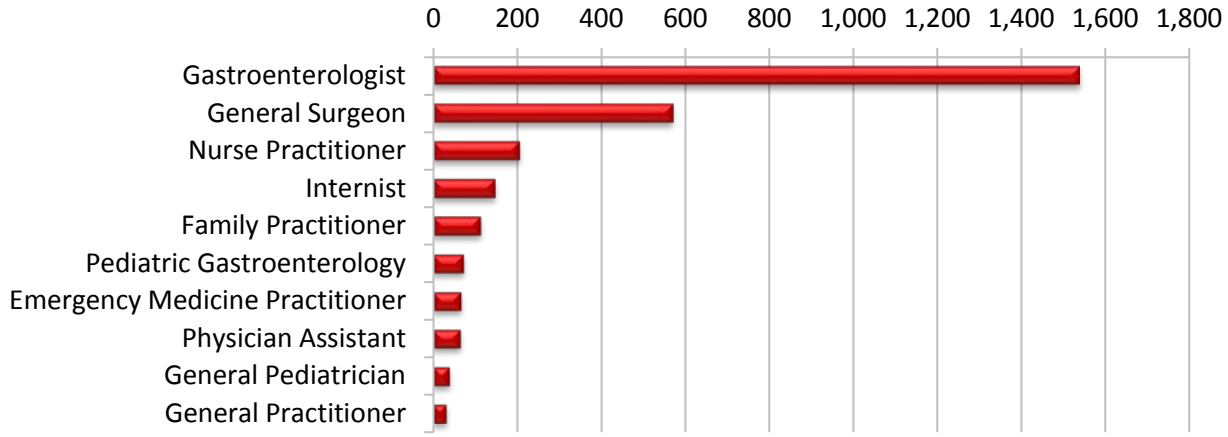
Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	2,887	3,267	$137,768.44	$42.17	$12.24	8,838,495	11,255
2017	2,630	2,915	$87,431.58	$29.99	$9.57	10,096,079	9,139
% Change	**-8.90%**	**-10.80%**	**-36.50%**	**-28.90%**	**-21.80%**	**14.20%**	**-18.80%**
Change	**-257**	**-352**	**-$50,336.86**	**-$12.18**	**-$2.67**	**1,257,584**	**-2,116**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

Demographics of Members Utilizing Bowel Preparation Medications



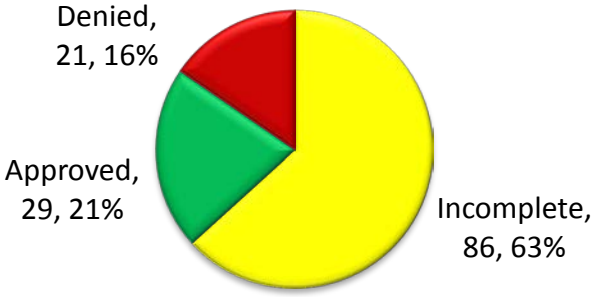
Top Prescriber Specialties of Bowel Preparation Medications by Number of Claims



Prior Authorization of Bowel Preparation Medications

There were 136 prior authorization requests submitted for bowel preparation medications during calendar year 2017. The following chart shows the status of the submitted petitions for calendar year 2017.

Status of Petitions



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

Anticipated Patent Expiration(s):

- Moviprep® [polyethylene glycol (PEG)-3350/sodium sulfate/sodium chloride/potassium chloride/sodium ascorbate/ascorbic acid]: September 2024
- Osmoprep® (sodium phosphate monobasic/sodium phosphate dibasic): June 2028
- Prepopik® (sodium picosulfate/magnesium oxide/anhydrous citric acid): October 2028
- Clenpiq™ (sodium picosulfate/magnesium oxide/anhydrous citric acid): June 2034

New U.S. Food and Drug Administration (FDA) Approval(s):

- **February 2017:** The FDA approved the first generic formulation of SUPREP® Bowel Prep Kit (sodium sulfate/potassium sulfate/magnesium sulfate) for cleansing of the colon in preparation for colonoscopy in adults. The National Average Drug Acquisition Cost (NADAC) of SUPREP® Bowel Prep Kit remains comparable to other prior authorized bowel preparation medications. The College of Pharmacy will continue to monitor the

cost of generic SUPREP® Bowel Prep Kit in comparison to the branded product, as well as other bowel preparation medications.

- **November 2017:** The FDA approved Clenpiq™ (sodium picosulfate/magnesium oxide/ anhydrous citric acid oral solution) for cleansing of the colon as a preparation for colonoscopy in adults. This is the only FDA-approved prescription colonoscopy prep that comes "ready-to-drink".

Pipeline:

- **Plenvu® (NER1006):** Plenvu® is a novel, low volume (1 liter) PEG-based bowel preparation product that has been developed to provide whole bowel cleansing, with an additional focus on the ascending colon. In June 2017, Salix Pharmaceuticals announced the FDA accepted a New Drug Application (NDA) for Plenvu®, with an expected Prescription Drug User Fee Act (PDUFA) date in the first quarter of 2018. The decision date was extended by the FDA in February 2018 to allow more time for additional review. The updated PDUFA date is expected mid-May 2018.

Clenpiq™ (Sodium Picosulfate/Magnesium Oxide/Anhydrous Citric Acid) Product Summary[6]

Indication(s): Clenpiq™ (sodium picosulfate/magnesium oxide/anhydrous citric acid oral solution) is a combination of sodium picosulfate, a stimulant laxative, and magnesium oxide and anhydrous citric acid, which form magnesium citrate, an osmotic laxative, indicated for cleansing of the colon as a preparation for colonoscopy in adults.

Dosing:

- Clenpiq™ is supplied in a carton containing two bottles, each holding 10mg of sodium picosulfate, 3.5 grams of magnesium oxide, and 12 grams of anhydrous citric acid in 160mL of cranberry-flavored, colorless to slightly yellow oral solution, along with an eight-ounce cup for measuring fluids for hydration.
- Clenpiq™ is ready-to-drink and does not require dilution prior to administration.
- Two doses of Clenpiq™ are required for a complete preparation for colonoscopy. The preferred method is the "split-dose" method (an alternative method is the "day-before" method).
    - Split-Dose Method: The first dose should be administered during the evening before the colonoscopy. Following the first dose, the patient should drink five 8-ounce cups (cup provided) of clear liquids within 5 hours and before bed. If severe bloating, distention, or abdominal pain occurs, following the first dose, the second dose should be delayed until the symptoms resolve. The second dose should be administered the next morning on the day of colonoscopy (approximately 5 hours prior to the colonoscopy). Following the second dose, the patient should drink at least three 8-ounce cups of clear liquids at least 2 hours before the colonoscopy.
    - Day-Before Method: The first dose should be taken in the afternoon or early evening before the colonoscopy (e.g., 4:00 to 6:00 PM). The patient should then drink five 8-ounce cups of clear liquids within 5 hours and before the next dose.

If severe bloating, distention, or abdominal pain occurs, following the first dose, the second dose should be delayed until the symptoms resolve. The second dose should be taken approximately 6 hours later in the evening the night before the colonoscopy (e.g., 10:00 PM to 12:00 AM). Following the second dose, the patient should drink three 8-ounce cups of clear liquids within 5 hours and before bed.

Contraindication(s):

- Patients with severe renal impairment [creatinine clearance (CrCl) <30mL/minute], which may result in accumulation of magnesium
- Gastrointestinal (GI) obstruction or ileus
- Bowel perforation
- Toxic colitis or toxic megacolon
- Gastric retention
- Hypersensitivity to any of the ingredients in Clenpiq™

Warnings and Precautions:

- Serious Fluid and Serum Chemistry Abnormalities: Patients should be advised to hydrate adequately before, during, and after the use of Clenpiq™. Caution should be exercised in patients with congestive heart failure (CHF) when replacing fluids. Approximately 20% of patients in clinical trials of another oral formulation of sodium picosulfate/magnesium oxide/anhydrous citric acid had orthostatic changes in blood pressure and/or heart rate on the day of colonoscopy and up to seven days post colonoscopy.
- Seizures: There have been reports of generalized tonic-clonic seizures (GTCS) with the use of bowel preparation products in patients with no prior history of seizures. The seizure cases were associated with electrolyte abnormalities and low serum osmolality.
- Use in Patients with Renal Impairment: As with other magnesium containing bowel preparations, caution should be used when prescribing Clenpiq™ for patients with impaired renal function or patients taking concomitant medications that may affect renal function [e.g., diuretics, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), or non-steroidal anti-inflammatory drugs (NSAIDs)]. These patients may be at increased risk for renal injury.
- Cardiac Arrhythmias: There have been rare reports of serious arrhythmias associated with the use of ionic osmotic laxative products for bowel preparation. Caution should be exercised when prescribing Clenpiq™ for patients at increased risk of arrhythmias [e.g., patients with a history of prolonged QT, uncontrolled arrhythmias, recent myocardial infarction (MI), unstable angina, CHF, cardiomyopathy]. Pre-dose and post-colonoscopy ECGs in patients at increased risk of serious cardiac arrhythmias should be considered.
- Colonic Mucosal Ulceration, Ischemic Colitis, and Ulcerative Colitis: Osmotic laxatives may produce colonic mucosal aphthous ulcerations and there have been reports of more serious cases of ischemic colitis requiring hospitalization. Concurrent use of additional stimulant laxatives with Clenpiq™ may increase this risk.

- Use in Patients with Significant GI Disease: If GI obstruction or perforation is suspected appropriate diagnostic studies should be performed before administering Clenpiq™ to rule out these conditions.
- Aspiration: Patients with impaired gag reflex are at risk for regurgitation or aspiration during the administration of Clenpiq™.

Adverse Reactions: The safety of Clenpiq™ was established from controlled trials of another orally administered formulation of sodium picosulfate/magnesium oxide/anhydrous citric acid. The most common adverse reactions (at least 1% of patients) experienced during those clinical trials included nausea, headache, and vomiting.

Drug Interactions:

- Drugs That May Increase Risks of Fluid and Electrolyte Abnormalities: Caution should be exercised when prescribing Clenpiq™ for patients with conditions or who are taking other drugs that increase the risk for fluid and electrolyte disturbances or may increase the risk of renal impairment, seizures, arrhythmias, or QT prolongation in the setting of fluid and electrolyte abnormalities.
- Potential for Reduced Drug Absorption: Clenpiq™ can reduce the absorption of other co-administered drugs:
    - Oral medications should be administered at least one hour before the start of administration of Clenpiq™.
    - Tetracycline and fluoroquinolone antibiotics, iron, digoxin, chlorpromazine, and penicillamine should be administered at least 2 hours before and not less than 6 hours after administration of Clenpiq™ to avoid chelation with magnesium.
- Antibiotics: Prior or concomitant use of antibiotics with Clenpiq™ may reduce the efficacy of Clenpiq™ as conversion of sodium picosulfate to its active metabolite bis-(p-hydroxyphenyl)-pyridyl-2-methane (BHPM) is mediated by colonic bacteria.

Use in Specific Populations:

- Pregnancy: There is no data with Clenpiq™ use in pregnant women to determine a drug-associated risk. In animal reproduction studies, no adverse developmental effects were observed in pregnant rats when sodium picosulfate/magnesium oxide/anhydrous citric acid were administered orally at doses 1.2 times the recommended human dose based on body surface area during organogenesis.
- Lactation: There are no data on the presence of magnesium oxide or anhydrous citric acid in either human or animal milk, the effects on the breastfed infant, or the effects on milk production. Published data on lactating women indicate that the active metabolite of sodium picosulfate, BHPM, remained below the limit of detection in breast milk after both single and multiple doses of 10mg/day.
- Pediatric Use: The safety and effectiveness of Clenpiq™ in pediatric patients have not been established.
- Geriatric Use: Of the 1,201 patients in clinical trials who received another oral formulation of sodium picosulfate/magnesium oxide/anhydrous citric acid, 215 (18%)

patients were 65 years of age or older. No overall differences in safety or effectiveness were observed between geriatric patients and younger patients.

- Renal Impairment: Clenpiq™ is contraindicated in patients with severe renal impairment (CrCl <30mL/min), as accumulation of magnesium in plasma may occur. Patients with less severe renal impairment or patients taking concomitant medications that may affect renal function may be at increased risk for renal injury.

Efficacy: The safety and efficacy of Clenpiq™ were established based on controlled studies of another oral formulation of sodium picosulfate/magnesium oxide/anhydrous citric acid.

Cost Comparison:

Medication	Cost per Course of Therapy
Clenpiq™ (sodium picosulfate/magnesium oxide/anhydrous citric acid)	**$128.00**
Prepopik® (sodium picosulfate/magnesium oxide/anhydrous citric acid)	$123.86
Moviprep® (PEG-3350/sodium sulfate/sodium chloride/potassium chloride/sodium ascorbate/ascorbic acid)	$95.79
Gavilyte®-G (PEG-3350/sodium sulfate/sodium bicarbonate/sodium chloride/potassium chloride)	$12.00

PEG-3350 = polyethylene glycol 3350
Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Cost (SMAC) if NADAC unavailable.

Recommendations

The College of Pharmacy recommends the prior authorization of Clenpiq™ with criteria similar to the other prior authorized bowel preparation medications:

Clenpiq™, ColPrep™ Kit, OsmoPrep®, Prepopik®, and SUPREP® Approval Criteria:

1. An FDA approved indication for use in cleansing of the colon as a preparation for colonoscopy; and
2. A patient-specific, clinically significant reason other than convenience why the member cannot use other bowel preparation medications available without prior authorization.
3. If the member requires a low volume polyethylene glycol electrolyte lavage solution, Moviprep® is available without prior authorization. Other medications currently available without a prior authorization include: Colyte®, Gavilyte®, Golytely®, and Trilyte®.

Utilization Details of Bowel Preparation Medications: Calendar Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS*	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
POLYETHYLENE GLYCOL ELECTROLYTE SOLUTION PRODUCTS					
GAVILYTE-G SOL	1,242	1,103	$24,360.64	1.13	$19.61
MOVIPREP SOL	399	392	$37,820.49	1.02	$94.79
PEG 3350 SOL ELECTROL	353	334	$5,279.88	1.06	$14.96
GAVILYTE-N SOL FLAV PK	343	324	$6,904.10	1.06	$20.13

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS*	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
PEG-3350/KCL SOL /SODIUM	246	219	$5,321.00	1.12	$21.63
PEG-3350 SOL ELECTROL	156	144	$3,117.41	1.08	$19.98
GAVILYTE-C SOL	92	90	$1,559.94	1.02	$16.96
TRILYTE SOL	61	58	$1,346.71	1.05	$22.08
GOLYTELY SOL	11	11	$212.33	1	$19.30
SUBTOTAL	**2,903**	**2,620**	**$85,922.50**	**1.11**	**$29.60**
SODIUM SULFATE SOLUTION PRODUCTS					
SUPREP BOWEL SOL PREP KIT	8	8	$714.30	1	$89.29
SUBTOTAL	**8**	**8**	**$714.30**	**1**	**$89.29**
SODIUM PHOSPHATE TABLET PRODUCTS					
OSMOPREP TAB 1.5GM	4	4	$794.78	1	$198.70
SUBTOTAL	**4**	**4**	**$794.78**	**1**	**$198.70**
TOTAL	**2,915**	**2,630***	**$87,431.58**	**1.11**	**$29.99**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

[1] U.S. Food and Drug Administration (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 03/2018. Last accessed 04/16/2018.

[2] FDA. Drugs@FDA: FDA Approved Drug Products. Abbreviated New Drug Application (ANDA): 202511. Available online at: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=BasicSearch.process&ApplNo=202511. Last revised 02/23/2017. Last accessed 04/16/2018.

[3] Ferring Pharmaceuticals, Inc. FDA Approves Ferring's Clenpiq™ (sodium picosulfate, magnesium oxide, and anhydrous citric acid) Oral Solution for Colonoscopy Prep. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/fda-approves-ferrings-clenpiq-sodium-picosulfate-magnesium-oxide-and-anhydrous-citric-acid-oral-solution-for-colonoscopy-prep-300563466.html. Issued 11/29/2017. Last accessed 04/16/2018.

[4] Salix Pharmaceuticals, Ltd. Salix Announces Filing Acceptance for Plenvu® Next Generation Bowel Cleansing Preparation for Colonoscopies. *PR Newswire*. Available online at: http://www.prnewswire.com/news-releases/salix-announces-filing-acceptance-for-plenvu-next-generation-bowel-cleansing-preparation-for-colonoscopies-300481172.html. Issued 06/28/2017. Last accessed 04/16/2018.

[5] Salix Pharmaceuticals, Ltd. Salix Provides Update on FDA Submission for PLENVU®. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/salix-provides-update-on-fda-submission-for-plenvu-300596423.html. Issued 02/09/2018. Last accessed 04/16/2018.

[6] Clenpiq™ (sodium picosulfate/magnesium oxide/anhydrous citric acid) Prescribing Information. Ferring Pharmaceuticals, Inc. Available online at: http://www.ferringusa.com/wp-content/uploads/2018/04/ClenpiqPI-11-2017.pdf. Last revised 11/2017. Last accessed 04/16/2018.

Appendix E

Calendar Year 2017 Annual Review of Otic Anti-Infective Medications and 30-Day Notice to Prior Authorize Otiprio® (Ciprofloxacin Otic Suspension)

Oklahoma Health Care Authority
May 2018

Current Prior Authorization Criteria

Otic Anti-Infective Medications 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.

Acetasol® HC and VoSol® HC (Acetic Acid/Hydrocortisone) Approval Criteria:

1. Diagnosis of acute otitis externa; and
2. Recent trials (within the last six months) 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.

Otic Anti-Infectives Medications		
Tier-1	**Tier-2**	**Special PA**
acetic acid (VoSol®, Acetasol®)	ciprofloxacin (Cetraxal®)	acetic acid/HC (Acetasol® HC, VoSol® HC)
ciprofloxacin/dexamethasone (Ciprodex®)	ciprofloxacin/fluocinolone (Otovel®)	
ciprofloxacin/HC (Cipro® HC)	finafloxacin (Xtoro™)	
neomycin/colistin/HC/ thonzonium (Coly-Mycin® S)	neomycin/polymyxin B/HC (Cortisporin®, Pediotic®)	
	ofloxacin (Floxin® Otic)	

PA = prior authorization; HC = hydrocortisone
Tier structure based on supplemental rebate participation, and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Utilization of Otic Anti-Infective Medications: Calendar Year 2017

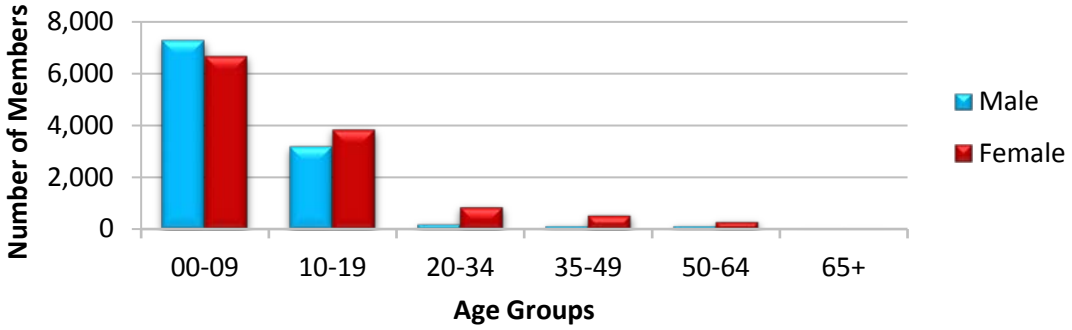
Comparison of Calendar Years

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	24,149	29,362	$5,255,081.12	$178.98	$15.95	234,078	329,387
2017	23,191	28,145	$5,448,231.85	$193.58	$17.81	216,447	305,958
% Change	**-4.00%**	**-4.10%**	**3.70%**	**8.20%**	**11.70%**	**-7.50%**	**-7.10%**
Change	**-958**	**-1,217**	**$193,150.73**	**$14.60**	**$1.86**	**-17,631**	**-23,429**

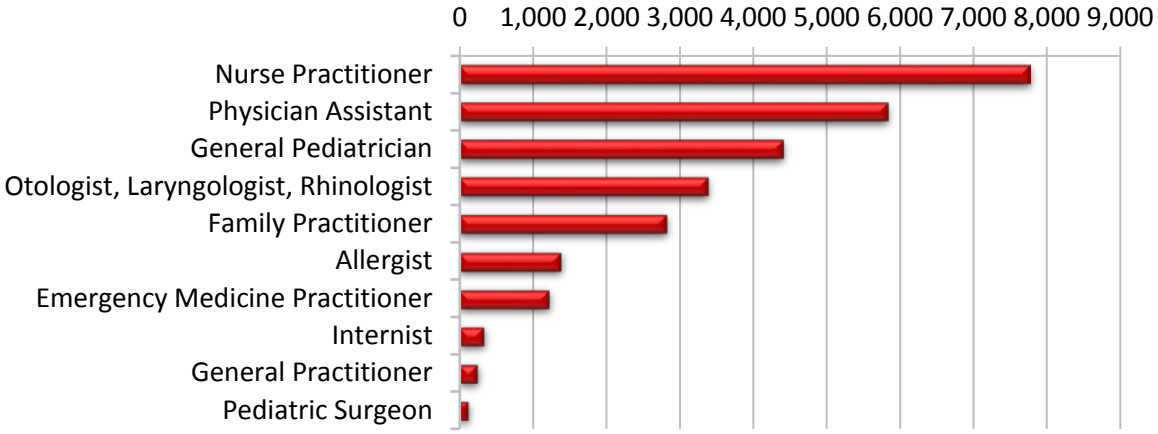
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

- Some Tier-1 products participate in supplemental rebates; therefore, costs shown do not reflect net costs.

Demographics of Members Utilizing Otic Anti-Infective Medications



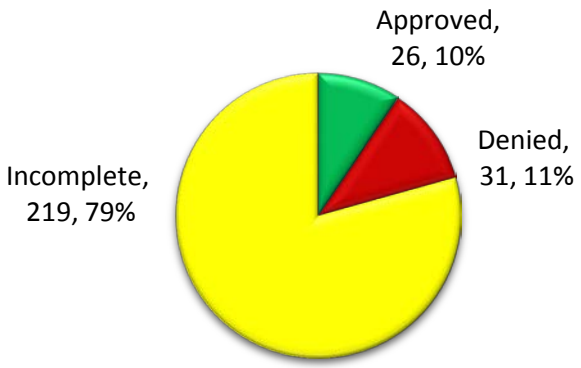
Top Prescriber Specialties of Otic Anti-Infective Medications by Number of Claims



Prior Authorization of Otic Anti-Infective Medications

There were 276 prior authorization requests submitted for otic anti-infective medications during calendar year 2017. The following chart shows the status of the submitted petitions for calendar year 2017.

Status of Petitions



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

Anticipated Patent Expiration(s):

- Ciprodex® (ciprofloxacin/dexamethasone): June 2025
- Otovel® (ciprofloxacin/fluocinolone): March 2030
- Xtoro™ (finafloxacin): November 2033
- Otiprio® (ciprofloxacin): July 2035

New U.S. Food and Drug Administration (FDA) Approvals:

- **March 2018:** The FDA approved Otiprio® (ciprofloxacin 6% otic suspension) for the treatment of acute otitis externa (AOE) in patients 6 months of age and older due to *Pseudomonas aeruginosa (P. aeruginosa)* and *Staphylococcus aureus (S. aureus)*. Otiprio® is the first single-dose antibacterial approved by the FDA for treating AOE. It is to be administered in an office setting by a health care professional. Otiprio® was previously approved in December 2015 for the treatment of bilateral otitis media with effusion (OME) in patients undergoing tympanostomy tube placement. Otiprio® is the only single-dose otic drop FDA approved for intratympanic administration. Other treatments commonly used during tympanostomy tube placement include ofloxacin or ciprofloxacin administered into the ear intraoperatively and then twice daily for five days following the procedure.

Otiprio® (Ciprofloxacin Otic Suspension) Product Summary[5]

Indication(s): Otiprio® (ciprofloxacin otic suspension) is a fluoroquinolone antibacterial indicated for the treatment of the following:

- Bilateral OME in patients 6 months of age and older undergoing tympanostomy tube placement
- AOE in patients 6 months of age and older due to *P. aeruginosa* and *S. aureus*

Dosing:

- Otiprio® is available as an otic suspension containing ciprofloxacin 6%. It is supplied in a single-dose, preservative-free glass vial containing 1mL of solution.
- Otiprio® is for intratympanic or otic administration by a healthcare professional only.
- Bilateral OME: The dose of 0.1mL (6mg) should be administered into the affected ear(s), following suctioning of middle ear effusion.
- AOE: The dose of 0.2mL (12mg) should be administered to external ear canal(s) of each affected ear.
- Any unused portion should be discarded after single-patient use.

Mechanism of Action:

- Ciprofloxacin, a fluoroquinolone antibiotic, interferes with enzyme deoxyribonucleic acid (DNA) gyrase, which is needed for the synthesis of bacterial DNA.

Contraindication(s):

- Known hypersensitivity to ciprofloxacin or other quinolones, or to any other components of Otiprio®

Warnings and Precautions:

- Potential for Microbial Overgrowth: Use of ciprofloxacin may result in overgrowth of non-susceptible bacteria and fungi. If such infections occur, alternative therapy should be instituted.

Adverse Reactions: The most common adverse reactions occurring in at least 2% of patients during clinical trials included:

- Nasopharyngitis
- Irritability
- Rhinorrhea
- Ear pruritus
- Headache
- Otitis media
- Ear discomfort

Use in Special Populations:

- Pregnancy: Ciprofloxacin is negligibly absorbed following otic administration and maternal use is not expected to result in fetal exposure to ciprofloxacin.
- Lactation: Ciprofloxacin is negligibly absorbed following otic administration and breastfeeding is not expected to result in infant exposure to ciprofloxacin.
- Pediatric Use: Ciprofloxacin has been studied in patients as young as 6 months of age in adequate and well-controlled clinical trials. No major differences in safety and effectiveness have been observed between adult and pediatric patients.
- Geriatric Use: Clinical studies of ciprofloxacin did not include sufficient numbers of subjects 65 years of age and older to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

Efficacy:

OME: Two randomized, multicenter, sham-controlled Phase 3 clinical trials were conducted in 532 pediatric patients with bilateral OME undergoing myringotomy with tympanostomy tube placement, to assess the safety and efficacy of Otiprio®. The primary efficacy endpoint for both trials was the cumulative proportion of treatment failures through Day 15, defined as the occurrence of otorrhea, otic or systemic antibacterial drug use for any reason post-surgery, and those who missed visits or were lost-to-follow-up.

- Trial 1: In the Otiprio® treatment arm, 25% of the patients had a recorded treatment failure through Day 15. In the sham treatment arm, 45% of the patients had a recorded treatment failure through Day 15.
- Trial 2: In the Otiprio® treatment arm, 21% of the patients had a recorded treatment failure through Day 15. In the sham treatment arm, 45% of the patients had a recorded treatment failure through Day 15.
- Otiprio® did not lead to any issues with hearing function, middle ear function, or tube patency in this trial.

AOE: One randomized, multicenter, sham-controlled clinical trial was conducted in 262 pediatric and adult patients with unilateral or bilateral AOE to assess the safety and efficacy of Otiprio® in patients 6 months of age and older. The primary efficacy endpoint was the proportion of patients with a clinical response at Day 8. Clinical response in the study was defined as the complete absence of signs and symptoms of AOE and no systemic or topical antibacterial drug given at or prior to the study visit.

- Intention to Treat: All subjects who were randomized and did not have group A streptococci cultured on Day 1. In the Otiprio® treatment arm, 69% of the patients achieved a clinical response at Day 8 compared to 46% in the sham treatment arm.
- Microbiological Intention to Treat: All intent to treat subjects who had a positive culture for *S. aureus* or *P. aeruginosa* on Day 1. In the Otiprio® treatment arm, 60% of the patients achieved a clinical response at Day 8 compared to 34% in the sham treatment arm.

Cost Comparison:

Medication	Cost per Vial or mL	Cost per Treatment
Otiprio® (ciprofloxacin 6%)	**$283.20**	**$283.20**
Ciprodex® (ciprofloxacin/dexamethasone 0.3%/0.1%)	$27.93	$209.48
Cipro® HC (ciprofloxacin/HC 0.2%/1%)	$28.50	$285.00
Coly-Mycin® S (colistin/neomycin/TZ/HC 3mg/3.3mg/10mg/0.5mg)	$20.34	$203.40

TZ = thonzonium; HC = hydrocortisone
Costs do not reflect rebated prices or net costs.
Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Recommendations

The College of Pharmacy recommends the placement of Otiprio® (ciprofloxacin otic suspension) into the Special Prior Authorization (PA) Tier of the Otic Anti-Infective Medications Product Based Prior Authorization (PBPA) category with the following criteria:

Otiprio® (Ciprofloxacin 6% Otic Suspension) Approval Criteria:

1. An FDA approved indication of one of the following:
   a. For the treatment of bilateral otitis media with effusion undergoing tympanostomy tube placement; or
   b. For the treatment of acute otitis externa due to *S. aureus* or *P. aeruginosa;* and
2. Member must be 6 months of age or older; and
3. Otiprio® must be administered by a health care professional; and
4. A patient-specific, clinically significant reason why appropriate lower tiered otic anti-infectives cannot be used; and
5. A quantity limit of 1 vial per treatment course will apply.

Otic Anti-Infectives Medications		
Tier-1	**Tier-2**	**Special PA**
acetic acid (VoSol®, Acetasol®)	ciprofloxacin 0.2% (Cetraxal®)	acetic acid/HC (Acetasol® HC, VoSol® HC)
ciprofloxacin/dexamethasone (Ciprodex®)	ciprofloxacin/fluocinolone (Otovel®)	**ciprofloxacin 6% (Otiprio®)**
ciprofloxacin/HC (Cipro® HC)	finafloxacin (Xtoro™)	
neomycin/colistin/HC/ thonzonium (Coly-Mycin® S)	neomycin/polymyxin B/HC (Cortisporin®, Pediotic®)	
	ofloxacin (Floxin® Otic)	

PA = prior authorization; HC = hydrocortisone
Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Utilization Details of Otic Anti-Infective Medications: Calendar Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ DAY	COST/ CLAIM
TIER-1 PRODUCTS						
CIPRODEX SUS 0.3-0.1% OTIC	26,816	22,206	$5,219,754.19	1.21	$18.64	$194.65
CIPRO HC SUS 0.2-1% OTIC	567	537	$153,737.57	1.06	$17.26	$271.14
ACETIC ACID SOL 2% OTIC	427	401	$13,481.27	1.06	$1.04	$31.57
COLY-MYCIN S SUS OTIC	314	297	$59,617.90	1.06	$15.87	$189.87
CORTISPORIN SUS - TC OTIC	1	1	$185.06	1	$9.25	$185.06
TIER-1 SUBTOTAL	**28,125**	**23,442**	**$5,446,775.99**	**1.21**	**$17.82**	**$193.66**
TIER-2 PRODUCTS						
OFLOXACIN DRO 0.3% OTIC	10	9	$855.91	1.11	$6.63	$85.59
NEO/POLY/HC SUS 1% OTIC	5	5	$293.72	1	$6.39	$58.74
NEO/POLY/HC SOL 1% OTIC	4	4	$230.55	1	$4.61	$57.64
TIER-2 SUBTOTAL	**19**	**18**	**$1,380.18**	**1.06**	**$6.13**	**$72.64**
SPECIAL PA PRODUCTS						
HC/ACET ACID SOL 1-2% OTIC	1	1	$75.68	1	$5.05	$75.68
SPECIAL PA SUBTOTAL	**1**	**1**	**$75.68**	**1**	**$5.05**	**$75.68**
TOTAL	**28,145**	**23,191***	**$5,448,231.85**	**1.21**	**$17.81**	**$193.58**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

- Some Tier-1 products participate in supplemental rebates; therefore, costs shown do not reflect net costs.

[1] U.S. Food and Drug Administration (FDA) Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm?resetfields=1. Last revised 03/2018. Last accessed 04/16/2018.
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Appendix F

Calendar Year 2017 Annual Review of Granulocyte Colony-Stimulating Factors (G-CSFs)

Oklahoma Health Care Authority
May 2018

Current Prior Authorization Criteria

Granix® (Tbo-filgrastim) and Zarxio® (Filgrastim-sndz) Approval Criteria:

1. An FDA approved diagnosis; and
2. A patient-specific, clinically significant reason why the member cannot use Neupogen® (filgrastim).

Currently, Neupogen® (filgrastim) and Neulasta® (pegfilgrastim) are available without prior authorization. Neulasta® was included in the implementation of the original prior authorization of G-CSFs in April 2016 (which also included Granix® and Zarxio®); however, after an analysis of cost-effectiveness, the prior authorization requirement for Neulasta® was removed in October 2016.

Utilization of G-CSFs: Calendar Year 2017

Comparison of Calendar Years for G-CSFs: Pharmacy Claims

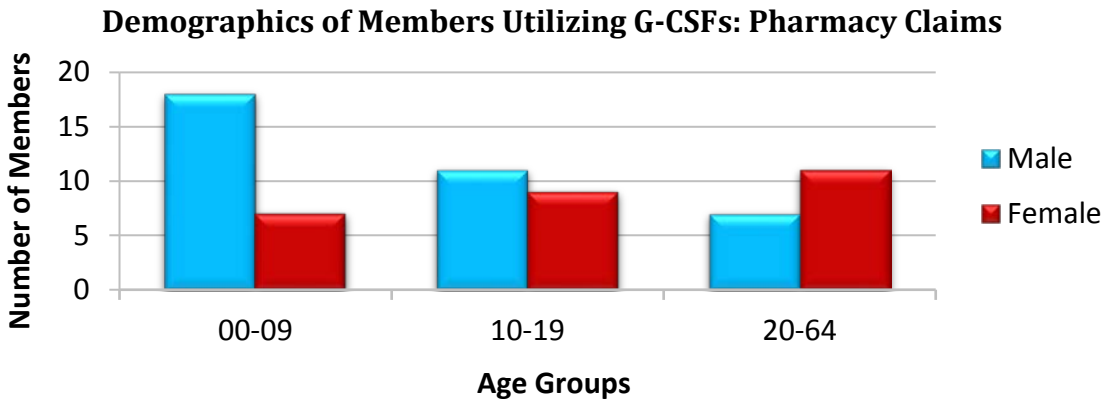
Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	105	419	$1,462,670.61	$3,490.86	$250.71	3,028	5,834
2017	63	222	$1,168,702.97	$5,264.43	$256.07	1,786	4,564
% Change	**-40.00%**	**-47.00%**	**-20.10%**	**50.80%**	**2.10%**	**-41.00%**	**-21.80%**
Change	**-42**	**-197**	**-$293,967.64**	**$1,773.57**	**$5.36**	**-1,242**	**-1,270**

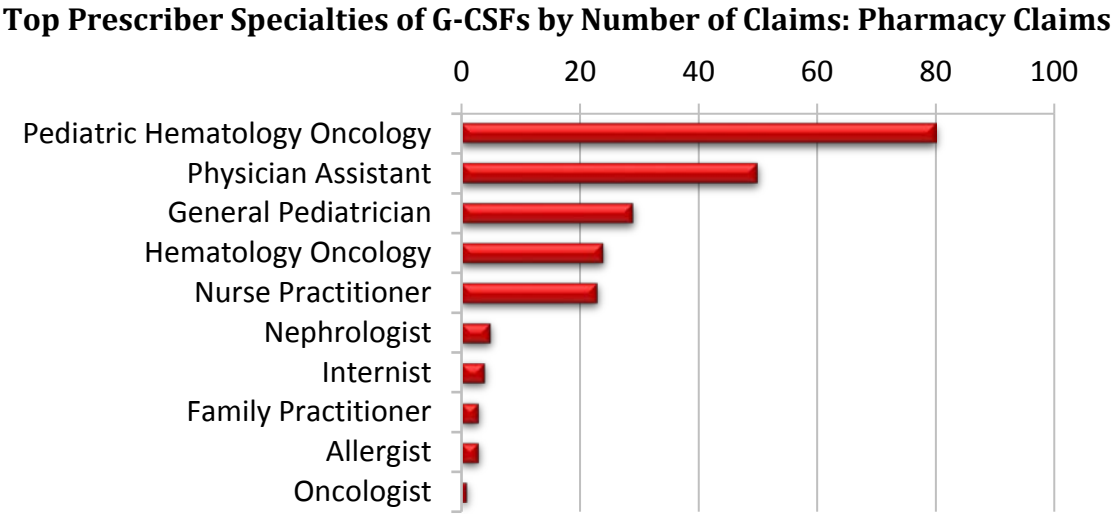
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

Calendar Year 2017 Utilization of G-CSFs: Medical Claims

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Claims/ Member
2017	233	796	$2,632,356.34	$3,306.98	3.4

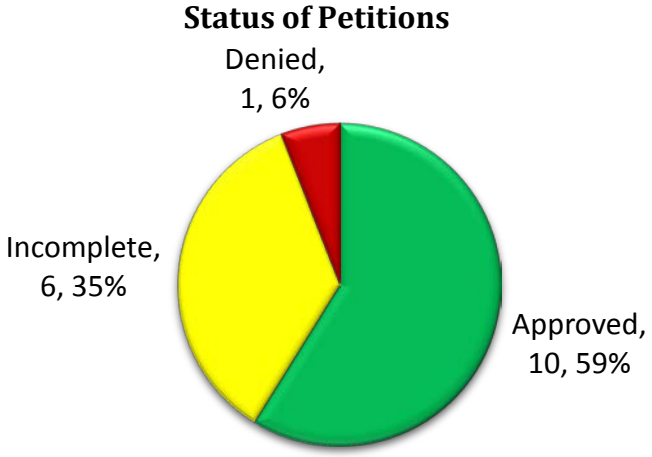
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.





Prior Authorization of G-CSFs

There were 17 prior authorization requests submitted for G-CSFs during calendar year 2017. The following chart shows the status of the submitted petitions for calendar year 2017.



Market News and Updates[1,2,3,4,5,6,7,8,9,10,11,12]

New U.S. Food and Drug Administration (FDA) Approval(s):

- **March 2018:** The FDA approved a supplemental Biologics License Application (sBLA) for Leukine® (sargramostim) for a new indication to increase survival in adult and pediatric patients acutely exposed to myelosuppressive doses of radiation [Hematopoietic Syndrome of Acute Radiation Syndrome (H-ARS)]. Leukine® is a granulocyte-macrophage colony-stimulating factor (GM-CSF) and was first FDA approved in 1991. Leukine® is the third FDA-approved medical countermeasure (MCM) that is indicated to increase survival in patients exposed to myelosuppressive doses of radiation and was approved by the FDA based on efficacy studies in animals, as efficacy studies in humans could not be ethically conducted. Neupogen® (filgrastim) and Neulasta® (pegfilgrastim) are also FDA approved for H-ARS. Myelosuppression occurs when radiation damages the bone marrow; suppression of the bone marrow blocks the production of blood cells. Use of Leukine®, Neupogen®, or Neulasta® can help patients with H-ARS by facilitating recovery of bone marrow cells that develop into white blood cells that help fight off infections. Acute Radiation Syndrome (ARS), sometimes referred to as radiation sickness or radiation toxicity, is an acute illness caused by irradiation of the entire body (or most of the body) by a high dose of penetrating radiation in a very short period of time, which causes depletion of immature parenchymal stem cells in specific tissues. There are three classic ARSs: bone marrow syndrome (also referred to as H-ARS), gastrointestinal syndrome, and cardiovascular/central nervous system syndrome, and four stages of ARS (prodromal stage, latent stage, manifest illness stage, and recovery or death). Examples of people who suffered from ARS are the survivors of the Hiroshima and Nagasaki atomic bombs, the firefighters that first responded after the Chernobyl Nuclear Power Plant event in 1986, and some unintentional exposures to sterilization irradiators.

News:

- **February 2017:** The labels for Granix® (tbo-filgrastim) and Zarxio® (filgrastim-sndz) were updated by the FDA to include glomerulonephritis in the *Warnings and Precautions* section, following postmarketing adverse event reports. If glomerulonephritis is suspected, patients should be evaluated for cause and a dose-reduction or interruption of Granix® or Zarxio® therapy should be considered if causality is likely. Glomerulonephritis is also included in the *Warnings and Precautions* section for Neupogen® (filgrastim) and Neulasta® (pegfilgrastim).

Pipeline:

- **Pegfilgrastim biosimilars:** An abbreviated Biologics License Application (aBLA) has been submitted to the FDA for proposed pegfilgrastim biosimilar products from four different pharmaceutical manufacturers since 2014; however, the FDA has not yet approved any of the proposed pegfilgrastim biosimilar products. Three of the pharmaceutical manufacturers have received complete response letters (CRLs) from the FDA regarding their proposed pegfilgrastim biosimilar product; all of which are working to resolve any issues cited in the CRL and are planning to resubmit the aBLA to the FDA in either 2018

or early 2019. There has also been ongoing litigation with Amgen regarding the possible patent infringement of Amgen's product, Neulasta® (pegfilgrastim).

Recommendations

The College of Pharmacy does not recommend any changes to the current G-CSF prior authorization at this time.

Utilization Details of G-CSFs: Calendar Year 2017

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
FILGRASTIM PRODUCTS						
NEUPOGEN INJ 300MCG	59	21	$331,889.04	$5,625.24	2.8	28.40%
NEUPOGEN INJ 480/0.8	25	13	$117,257.51	$4,690.30	1.9	10.03%
NEUPOGEN INJ 300/0.5	24	11	$209,897.23	$8,745.72	2.2	17.96%
ZARXIO INJ 300/0.5	6	2	$0.00^	$0.00^	3	0.00%
NEUPOGEN INJ 480MCG	3	3	$13,689.05	$4,563.02	1	1.17%
SUBTOTAL	**117**	**50**	**$672,732.83**	**$5,749.85**	**2.3**	**57.56%**
PEGFILGRASTIM PRODUCTS						
NEULASTA INJ 6MG/0.6	105	25	$495,970.14	$4,723.53	4.2	42.44%
SUBTOTAL	**105**	**25**	**$495,970.14**	**$4,723.53**	**4.2**	**42.44%**
TOTAL	**222**	**63***	**$1,168,702.97**	**$5,264.43**	**3.5**	**100%**

^SoonerCare was not the primary coverage on claims for this medication; therefore, costs do not reflect actual drug costs.
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
PEGFILGRASTIM PRODUCTS						
NEULASTA J2505	620	208	$2,559,018.72	$4,127.45	3	97.21%
SUBTOTAL	**620**	**208***	**$2,559,018.72**	**$4,127.45**	**3**	**97.21%**
FILGRASTIM PRODUCTS						
NEUPOGEN J1442	175	38	$72,977.62	$417.01	4.6	2.77%
ZARXIO Q5101	1	1	$360.00	$360.00	1	0.01%
SUBTOTAL	**176**	**39***	**$73,337.62**	**$416.69**	**4.5**	**2.79%**
TOTAL	**796**	**233***	**$2,632,356.34**	**$3,306.98**	**3.4**	**100%**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

[1] U.S. Food and Drug Administration (FDA). sBLA Approval: Leukine® (sargramostim). Available online at: https://www.fda.gov/downloads/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/AboutMCMi/UCM603226.pdf. Issued 03/29/2018. Last accessed 04/17/2018.
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[11] Brennan Z. The Battle Over Neulasta Biosimilars in the U.S.: What's Coming in 2018. *Regulatory Affairs Professionals Society*. Available online at: https://www.raps.org/regulatory-focus%E2%84%A2/news-articles/2018/1/the-battle-over-neulasta-biosimilars-in-the-us-what-s-coming-in-2018. Issued 01/18/2018. Last accessed 04/18/2018.
[12] Cottler M, Whitehill J, Siedor A. The 2018 Biosimilar Litigation Landscape: A Primer. *Biopharma Dive*. Available online at: https://www.biopharmadive.com/news/the-2018-biosimilar-litigation-landscape-a-primer/512982/. Issued 12/14/2017. Last accessed 04/18/2018.

Appendix G

Calendar Year 2017 Annual Review of Elaprase® (Idursulfase)

Oklahoma Health Care Authority
May 2018

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

Hunter syndrome, also known as mucopolysaccharidosis type II or MPS II, is an X-linked recessive genetic disorder caused by insufficient levels of the lysosomal enzyme iduronate-2-sulfatase (I2S). Due to the missing or defective I2S enzyme in patients with Hunter syndrome, glycosaminoglycans (GAGs) progressively accumulate in the lysosomes of a variety of cells, leading to cellular engorgement, organomegaly, tissue destruction, and organ system dysfunction. The vast majority of affected individuals are male. It is estimated that Hunter syndrome occurs in approximately 1 in 100,000 to 1 in 170,000 males. Hunter syndrome is a progressively debilitating disorder; however, age of onset, disease severity, and rate of progression vary significantly among affected individuals. In individuals with early progressive disease, central nervous system (CNS) involvement (manifested primarily by progressive cognitive deterioration), progressive airway disease, and cardiac disease frequently result in death in the first or second decade of life. Survival into the early adult years with normal intelligence is common in the slowly progressing form of the disease. Additional findings in both forms of Hunter syndrome include short stature, macrocephaly with or without communicating hydrocephalus, macroglossia, hoarse voice, conductive and sensorineural hearing loss, hepatosplenomegaly, dysostosis multiplex, spinal stenosis, and carpal tunnel syndrome.

Elaprase® (idursulfase) was approved by the U.S. Food and Drug Administration (FDA) in 2006 as the first enzyme replacement therapy for patients with Hunter syndrome. Idursulfase is a recombinant form of human I2S, produced by recombinant DNA technology in a human cell line and is intended to provide exogenous enzyme for uptake into cellular lysosomes. Idursulfase has a boxed warning for the risk of life-threatening anaphylactic reactions. The recommended dosage regimen of idursulfase is 0.5mg per kilogram (kg) of body weight administered once weekly as an intravenous (IV) infusion.

Cost: The wholesale acquisition cost (WAC) of Elaprase® (idursulfase) is $3,135.84 per 6mg/3mL single-use vial for IV use.

Patient Weight	Dosing Regimen	Vials Per Infusion	Cost Per Weekly Infusion	Cost Per Year
10kg	5mg once weekly	1	$3,135.84	$163,063.68
20kg	10mg once weekly	2	$6,271.68	$326,127.36
55kg	27.5mg once weekly	5	$15,679.20	$815,318.40

Costs based on WAC and do not reflect rebated prices or net costs. Cost per year based on 52 weekly infusions.

Current Prior Authorization Criteria

Elaprase® (Idursulfase) Approval Criteria:

1. An FDA approved diagnosis of Hunter syndrome (mucopolysaccharidosis type II; MPS II) confirmed by:
    a. Enzyme assay demonstrating a deficiency of iduronate-2-sulfatase enzyme activity; or
    b. Molecular genetic testing confirming a hemizygous pathogenic variant in the *IDS* gene; and
2. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling.

Utilization of Elaprase® (Idursulfase): Calendar Year 2017

Comparison of Calendar Years: Pharmacy Claims

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	1	8	$488,559.17	$61,069.90	$2,181.07	468	224
2017	1	10	$699,806.31	$69,980.63	$2,499.31	672	280
% Change	**0.00%**	**25.00%**	**43.20%**	**14.60%**	**14.60%**	**43.60%**	**25.00%**
Change	**0**	**2**	**$211,247.14**	**$8,910.73**	**$318.24**	**204**	**56**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

- There were no paid medical claims for Elaprase® (idursulfase) during calendar year 2017.

Demographics of Members Utilizing Elaprase® (Idursulfase)

- Due to the small number of members utilizing Elaprase® (idursulfase) during calendar year 2017, detailed demographic information could not be provided.

Top Prescriber Specialties of Elaprase® (Idursulfase) by Number of Claims

- The only prescriber specialty listed on paid claims for Elaprase® (idursulfase) during calendar year 2017 was general pediatrician.

Prior Authorization of Elaprase® (Idursulfase)

Prior authorization of Elaprase® (idursulfase) was implemented on September 1, 2017. There was one member on Elaprase® (idursulfase) when the prior authorization was implemented and a pre-emptive approval was granted for this member. There were no additional prior authorization requests submitted for Elaprase® (idursulfase) during calendar year 2017.

Market News and Updates[6]

Pipeline:

- **November 2017:** Sangamo Therapeutics, Inc. announced the first patient in the Phase 1/2 clinical trial evaluating SB-913 had received treatment. SB-913 is an investigational *in vivo* genome editing therapy for individuals with Hunter syndrome. Sangamo received Fast Track, Orphan Drug, and Rare Pediatric Disease designations for the genome editing therapy.

Recommendations

The College of Pharmacy does not recommend any changes to the current Elaprase® (idursulfase) prior authorization criteria at this time.

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[1] Jones S, Wynn R. Mucopolysaccharidoses: Clinical features and diagnosis. *UpToDate*. Available online at: http://www.uptodate.com/contents/mucopolysaccharidoses-clinical-features-and-diagnosis?search=hunter+syndrome&sectionRank=1&anchor=H8&source=machineLearning&selectedTitle=1%7E38#H8. Last revised 09/12/2017. Last accessed 04/18/2018.

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[6] Sangamo Therapeutics, Inc. Sangamo Announces Treatment of First Patient in Landmark Phase 1/2 Clinical Trial Evaluating In Vivo Genome Editing for MPS II. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/sangamo-announces-treatment-of-first-patient-in-landmark-phase-12-clinical-trial-evaluating-in-vivo-genome-editing-for-mps-ii-300556189.html. Issued 11/15/2017. Last accessed 05/01/2018.

Appendix H

Calendar Year 2017 Annual Review of Kuvan® (Sapropterin)

Oklahoma Health Care Authority
May 2018

Introduction[1,2]

Phenylketonuria (PKU) is a disorder affecting the aromatic amino acid, phenylalanine (Phe). It results from a deficiency of phenylalanine hydroxylase (PAH), and if untreated is characterized by intellectual disability. The incidence of PKU is 1 in 13,500 to 19,000 births in the United States. The hepatic enzyme, PAH, catalyzes the conversion of the essential amino acid Phe to tyrosine. Tetrahydrobiopterin (BH4) is a cofactor required for PAH activity. This pathway accounts for most of the catabolism and is responsible for the disposal of approximately 75% of dietary Phe, with the remainder used for protein synthesis. This results in elevated blood and urine concentrations of Phe and its metabolites, phenylacetate and phenyllactate. Defects in BH4 metabolism account for approximately 2% of patients with elevated Phe levels.

Kuvan® (sapropterin) is a PAH activator indicated to reduce blood Phe levels in patients with hyperphenylalaninemia (HPA) due to BH4-responsive PKU. Sapropterin is to be used in conjunction with a Phe-restricted diet. Sapropterin is supplied as 100mg soluble tablets and as 100mg and 500mg powder packets for oral solution.

Current Prior Authorization Criteria

Kuvan® (Sapropterin) Approval Criteria:

1. An FDA approved diagnosis of phenylketonuria; and
2. Documentation of active management with a phenylalanine restricted diet; and
3. Member must not have two null mutations in *trans*; and
4. Initial approvals will be for the duration of 30 days. After which time, the prescriber must verify that the member responded to treatment as defined by laboratory documentation of ≥30% decrease in blood phenylalanine levels from baseline.
    a. If the member was initiated at 10mg/kg/day dose, then a subsequent trial of 20mg/kg/day for a duration of 30 days can be approved. After which time, the prescriber must verify that the member responded to treatment as defined by laboratory documentation of ≥30% decrease in blood phenylalanine levels from baseline.
    b. If the member was initiated at 20mg/kg/day dose, then no additional approvals will be granted after a trial period of 30 days if the member did not respond to treatment as defined by laboratory documentation of ≥30% decrease in blood phenylalanine levels from baseline.
5. Subsequent approvals will be for the duration of one year.

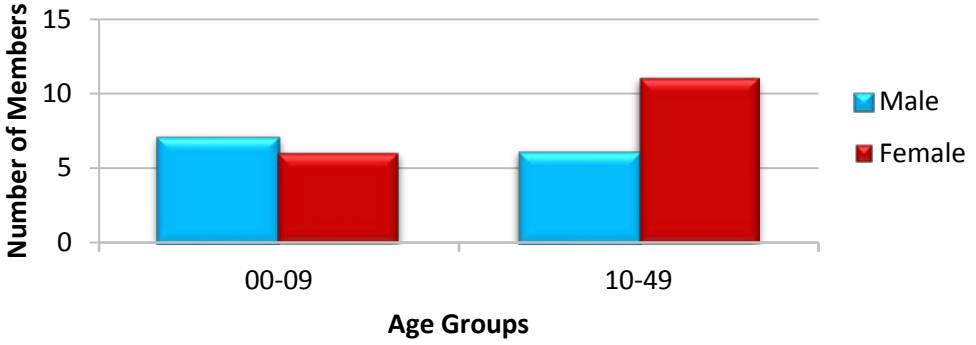
Utilization of Kuvan® (Sapropterin): Calendar Year 2017

Comparison of Calendar Years

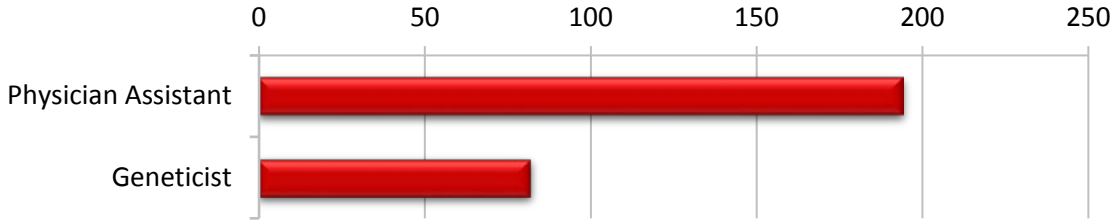
Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	26	250	$1,468,182.41	$5,872.73	$195.81	37,710	7,498
2017	30	276	$1,881,559.75	$6,817.25	$226.91	43,440	8,292
% Change	**15.40%**	**10.40%**	**28.20%**	**16.10%**	**15.90%**	**15.20%**	**10.60%**
Change	**4**	**26**	**$413,377.34**	**$944.52**	**$31.10**	**5,730**	**794**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

Demographics of Members Utilizing Kuvan® (Sapropterin)



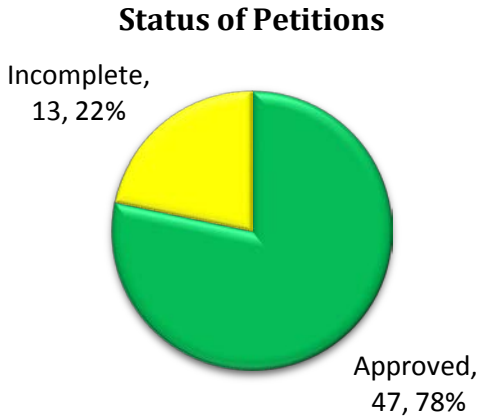
Top Prescriber Specialties of Kuvan® (Sapropterin) by Number of Claims



- After further analysis, the physician assistant's supervising physician was found to be a geneticist.

Prior Authorization of Kuvan® (Sapropterin)

There were 60 prior authorization requests submitted for Kuvan® (sapropterin) during calendar year 2017. The prior authorization of Kuvan® (sapropterin) was implemented on August 30, 2017. Members currently utilizing Kuvan® (sapropterin) at the time of implementation were grandfathered and given pre-emptive approvals, as reflected by the high approval rate in the following chart. The following chart shows the status of the submitted petitions for calendar year 2017.



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

Anticipated Patent Expiration(s):

- Kuvan® (sapropterin) tablet: May 2026
- Kuvan® (sapropterin) powder: November 2032

News:

- **April 2017:** BioMarin Pharmaceutical, Inc. announced that it has entered into a settlement agreement with Par Pharmaceutical that resolved patent litigation in the United States related to BioMarin's Kuvan® (sapropterin). Under the terms of the settlement, BioMarin will grant Par a non-exclusive license to its patents related to Kuvan® to allow Par to market a generic version of sapropterin 100mg tablets and powder for oral solution in 100mg and 500mg sachets for the indications approved for Kuvan® beginning October 1, 2020 or earlier under certain circumstances.

Pipeline:

- **October 2017:** Synlogic, a clinical stage company applying synthetic biology to probiotics to develop novel living medicines, announced that the U.S. Food and Drug Administration (FDA) has granted Orphan Drug designation to SYNB1618, Synlogic's preclinical-stage drug candidate for the treatment of PKU. SYNB1618, an oral medication, is designed to complement the missing function in patients with PKU by providing alternative metabolic pathways to consume Phe. Synlogic plans to file an Investigational New Drug Application (IND) with the FDA for SYNB1618 for the potential treatment of PKU in early 2018.
- **December 2017:** BioMarin Pharmaceutical, Inc. announced that the FDA will require additional time to complete its review of the Biologics License Application (BLA) for the investigational therapy pegvaliase. It is a PEGylated recombinant phenylalanine ammonia lyase enzyme product intended to reduce blood Phe levels in adult patients with PKU who have uncontrolled blood Phe levels on existing management. In a notice received from the FDA, the Prescription Drug User Fee Act (PDUFA) goal date for pegvaliase has been extended by three months to May 2018. Previously, the FDA had requested additional information on Chemistry, Manufacturing, and Controls (CMC), which was likely to be the reason for the three month extension of the PDUFA date.

Recommendations

The College of Pharmacy does not recommend any changes to the current Kuvan® (sapropterin) prior authorization criteria at this time.

Utilization Details of Kuvan® (Sapropterin): Calendar Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
KUVAN TAB 100MG	153	16	$1,212,406.15	$266.93	$7,924.22	64.44%
KUVAN POW 100MG	65	11	$172,455.65	$88.44	$2,653.16	9.16%
KUVAN POW 500MG	58	9	$496,697.95	$275.94	$8,563.76	26.40%
TOTAL	**276**	**30***	**$1,881,559.75**	**$226.91**	**$6,817.25**	**100.00%**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

[1] Bodamer OA. Overview of phenylketonuria. *UpToDate*. Available online at: http://www.uptodate.com/contents/overview-of-phenylketonuria?search=pku&source=search_result&selectedTitle=1%7E118. Last revised 06/21/2016. Last accessed 04/17/2018.
[2] Kuvan® Prescribing Information. BioMarin Pharmaceutical Inc. Available online at: https://www.kuvan.com/hcp/wp-content/file/KUVAN_Prescribing_Information1.pdf. Last revised 08/2016. Last accessed 04/17/2018.
[3] U.S. Food and Drug Administration (FDA) Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: https://www.accessdata.fda.gov/scripts/cder/ob/. Last revised 03/2018. Last accessed 04/17/2018.
[4] BioMarin Pharmaceutical Inc. BioMarin Announces Kuvan® (sapropterin dihydrochloride) Patent Challenge Settlement. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/biomarin-announces-kuvan-sapropterin-dihydrochloride-patent-challenge-settlement-300439214.html. Issued 04/13/2017. Last accessed 04/17/2018.
[5] Synlogic. News Release. Synlogic Receives Orphan Drug Designation for SYNB1618, a Synthetic BioticTM Medicine for the Treatment of Phenylketonuria. Available online at: https://investor.synlogictx.com/news-releases/news-release-details/synlogic-receives-orphan-drug-designation-synb1618-synthetic. Issued 10/24/2017. Last accessed 04/17/2018.
[6] BioMarin Pharmaceutical Inc. BioMarin Receives Anticipated Notification of PDUFA Extension for Pegvaliase Biologics License Application (BLA) to May 28, 2018. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/biomarin-receives-anticipated-notification-of-pdufa-extension-for-pegvaliase-biologics-license-application-bla-to-may-28-2018-300574811.html. Issued 12/22/2017. Last accessed 04/17/2018.

Appendix I

Calendar Year 2017 Annual Review of Ophthalmic Anti-Inflammatories

Oklahoma Health Care Authority
May 2018

Current Prior Authorization Criteria

Ophthalmic Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)	
Tier-1	**Tier-2**
diclofenac (Voltaren®) 0.1% soln	bromfenac (Bromday®) 0.09% soln
flurbiprofen (Ocufen®) 0.03% soln$^{\Delta}$	bromfenac (BromSite™) 0.075% soln
ketorolac (Acular®) 0.5% soln	bromfenac (Prolensa®) 0.07% soln
nepafenac (Ilevro®) 0.3% susp*	ketorolac (Acular LS®) 0.4% soln
	ketorolac (Acuvail®) 0.45% soln
	nepafenac (Nevanac®) 0.1% susp

soln = solution; susp = suspension
$^{\Delta}$ Not a required Tier-1 trial. Does not have to be attempted for approval of a Tier-2 medication.
*Ilevro® (nepafenac) 0.3% suspension was moved from Tier-2 to Tier-1 by the Oklahoma Health Care Authority (OHCA) on 01/01/2018 as a result of supplemental rebate participation.
Tier structure based on supplemental rebate participation, and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Ophthalmic Non-Steroidal Anti-Inflammatory Drug (NSAIDs) Tier-2 Approval Criteria:

1. Documented trials of all Tier-1 ophthalmic NSAIDs (from different medication lines) in the last 30 days that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or
2. Contraindication(s) to all lower tiered medications; or
3. A unique indication for which the Tier-1 ophthalmic NSAIDs lack.

Ophthalmic Corticosteroids	
Tier-1	**Tier-2**
dexamethasone sodium phosphate 0.1% soln	fluorometholone (FML Forte®) 0.25% susp
dexamethasone (Maxidex®) 0.1% susp	fluorometholone (FML S.O.P®) 0.1% oint
difluprednate (Durezol®) 0.05% emul	loteprednol (Lotemax®) 0.5% gel
fluorometholone (FML Liquifilm®) 0.1% susp	loteprednol (Lotemax®) 0.5% oint
fluorometholone (Flarex®) 0.1% susp	Pred Forte® (brand) prednisolone acetate 1% susp
loteprednol (Lotemax®) 0.5% susp	
prednisolone acetate (Omnipred®) 1% susp	
prednisolone acetate (Pred Mild®) 0.12% susp	
prednisolone sodium phosphate 1% soln	
rimexolone (Vexol®) 1% susp	

soln = solution; susp = suspension; emul = emulsion; oint = ointment
Tier structure based on supplemental rebate participation, and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Ophthalmic Corticosteroids Tier-2 Approval Criteria:

1. Documented trials of all Tier-1 ophthalmic corticosteroids (from different product lines) in the last 30 days that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or
2. Contraindication(s) to all lower-tiered medications; or
3. A unique indication for which the Tier-1 ophthalmic corticosteroids lack.

Utilization of Ophthalmic Anti-Inflammatories: Calendar Year 2017

Comparison of Calendar Years: Ophthalmic NSAIDs

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	569	738	$9,770.89	$13.24	$0.63	3,904	15,523
2017	580	740	$12,458.37	$16.84	$0.78	4,016	15,940
% Change	**1.90%**	**0.30%**	**27.50%**	**27.20%**	**23.80%**	**2.90%**	**2.70%**
Change	**11**	**2**	**$2,687.48**	**$3.60**	**$0.15**	**112**	**417**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

- Some Tier-1 products participate in supplemental rebates; therefore, costs shown do not reflect net costs.

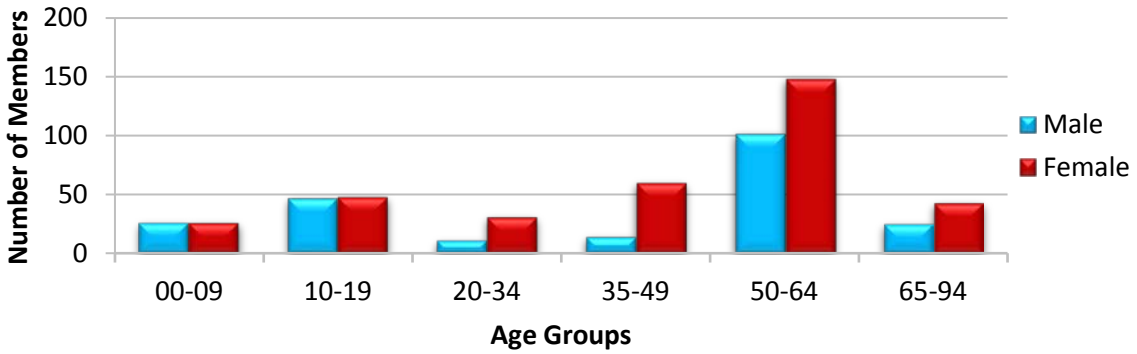
Comparison of Calendar Years: Ophthalmic Corticosteroids

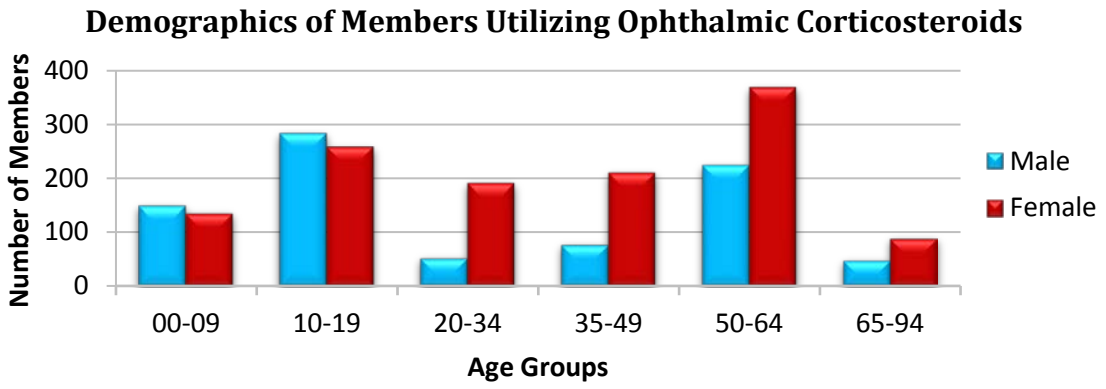
Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	2,153	3,096	$287,015.50	$92.71	$3.67	21,424	78,212
2017	2,089	3,019	$272,779.46	$90.35	$3.54	20,818	77,071
% Change	**-3.00%**	**-2.50%**	**-5.00%**	**-2.50%**	**-3.50%**	**-2.80%**	**-1.50%**
Change	**-64**	**-77**	**-$14,236.04**	**-$2.36**	**-$0.13**	**-606**	**-1,141**

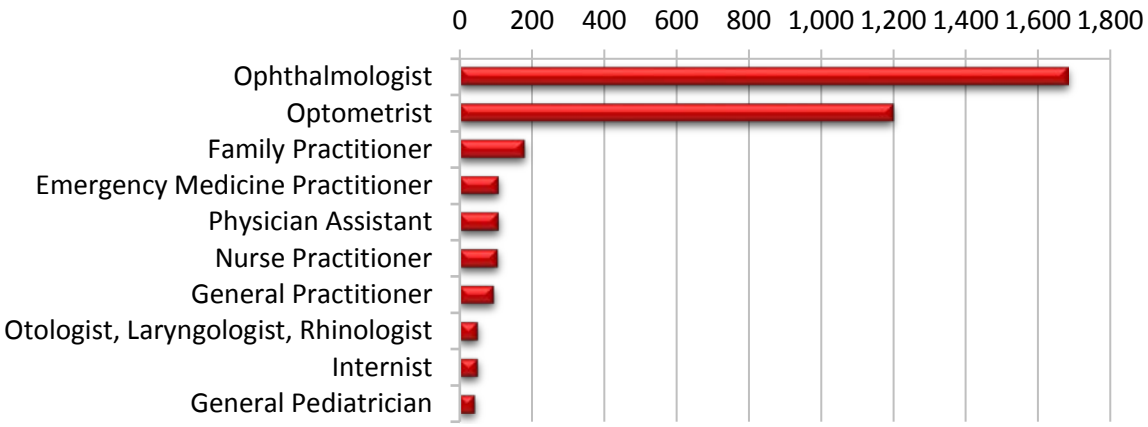
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

- Some Tier-1 products participate in supplemental rebates; therefore, costs shown do not reflect net costs.

Demographics of Members Utilizing Ophthalmic NSAIDs

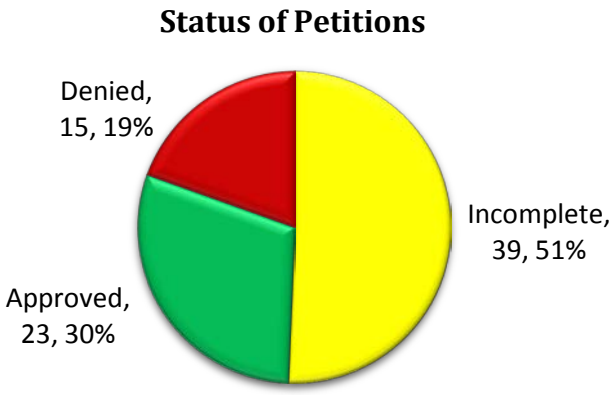






Prior Authorization of Ophthalmic Anti-Inflammatories

There were 77 prior authorization requests submitted for ophthalmic anti-inflammatories during calendar year 2017. The following chart shows the status of the submitted petitions for calendar year 2017.



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

Anticipated Patent Expiration(s):

- Durezol® (difluprednate 0.05%): November 2019

- Nevanac® (nepafenac 0.1%): January 2027
- Acular LS® (ketorolac 0.4%): November 2027
- Acuvail® (ketorolac 0.45%): August 2029
- BromSite™ (bromfenac 0.075%): September 2029
- Ilevro® (nepafenac 0.3%): March 2032
- Prolensa® (bromfenac 0.07%): November 2033

News:

- **June 2016:** Vexol® (rimexolone) 1% suspension was discontinued by Alcon. The U.S. Food and Drug Administration (FDA) indicates it was discontinued for reasons other than safety or efficacy.
- **February 2017:** Allergan discontinued Ocufen® (flurbiprofen) ophthalmic solution. Allergan made a business decision to permanently discontinue manufacturing the branded, authorized generic, and a repackaged version of the branded drug. After a shortage due to delays in manufacturing, Valeant Pharmaceuticals has made a generic formulation of flurbiprofen sodium ophthalmic solution 0.03% available in a 2.5mL bottle.

Recommendations

The College of Pharmacy recommends removing Vexol® (rimexolone) 1% suspension from the ophthalmic corticosteroid tier chart due to product discontinuation. The recommended change is shown in red in the following tier chart.

Ophthalmic Corticosteroids	
Tier-1	**Tier-2**
dexamethasone sodium phosphate 0.1% soln	fluorometholone (FML Forte®) 0.25% susp
dexamethasone (Maxidex®) 0.1% susp	fluorometholone (FML S.O.P®) 0.1% oint
difluprednate (Durezol®) 0.05% emul	loteprednol (Lotemax®) 0.5% gel
fluorometholone (FML Liquifilm®) 0.1% susp	loteprednol (Lotemax®) 0.5% oint
fluorometholone (Flarex®) 0.1% susp	Pred Forte® (brand) prednisolone acetate 1% susp
loteprednol (Lotemax®) 0.5% susp	
prednisolone acetate (Omnipred®) 1% susp	
prednisolone acetate (Pred Mild®) 0.12% susp	
prednisolone sodium phosphate 1% soln	
~~rimexolone (Vexol®) 1% susp~~	

soln = solution; susp = suspension; emul = emulsion; oint = ointment
Tier structure based on supplemental rebate participation, and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Utilization Details of Ophthalmic NSAIDs: Calendar Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
TIER-1 MEDICATIONS						
KETOROLAC PRODUCTS						
KETOROLAC SOL 0.5%	554	433	$9,389.98	$0.76	$16.95	75.36%
SUBTOTAL	**554**	**433**	**$9,389.98**	**$0.76**	**$16.95**	**75.36%**
DICLOFENAC PRODUCTS						
DICLOFENAC SOL 0.1%	182	147	$2,780.31	$0.79	$15.28	22.32%
SUBTOTAL	**182**	**147**	**$2,780.31**	**$0.79**	**$15.28**	**22.32%**
FLURBIPROFEN PRODUCTS						
FLURBIPROFEN SOL 0.03%	3	3	$39.26	$1.27	$13.09	0.32%
SUBTOTAL	**3**	**3**	**$39.26**	**$1.27**	**$13.09**	**0.32%**
TIER-1 SUBTOTAL	**739**	**583**	**$12,209.55**	**$0.77**	**$16.52**	**98.00%**
TIER-2 MEDICATIONS						
NEPAFENAC PRODUCTS						
NEVANAC SUS 0.1%	1	1	$248.82	$16.59	$248.82	2.00%
SUBTOTAL	**1**	**1**	**$248.82**	**$16.59**	**$248.82**	**2.00%**
TIER-2 SUBTOTAL	**1**	**1**	**$248.82**	**$16.59**	**$248.82**	**2.00%**
TOTAL	**740**	**580***	**$12,458.37**	**$0.78**	**$16.84**	**100.00%**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

- Some Tier-1 products participate in supplemental rebates; therefore, costs shown do not reflect net costs.

Utilization Details of Ophthalmic Corticosteroids: Calendar Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
TIER-1 MEDICATIONS						
PREDNISOLONE PRODUCTS						
PREDNISOLONE SUS 1%	2,002	1,437	$119,480.92	$2.24	$59.68	43.80%
PRED MILD SUS 0.12%	28	15	$4,811.71	$6.45	$171.85	1.76%
PRED SOD PHO SOL 1%	5	5	$287.84	$2.50	$57.57	0.11%
SUBTOTAL	**2,035**	**1,457**	**$124,580.47**	**$2.30**	**$61.22**	**45.67%**
DIFLUPREDNATE PRODUCTS						
DUREZOL EMU 0.05%	365	228	$60,878.63	$6.63	$166.79	22.32%
SUBTOTAL	**365**	**228**	**$60,878.63**	**$6.63**	**$166.79**	**22.32%**
LOTEPREDNOL PRODUCTS						
LOTEMAX SUS 0.5%	229	169	$55,547.36	$8.90	$242.56	20.36%
SUBTOTAL	**229**	**169**	**$55,547.36**	**$8.90**	**$242.56**	**20.36%**
FLUOROMETHOLONE PRODUCTS						
FLUOROMETH SUS 0.1%	186	155	$16,397.35	$4.01	$88.16	6.01%
FML LIQUIFLM SUS 0.1%	18	13	$2,741.01	$7.05	$152.28	1.00%
FLAREX SUS 0.1%	5	5	$372.66	$4.23	$74.53	0.14%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
SUBTOTAL	**209**	**173**	**$19,511.02**	**$4.27**	**$93.35**	**7.15%**
DEXAMETHASONE PRODUCTS						
DEXAMETH PHOS SOL 0.1%	160	142	$9,948.11	$3.93	$62.18	3.65%
MAXIDEX SUS 0.1%	13	11	$1,231.85	$5.55	$94.76	0.45%
SUBTOTAL	**173**	**153**	**$11,179.96**	**$4.06**	**$64.62**	**4.10%**
TIER-1 SUBTOTAL	**3,011**	**2,180**	**$271,697.44**	**$3.53**	**$90.23**	**99.60%**
TIER-2 MEDICATIONS						
FLUOROMETHOLONE PRODUCTS						
FML OIN 0.1%	8	3	$1,082.02	$5.64	$135.25	0.40%
SUBTOTAL	**8**	**3**	**$1,082.02**	**$5.64**	**$135.25**	**0.40%**
TIER-2 SUBTOTAL	**8**	**3**	**$1,082.02**	**$5.64**	**$135.25**	**0.40%**
TOTAL	**3,019**	**2,089***	**$272,779.46**	**$3.54**	**$90.35**	**100.00%**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

- Some Tier-1 products participate in supplemental rebates; therefore, costs shown do not reflect net costs.

[1] U.S. Food and Drug Administration (FDA) Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: https://www.accessdata.fda.gov/scripts/cder/ob/. Last revised 03/2018. Last accessed 04/17/2018.
[2] American Society of Health-System Pharmacists (ASHP). Drug Shortages. Flurbiprofen Sodium Ophthalmic Solution. Available online at: https://www.ashp.org/drug-shortages/current-shortages/Drug-Shortage-Detail.aspx?id=342. Issued 03/01/2018. Last accessed 04/17/2018.
[3] Han DH. Ocufen Eye Drops No Longer Available. *MPR*. Available online at: https://www.empr.com/news/ocufen-eye-drops-no-longer-available/article/575382/. Issued 11/28/2016. Last accessed 04/17/2018.
[4] FDA. Drug Approvals and Databases: Additions/Deletions for Prescription and OTC Drug Product Lists: June 2016. Available online at: https://www.fda.gov/Drugs/InformationOnDrugs/ucm086229.htm. Issued 07/15/2016. Last accessed 04/20/2018.

Appendix J

Calendar Year 2017 Annual Review of Topical Acne Products

Oklahoma Health Care Authority
May 2018

Current Prior Authorization Criteria

Aczone® (Dapsone Gel) Approval Criteria:

1. An FDA approved indication of acne vulgaris; and
2. Member must be 20 years of age or younger; and
3. A previous trial of benzoyl peroxide or a patient-specific, clinically significant reason why benzoyl peroxide is not appropriate for the member; and
4. A previous trial of a topical antibiotic, such as clindamycin or erythromycin, or a patient-specific, clinically significant reason why a topical antibiotic is not appropriate for the member.

Tazorac® (Tazarotene Cream and Gel) Approval Criteria:

1. An FDA approved indication of acne vulgaris or plaque psoriasis; and
2. Female members must not be pregnant and must be willing to use an effective method of contraception during treatment; and
3. Authorization of ~~generic~~ tazarotene 0.1% cream will require a patient-specific, clinically significant reason why the member cannot use the other formulations of tazarotene (brand Tazorac® 0.05% cream, 0.05% gel, and 0.1% gel are preferred) ~~will require a patient-specific, clinically significant reason why the member cannot use the brand formulation (brand formulation is preferred)~~; and
4. For a diagnosis of acne vulgaris, the following must be met:
   a. Member must be 20 years of age or younger; and
   b. Based on current net costs, Tazorac® 0.05% gel, 0.05% cream, and 0.1% gel will not require prior authorization for members 20 years of age or younger; and
5. A quantity limit of 60 grams per 30 days will apply.

Utilization of Topical Acne Products: Calendar Year 2017

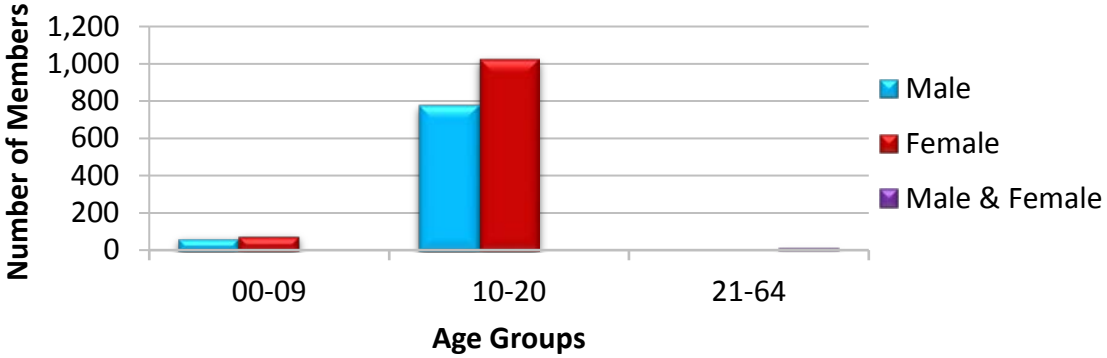
Comparison of Calendar Years: Topical Acne Products

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	2,134	3,424	$1,570,584.60	$458.70	$18.29	143,115	85,878
2017	1,952	2,955	$1,265,767.02	$428.35	$17.15	119,285	73,788
% Change	**-8.50%**	**-13.70%**	**-19.40%**	**-6.60%**	**-6.20%**	**-16.70%**	**-14.10%**
Change	**-182**	**-469**	**-$304,817.58**	**-$30.35**	**-$1.14**	**-23,830**	**-12,090**

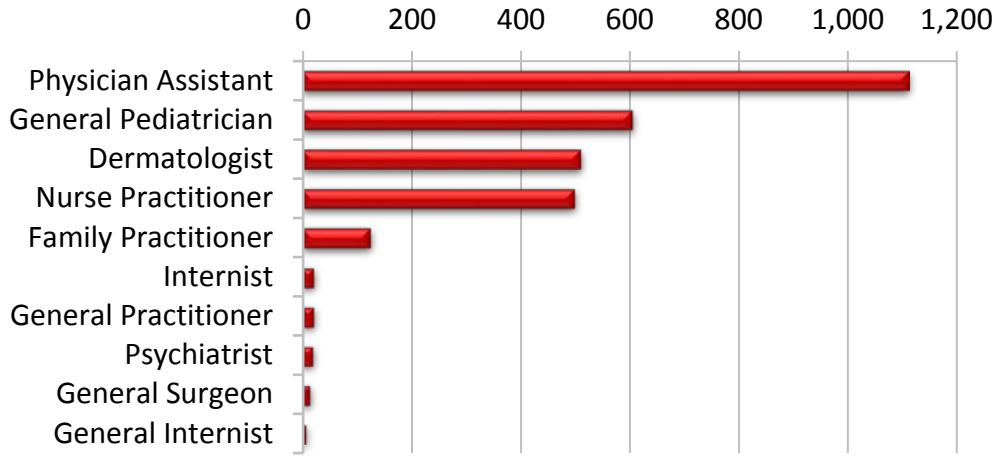
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

- Please note, Aczone® and Tazorac® both have significant federal rebates and costs included in this report do not reflect rebated prices or net costs.

Demographics of Members Utilizing Topical Acne Products



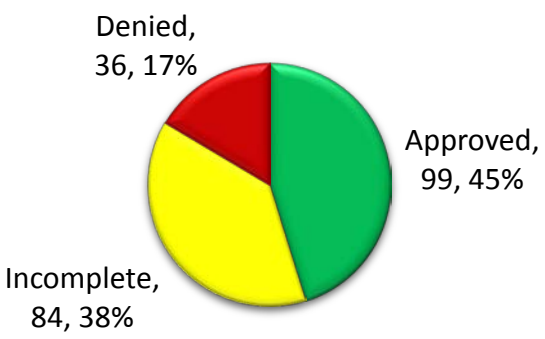
Top Prescriber Specialties of Topical Acne Products by Number of Claims



Prior Authorization of Topical Acne Products

There were 219 prior authorization requests submitted for topical acne products during calendar year 2017. The current prior authorization criteria for topical acne products went into effect on December 4, 2017. The following chart shows the status of the submitted petitions for calendar year 2017.

Status of Petitions



Market News and Updates[1]

Anticipated Patent Expiration(s):

- Aczone® (dapsone 7.5% gel): November 2033

Recommendations

The College of Pharmacy recommends the changes noted in red, based on current net costs, in the *Current Prior Authorization* section of this report. These changes will be voted on in the following live meeting.

Utilization Details of Topical Acne Products: Calendar Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
TAZAROTENE PRODUCTS						
TAZORAC CRE 0.05%	1,736	1,254	$742,168.80	$427.52	1.4	58.63%
TAZAROTENE CRE 0.1%	412	295	$149,160.28	$362.04	1.4	11.78%
TAZORAC GEL 0.05%	279	211	$119,070.86	$426.78	1.3	9.41%
TAZORAC CRE 0.1%	274	213	$131,135.76	$478.60	1.3	10.36%
TAZORAC GEL 0.1%	226	162	$108,983.86	$482.23	1.4	8.61%
SUBTOTAL	**2,927**	**2,135**	**$1,250,519.56**	**$427.24**	**1.4**	**98.80%**
DAPSONE PRODUCTS						
ACZONE GEL 7.5%	28	20	$15,247.46	$544.55	1.4	1.20%
SUBTOTAL	**28**	**20**	**$15,247.46**	**$544.55**	**1.4**	**1.20%**
TOTAL	**2,955**	**1,952***	**$1,265,767.02**	**$428.35**	**1.5**	**100%**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

- Please note, Aczone® and Tazorac® both have significant federal rebates and costs included in this report do not reflect rebated prices or net costs.

[1] U.S. Food and Drug Administration (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 03/2018. Last accessed 04/19/2018.

Appendix K

Industry News and Updates

Oklahoma Health Care Authority
May 2018

Introduction

The following report is an overview of recent issues, important literature, and select guideline updates impacting pharmacy and health care. Information that is expected to have a particular impact in the SoonerCare population has been included for review.

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

News:

- **Neonatal Abstinence Syndrome (NAS):** Researchers found that in 2014 alone, hospital costs for infants covered by Medicaid born with NAS totaled over $460 million. Dr. Tyler N.A. Winkelman, MD, of Hennepin County Medical Center in Minneapolis reported that NAS incidence among infants covered by Medicaid increased from 2.8 per 1,000 births in 2004 to 14.4 per 1,000 births in 2014. Infants covered by Medicaid with NAS were more likely to be boys, have comorbidities "reflective of the syndrome", and live in a rural county, compared with infants covered by Medicaid without NAS. Researchers examined hospital birth data from 2004 to 2014 in the National Inpatient Sample. The authors found that, in this pooled national sample, Medicaid was the primary payer for 43.9% of hospital births. According to the researchers, Medicaid was found to be the primary payer for 73.7% of NAS-related births in 2004 and 82% of these births in 2014. Compared to infants with NAS on private insurance, infants covered by Medicaid with NAS were significantly more likely to be transferred to another hospital for care (8.6% vs. 7.1%; P=0.02) and have longer lengths of stay (16.5 vs. 14.6 days; P<0.001). The researchers stated that limitations included potential misclassification bias from National Inpatient Sample data, and that reasons for the rising incidence of NAS could be improved awareness and recognition of it.
- **Low-Dose Naltrexone (LDN):** According to Jarred W. Younger, PhD, director of the Neuroinflammation, Pain, and Fatigue Lab at the University of Alabama, LDN may be a low-cost, nonaddictive opioid alternative for patients with chronic pain, pending further study. Naltrexone is an opioid antagonist currently available as a 50mg tablet for the treatment of alcohol and opioid dependence. The medication may also exert anti-inflammatory effects via a separate mechanism targeting microglial cells. The dose found to reduce pain is roughly one-tenth the substance abuse treatment dose and is not approved by the U.S. Food and Drug Administration (FDA); therefore, it must be specially compounded. Younger noted that in studies of several known inflammatory conditions, such as inflammatory bowel disease and multiple sclerosis, LDN reduced self-reported pain, objective markers of inflammation, and disease severity. At a 2-day summit held in Salt Lake City in March 2018, a panel of 13 clinicians who specialize in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) selected LDN as a top

medication for that patient population. The panel of clinicians also placed LDN at the top of a wish list for randomized clinical trials for the treatment of ME/CFS. Currently, there is no FDA approved treatment for ME/CFS and treatment of the condition focuses on the relief of symptoms. Patients with ME/CFS also often times meet clinical criteria for fibromyalgia and LDN has shown benefit in several of Younger's studies. Companies are currently working to gain FDA approval for naltrexone 1mg and 4.5mg.

- **Deprescribing Antipsychotics:** A clinical practice guideline is to be published in a series developed by the Deprescribing guidelines for the elderly project, based at the Bruyère Research Institute in Ontario, Canada. The practice guideline is focused on antipsychotic drugs. The other guidelines in the series have discussed proton pump inhibitors, antihyperglycemics, and cholinesterase inhibitors. The aim of the new guideline is to help clinicians determine whether an antipsychotic medication is being used appropriately and whether the medication can be discontinued. Antipsychotics are used for the treatment of many psychiatric disorders, such as schizophrenia and bipolar disorder; however, they are also widely used for the control of behavioral and psychological symptoms of dementia (BPSD) in elderly patients. BPSD includes delusions, hallucinations, aggression, agitation, anxiety, irritability, depression, and psychosis. Clinical studies of antipsychotic medications showed small but statistically significant improvements in BPSD compared with placebo; however, treatment was associated with an increased risk of adverse events, including stroke, death, extrapyramidal symptoms, and major cardiovascular events. The FDA issued warnings regarding the increased risk of mortality associated with antipsychotic medication use in older adults with dementia and these medications now carry a "boxed warning" about the risk. The 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults advises that antipsychotics should be avoided for BPSD unless nonpharmacologic options such as behavioral intervention have failed or are not possible and the patient is threatening "substantial" self-harm or harm to others. However, despite these warnings, antipsychotics are often prescribed for BPSD. The practice guideline and algorithm are based on data from studies of withdrawal versus continuation of antipsychotic medications used for BPSD. These studies suggest that many older patients with BPSD can have their chronic antipsychotic medication withdrawn without detrimental effects on their behavior. Recommendations on the use of antipsychotics in treating insomnia were based on a systematic review of studies on the efficacy of antipsychotics in treating insomnia because no deprescribing studies in this setting had been published. The authors concluded that atypical antipsychotics should be avoided as first-line treatment of primary insomnia until further evidence is available and additional studies are needed. According to the guideline algorithm, if a patient with dementia has been treated with an antipsychotic for 3 months or more and their symptoms are controlled or they have not had a response, consideration should be given to discontinuing the medication. There is currently no evidence to show that one tapering approach is better than another. The guideline suggests a 25 to 50% reduction in dose every 1 to 2 weeks. If symptoms return and are completely unmanageable, another antipsychotic might be worth considering. Furthermore, it may be helpful to

consult a geriatric psychiatrist if three or four approaches to managing a patient's behavioral symptoms have failed.

- **Stimulant Epidemic:** Drug forecasting experts say a new wave of addiction is coming. Abuse of stimulants, such as methamphetamine (meth), cocaine, and prescription medications like Adderall® and Ritalin®, is surging across the United States. According to John Eadie, coordinator for the National Emerging Threat Initiative, which provides research to the government's High Intensity Drug Trafficking Areas program, for every kilogram of heroin seized over the last 5 years by drug enforcement agents, 15 kilograms of stimulants have been seized. Data from government surveys on drug use show that stimulant use is rising and in some cases outpaces opioid use. Additionally, the number of people who are dying from stimulants is also rising. The reasons for the increase are not well understood. Historically, drug abuse tends to happen in cycles. Melvin Patterson, a spokesperson for the Drug Enforcement Administration (DEA) in Washington, D.C., states people who take stimulants generally crave a different kind of high than those who abuse opioids, so he states a stimulant epidemic is likely to affect a different pool of users. However, there is some overlap. People who are addicted to opioids are also using stimulants to help them function. Ed Craft, DrPH, a public health analyst for the Substance Abuse and Mental Health Services Administration in Washington, D.C., states that the National Institute on Drug Abuse is working to develop medications for stimulant abuse. He says that demand for meth addiction treatment services is on the rise in some parts of the country. In 2005, Congress made it more difficult to obtain pseudoephedrine in the United States. This helped to decrease domestic supplies of meth; however, production moved to Mexico. In Mexico, the drug is made with a potent chemical normally used to clean swimming pools called phenyl-2-propanone, or P2P. Craft states that "As a result of using this product, meth is a lot purer now and a lot cheaper and in plentiful supply. Because it's purer and cheaper, more people are using it, and more people are using more." This powerful meth can cause psychotic reactions, which may lead to some people needing ongoing residential treatment after a psychotic breakdown. Cocaine supplies are also up due to a record crop production in Colombia. In Colombia, the government made a deal with farmers to not destroy coca plants and instead offered to pay them if they switched to other crops. The plan has so far backfired as more farmers began growing coca to qualify for the cash. According to the DEA, in 2016 cocaine availability and use were at their highest levels in a decade. Furthermore, prescriptions for stimulant medications are up for all age groups according to data from prescription drug monitoring programs.
- **Patient Advocacy Groups:** Kaiser Health News (KHN) has created a first-of-its kind database, called Pre$cription for Power, to track donations from drug manufacturers to patient advocacy groups. The new database logged 12,000 donations from large publicly traded pharmaceutical companies to patient advocacy groups in 2015 and revealed that these companies gave at least $116 million to patient advocacy organizations. Companies do not have to report payments to patient advocacy groups, unlike payments to doctors or lobbying expenses. KHN examined the 20 pharmaceutical companies included in the S&P 500, noting that 14 were transparent, in varying degrees, about the money given to patient groups. The database is based on information within

charitable giving reports from company websites and federal 990 regulatory filings. While the primary mission of patient advocacy groups is to focus attention on the needs of patients with a particular disease, some groups effectively supplement the work of lobbyists by providing patients to testify on Capitol Hill and organizing letter-writing and social media campaigns that are beneficial to pharmaceutical companies. The data shows that six pharmaceutical companies contributed a million dollars or more to individual groups that represent patients who rely on their medications. The financial ties between pharmaceutical companies and patient advocacy groups that represent those who use their medications has been a growing concern as drug prices escalate. The Senate investigated conflicts of interest prior to the passage of the 2010 Physician Payments Sunshine Act, a law that requires payments to physicians from pharmaceutical companies to be registered on a public website, but patient advocacy groups were not addressed in the bill. The Pre$cription for Power database will continue to expand to include new disclosures; however, not all pharmaceutical companies are willing to disclose their company giving.

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[2] Tucker ME. Low-dose Naltrexone Explored as Option for Chronic Pain. *Medscape*. Available online at: https://www.medscape.com/viewarticle/894020?nlid=121316_745&src=WNL_mdplsfeat_180320_mscpedit_phar&uac=163910MN&spon=30&impID=1585828&faf=1#vp_1. Issued 03/16/2018. Last accessed 03/28/2018.

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[4] Goodman B. Experts Warn of Emerging 'Stimulant Epidemic'. *Medscape*. Available online at: https://www.medscape.com/viewarticle/894794#vp_2. Issued 04/04/2018. Last accessed 04/10/2018.

[5] Kopp E, Lupkin S, Lucas E. Patient Advocacy Groups Take in Millions From Drugmakers. Is there a Payback? *Kaiser Health News*. Available online at: https://khn.org/news/patient-advocacy-groups-take-in-millions-from-drugmakers-is-there-a-payback/. Issued 04/06/2018. Last accessed 04/11/2018.

Appendix L

U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates (additional information can be found at http://www.fda.gov/Drugs/default.htm)

FDA NEWS RELEASE

For Immediate Release: April 6th, 2018

FDA approves rucaparib for maintenance treatment of recurrent ovarian, fallopian tube, or primary peritoneal cancer

On April 6, 2018, the FDA approved rucaparib (Rubraca®, Clovis Oncology Inc.), a poly ADP-ribose polymerase (PARP) inhibitor, for the maintenance treatment of recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy.
Approval was based on ARIEL3 (NCT01968213), a randomized, double-blind, placebo-controlled trial in 561 patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who had been treated with at least two prior treatments of platinum-based chemotherapy and were in complete or partial response to the most recent platinum-based chemotherapy. Patients were randomized (2:1) to rucaparib 600mg orally twice daily (N=372) or placebo (N=189) and were treated until disease progression or unacceptable toxicity. Tumor tissue samples were examined with a next-generation sequencing assay to determine whether DNA contained a deleterious somatic or germline BRCA mutation (tBRCA). This test was also used to determine the percentage of genomic loss of heterozygosity (LOH). Positive homologous recombination deficiency (HRD) status was defined as tBRCA-positive and/or LOH high. Three patient outcomes analyses were performed on the following groups: all patients, HRD subgroup, and tBRCA subgroup.
ARIEL3 demonstrated a statistically significant improvement in estimated median progression-free survival (PFS) assessed by investigator for patients randomized to rucaparib compared with placebo in all patients (median PFS 10.8 vs. 5.4 months, HR 0.36; 95% CI: 0.30, 0.45; P<0.0001), in the HRD subgroup (median PFS 13.6 vs. 5.4 months, HR 0.32; 95% CI: 0.24, 0.42; P<0.0001), and in the tBRCA subgroup (median PFS 16.6 vs. 5.4 months, HR 0.23; 95% CI: 0.16, 0.34; P<0.0001).
The FDA also concurrently approved the complementary diagnostic test, FoundationFocus™ CDx BRCA LOH, for tumor samples to determine HRD status.
In ARIEL3, the most common adverse reactions in at least 20% of patients treated with rucaparib included nausea, fatigue (including asthenia), abdominal pain/distension, rash, dysgeusia, anemia, ALT/AST elevation, constipation, vomiting, diarrhea, thrombocytopenia, nasopharyngitis/URI, stomatitis, decreased appetite, and neutropenia. Myelodysplastic syndrome and/or acute myeloid leukemia occurred in 7 of 372 (1.9%) patients treated with rucaparib and in 1 of 189 (0.5%) patients assigned to placebo. Discontinuation due to adverse reactions occurred in 15% of patients receiving rucaparib and 2% of those assigned to placebo.
The recommended rucaparib dose is 600mg (two 300mg tablets) taken orally twice daily with or without food.
Full prescribing information is available at:
https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/209115s003lbl.pdf.
The FDA granted this application priority review.
Health care professionals should report all serious adverse events suspected to be associated with the use of any medicine and device to the FDA's MedWatch Reporting System.

Safety Announcements

FDA Drug Safety Communication: FDA warns of serious immune system reaction with seizure and mental health medicine lamotrigine (Lamictal®)

[04/25/2018] The FDA is warning that the medicine lamotrigine (Lamictal®) for seizures and bipolar disorder can cause a rare but very serious reaction that excessively activates the body's infection-fighting immune system. This can cause severe inflammation throughout the body and lead to hospitalization and death, especially if the reaction is not diagnosed and treated quickly. As a result, the FDA is requiring a new warning about this risk be added to the prescribing information in the lamotrigine drug labels.
The immune system reaction, called hemophagocytic lymphohistiocytosis (HLH), causes an uncontrolled response by the immune system. HLH typically presents as a persistent fever, usually greater than 101°F, and it can lead to severe problems with blood cells and organs throughout the body such as the liver, kidneys, and

lungs. Lamotrigine is used alone or with other medicines to treat seizures in patients two years and older. It may also be used as maintenance treatment in patients with bipolar disorder to help delay the occurrence of mood episodes such as depression, mania, or hypomania. Stopping lamotrigine without first talking to a prescriber can lead to uncontrolled seizures, or new or worsening mental health problems. Lamotrigine has been approved and on the market for 24 years, and is available under the brand name Lamictal® and as generics.

Health care professionals should be aware that prompt recognition and early treatment is important for improving HLH outcomes and decreasing mortality. Diagnosis is often complicated because early signs and symptoms such as fever and rash are not specific. HLH may also be confused with other serious immune-related adverse reactions such as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS). Patients who develop fever or rash should be evaluated promptly, and lamotrigine should be discontinued if HLH or another serious immune-related adverse reaction is suspected and an alternative etiology for the signs and symptoms cannot be established. Patients should be advised to seek immediate medical attention if they experience symptoms of HLH during lamotrigine treatment. A diagnosis of HLH can be established if a patient has at least five of the following eight signs or symptoms:

- Fever and rash
- Enlarged spleen
- Cytopenias
- Elevated levels of triglycerides or low blood levels of fibrinogen
- High levels of blood ferritin
- Hemophagocytosis identified through bone marrow, spleen, or lymph node biopsy
- Decreased or absent Natural Killer (NK) Cell activity
- Elevated blood levels of CD25 showing prolonged immune cell activation

Patients or their caregivers should contact their health care professionals right away if they experience any symptom of HLH while taking lamotrigine. HLH can occur within days to weeks after starting treatment. A physical examination and specific laboratory blood tests and other evaluations are used to diagnose HLH. Signs and symptoms of HLH include but are not limited to:

- Fever
- Enlarged liver; symptoms may include pain, tenderness, or unusual swelling over the liver area in the upper right belly
- Swollen lymph nodes
- Skin rashes
- Yellow skin or eyes
- Unusual bleeding
- Nervous system problems, including seizures, trouble walking, difficulty seeing, or other visual disturbances

The patient Medication Guide, which explains the benefits and risks of lamotrigine, should be read every time a patient receives a new prescription because the information may change. Patients should not stop taking lamotrigine without talking to their health care professional first as doing so can cause serious problems.

In the 24 years since lamotrigine's 1994 approval, the FDA identified eight cases worldwide of confirmed or suspected HLH associated with the medicine in children and adults. This number includes only reports submitted to FDA and found in the medical literature, so there are likely additional cases about which the FDA is unaware. The FDA determined there was reasonable evidence that lamotrigine was the cause of HLH in these eight cases based on the timing of events and the order in which they occurred. The patients in these cases required hospitalization and received drug and other medical treatments, with one dying.

The FDA previously communicated safety information associated with in September 2006 (possible association between lamotrigine exposure during pregnancy and oral clefts in newborns) and August 2010 (aseptic meningitis warning). Lamotrigine was also covered as part of a May 2009 safety alert concerning suicidal thoughts and behavior with the entire class of anti-seizure medicines.

The FDA urges health care professionals and patients to report side effects involving lamotrigine and other medicines to the FDA MedWatch program.

Current Drug Shortages Index (as of April 30th, 2018):

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

Abciximab (ReoPro) Injection	***Currently in Shortage***
Amino Acids	***Currently in Shortage***
Aminocaproic Acid Injection, USP	***Currently in Shortage***
Amoxapine Tablets	***Currently in Shortage***
Asparaginase Erwinia Chrysanthemi (Erwinaze)	***Currently in Shortage***
Atenolol Tablets	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Belatacept (Nulojix) Lyophilized Powder for Injection	***Currently in Shortage***
Bumetanide Injection, USP	***Currently in Shortage***
Bupivacaine Hydrochloride and Epinephrine Injection, USP	***Currently in Shortage***
Bupivacaine Hydrochloride Injection, USP	***Currently in Shortage***
Calcium Chloride Injection, USP	***Currently in Shortage***
Calcium Gluconate Injection	***Currently in Shortage***
Carbidopa and Levodopa Extended Release Tablets	***Currently in Shortage***
Cefepime Injection	***Currently in Shortage***
Cefotaxime Sodium (Claforan) Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***
Cromolyn Sodium Inhalation Solution, USP	***Currently in Shortage***
Deferoxamine Mesylate for Injection, USP	***Currently in Shortage***
Dexrazoxane Injection	***Currently in Shortage***
Dextrose 5% Injection Bags	***Currently in Shortage***
Dextrose 50% Injection	***Currently in Shortage***
Diazepam Injection, USP	***Currently in Shortage***
Diltiazem Hydrochloride	***Currently in Shortage***
Disopyramide Phosphate (Norpace) Capsules	***Currently in Shortage***
Dobutamine Hydrochloride Injection	***Currently in Shortage***
Dopamine Hydrochloride Injection	***Currently in Shortage***
Dorzolamide Hydrochloride and Timolol Maleate (Cosopt) Ophthalmic Solution	***Currently in Shortage***
Dorzolamide Hydrochloride Ophthalmic Solution	***Currently in Shortage***
Eflornithine Hydrochloride (Vaniqa) Cream	***Currently in Shortage***
Epinephrine Injection, 0.1 mg/mL	***Currently in Shortage***
Ethiodized Oil (Lipiodol) Injection	***Currently in Shortage***
Etoposide Injection	***Currently in Shortage***
Etoposide Phosphate (Etopophos) Injection	***Currently in Shortage***
Fentanyl Citrate (Sublimaze) Injection	***Currently in Shortage***
Fluorescein Strips	***Currently in Shortage***
Folic Acid Injection	***Currently in Shortage***
Gemifloxacin Mesylate (Factive) Tablets	***Currently in Shortage***
Guanfacine Hydrochloride Tablets	***Currently in Shortage***
Heparin Sodium and Sodium Chloride 0.9% Injection	***Currently in Shortage***
Hydromorphone Hydrochloride Injection, USP	***Currently in Shortage***
Imipenem and Cilastatin for Injection, USP	***Currently in Shortage***
Ketamine Injection	***Currently in Shortage***
Ketorolac Tromethamine Injection	***Currently in Shortage***
L-Cysteine Hydrochloride Injection	***Currently in Shortage***
Labetalol Hydrochloride Injection	***Currently in Shortage***
Leucovorin Calcium Lyophilized Powder for Injection	***Currently in Shortage***
Leuprolide Acetate Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) and Dextrose Injection Solution-Premix Bags	***Currently in Shortage***

Lidocaine Hydrochloride (Xylocaine) Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection with Epinephrine	***Currently in Shortage***
Liotrix (Thyrolar) Tablets	***Currently in Shortage***
Magnesium Sulfate Injection	***Currently in Shortage***
Methadone Hydrochloride Injection	***Currently in Shortage***
Methotrexate Sodium Injection	***Currently in Shortage***
Methylphenidate Hydrochloride (QUILLICHEW ER) Extended-Release Chewable Tablets	***Currently in Shortage***
Methylphenidate Hydrochloride (QUILLIVANT XR) for Extended-Release Oral Suspension	***Currently in Shortage***
Metoclopramide Injection, USP	***Currently in Shortage***
Metronidazole Injection, USP	***Currently in Shortage***
Molindone Hydrochloride Tablets	***Currently in Shortage***
Morphine Sulfate Injection, USP	***Currently in Shortage***
Multi-Vitamin Infusion (Adult and Pediatric)	***Currently in Shortage***
Mupirocin Calcium Nasal Ointment	***Currently in Shortage***
Ondansetron Hydrochloride Injection	***Currently in Shortage***
Pantoprazole (Protonix) Powder for Injection	***Currently in Shortage***
Penicillamine (Depen) Titratable Tablets	***Currently in Shortage***
Penicillin G Benzathine (Bicillin L-A) Injection	***Currently in Shortage***
Penicillin G Benzathine and Penicillin G Procaine (Bicillin C-R) Injection	***Currently in Shortage***
Penicillin G Procaine Injection	***Currently in Shortage***
Peritoneal Dialysis Solutions	***Currently in Shortage***
Phenytoin Sodium Injection, USP	***Currently in Shortage***
Phosphate Injection Products	***Currently in Shortage***
Piperacillin and Tazobactam (Zosyn) Injection	***Currently in Shortage***
Potassium Chloride Injection	***Currently in Shortage***
Potassium Phosphate Injection	***Currently in Shortage***
Procainamide Hydrochloride Injection, USP	***Currently in Shortage***
Progesterone Injection, USP	***Currently in Shortage***
Promethazine (Phenergan) Injection	***Currently in Shortage***
Ranitidine Injection, USP	***Currently in Shortage***
Remifentanil (Ultiva) Lyophilized Powder for Solution Injection	***Currently in Shortage***
Rocuronium Bromide Injection	***Currently in Shortage***
Ropivacaine Hydrochloride injection	***Currently in Shortage***
Sacrosidase (Sucraid) Oral Solution	***Currently in Shortage***
Sclerosol Intrapleural Aerosol	***Currently in Shortage***
Sincalide (Kinevac) Lyophilized Powder for Injection	***Currently in Shortage***
Sodium Acetate Injection, USP	***Currently in Shortage***
Sodium Bicarbonate Injection, USP	***Currently in Shortage***
Sodium Chloride 0.9% Injection Bags	***Currently in Shortage***
Sodium Chloride 23.4% Injection	***Currently in Shortage***
Sodium Phosphate Injection	***Currently in Shortage***
Sterile Talc Powder	***Currently in Shortage***
Sterile Water	***Currently in Shortage***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***
Thioridazine Hydrochloride Tablets	***Currently in Shortage***
Zolpidem Tartrate (Edluar) Sublingual Tablets	***Currently in Shortage***