Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
October 10, 2018
4:00pm

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 DUR Board Meeting – October 10, 2018

DATE: September 28, 2018

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

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

Call to Order

Public Comment Forum

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

Action Item – 2019 DUR Board Meeting Dates – Appendix B

Update on Medication Coverage Authorization Unit/SoonerPsych Program Update – Appendix C

Action Item – Vote to Prior Authorize NutreStore® (L-Glutamine) and Siklos® (Hydroxyurea) – Appendix D

Action Item – Vote to Prior Authorize Palynziq™ (Pegvaliase-pqpz) – Appendix E

Action Item – Vote to Prior Authorize Galafold™ (Migalastat) – Appendix F

Action Item – Vote to Prior Authorize Qbrexza™ (Glycopyrronium) – Appendix G

Action Item – Vote to Prior Authorize FloLipid® (Simvastatin Oral Suspension) and Update the Prior Authorization Criteria for Antihyperlipidemics – Appendix H

Action Item – Vote to Prior Authorize Verzenio™ (Abemaciclib), Ogivri™ (Trastuzumab-dkst), and Lynparza® (Olaparib) – Appendix I

Annual Review of Acute Lymphoblastic Leukemia (ALL) and Chronic Myeloid Leukemia (CML) Medications and 30-Day Notice to Prior Authorize Yescarta® (Axicabtagene) – Appendix J

Annual Review of Skin Cancer Medications and 30-Day Notice to Prior Authorize Braftovi™ (Encorafenib), Mektovi® (Binimetinib), and Libtayo® (Cemiplimab-rwlc) – Appendix K

Annual Review of Targeted Immunomodulator Agents and 30-Day Notice to Prior Authorize Ilumya™ (Tildrakizumab-asmn) and Olumiant® (Baricitinib) – Appendix L

Annual Review of Gonadotropin-Releasing Hormone (GnRH) Medications and 30-Day Notice to Prior Authorize Triptodur® (Triptorelin) and Orilissa™ (Elagolix) – Appendix M

Annual Review of Bladder Control Medications and 30-Day Notice to Prior Authorize Nocdurna® (Desmopressin Acetate Sublingual Tablet) – Appendix N

Action Item – Annual Review of Constipation and Diarrhea Medications – Appendix O

Annual Review of Topical Corticosteroids and 30-Day Notice to Prior Authorize Impoyz™ (Clobetasol Propionate 0.025% Cream) – Appendix P

Annual Review of Gout Medications and 30-Day Notice to Prior Authorize Krystexxa® (Pegloticase) – Appendix Q

Industry News and Updates – Appendix R

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

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – October 10, 2018 @ 4:00pm

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

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

1. Call to Order

A. Roll Call – Dr. Cothran

Items to be presented by Dr. Muchmore, Chairman:

2. Public Comment Forum

A. Acknowledgment of Speakers for Public Comment

Items to be presented by Dr. Muchmore, Chairman:

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

A. September 12, 2018 DUR Minutes – Vote
B. September 12, 2018 DUR Recommendations Memorandum

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

4. Action Item – 2019 Drug Utilization Review (DUR) Board Meeting Dates – See Appendix B

A. 2019 DUR Board Meeting Dates – Vote

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

5. Updates on Medication Coverage Authorization Unit/SoonerPsych Program Update – See Appendix C

A. Medication Coverage Activity for September 2018
B. Pharmacy Helpdesk Activity for September 2018
C. SoonerPsych Program Update

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

6. Action Item – Vote to Prior Authorize NutreStore® (L-Glutamine) and Siklos® (Hydroxyurea) – See Appendix D

A. Introduction
B. College of Pharmacy Recommendations

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

7. Action Item – Vote to Prior Authorize Palynziq™ (Pegvaliase-pqpz) – See Appendix E

A. Phenylketonuria Pharmacotherapy
B. College of Pharmacy Recommendations

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

8. Action Item – Vote to Prior Authorize Galafold™ (Migalastat) – See Appendix F

A. Introduction
B. College of Pharmacy Recommendations

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

9. Action Item – Vote to Prior Authorize Qbrexza™ (Glycopyrronium) – See Appendix G

A. Introduction
B. College of Pharmacy Recommendations

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

10. Action Item – Vote to Prior Authorize FloLipid® (Simvastatin Oral Suspension) and Update the Prior Authorization Criteria for Antihyperlipidemics – See Appendix H

A. Introduction
B. College of Pharmacy Recommendations

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

11. Action Item – Vote to Prior Authorize Verzenio™ (Abemaciclib), Ogivri™ (Trastuzumab-dkst), and Lynparza® (Olaparib) – See Appendix I

A. Introduction
B. Product Summaries
C. Recommendations

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

12. Annual Review of Acute Lymphoblastic Leukemia (ALL) and Chronic Myeloid Leukemia (CML) Medications and 30-Day Notice to Prior Authorize Yescarta® (Axicabtagene) – See Appendix J

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of ALL/CML Medications
D. Prior Authorization of ALL/CML Medications
E. Market News and Updates
F. Yescarta® (Axicabtagene) Product Summary
G. Recommendations
H. Utilization Details of ALL/CML Medications

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

13. Annual Review of Skin Cancer Medications and 30-Day Notice to Prior Authorize Braftovi™ (Encorafenib), Mektovi® (Binimetinib), and Libtayo® (Cemiplimab-rwlc) – See Appendix K

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Skin Cancer Medications
D. Prior Authorization of Skin Cancer Medications
E. Market News and Updates
F. Product Summaries
G. Recommendations
H. Utilization Details of Skin Cancer Medications

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

14. Annual Review of Targeted Immunomodulator Agents and 30-Day Notice to Prior Authorize Ilumya™ (Tildrakizumab-asmn) and Olumiant® (Baricitinib) – See Appendix L

A. Current Prior Authorization Criteria
B. Utilization of Targeted Immunomodulator Agents
C. Prior Authorization of Targeted Immunomodulator Agents
D. Market News and Updates
E. Ilumya™ (Tildrakizumab-asmn) Product Summary
F. Olumiant® (Baricitinib) Product Summary
G. Pemphigus Vulgaris (PV) Summary
H. College of Pharmacy Recommendations
I. Utilization Details of Targeted Immunomodulator Agents

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

15. Annual Review of Gonadotropin-Releasing Hormone (GnRH) Medications and 30-Day Notice to Prior Authorize Triptodur® (Triptorelin) and Orilissa™ (Elagolix) – See Appendix M

A. Current Prior Authorization Criteria
B. Utilization of GnRH Medications
C. Prior Authorization of GnRH Medications
D. Market News and Updates

E. Triptodur® (Triptorelin) Product Summary
F. Orilissa™ (Elagolix) Product Summary
G. College of Pharmacy Recommendations
H. Utilization Details of GnRH Medications

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

16. Annual Review of Bladder Control Medications and 30-Day Notice to Prior Authorize Nocdurna® (Desmopressin Acetate Sublingual Tablets) – See Appendix N

A. Current Prior Authorization Criteria
B. Utilization of Bladder Control Medications
C. Prior Authorization of Bladder Control Medications
D. Market News and Updates
E. Nocdurna® (Desmopressin Acetate Sublingual Tablets) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Bladder Control Medications

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

17. Action Item – Annual Review of Constipation and Diarrhea Medications – See Appendix O

A. Current Prior Authorization Criteria
B. Utilization of Constipation and Diarrhea Medications
C. Prior Authorization of Constipation and Diarrhea Medications
D. Market News and Updates
E. Cost Comparison: Constipation Medications
F. College of Pharmacy Recommendations
G. Utilization Details of Constipation and Diarrhea Medications

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

18. Annual Review of Topical Corticosteroids and 30-Day Notice to Prior Authorize Impoyz™ (Clobetasol Propionate 0.025% Cream) – See Appendix P

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

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

19. Annual Review of Gout Medications and 30-Day Notice to Prior Authorize Krystexxa® (Pegloticase) – See Appendix Q

A. Current Prior Authorization Criteria
B. Utilization of Gout Medications
C. Prior Authorization of Gout Medications
D. Market News and Updates
E. Krystexxa® (Pegloticase) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Gout Medications

Non-Presentation; Questions Only:

20. Industry News and Updates – See Appendix R

A. Introduction
B. News and Updates

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

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

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

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

A. Hepatitis C Medications
B. Hemophilia Medications
C. Onpattro™ (Patisiran)
D. Systemic Antibiotics
E. Cystic Fibrosis Medications
**Future business subject to change.*

23. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF SEPTEMBER 12, 2018

BOARD MEMBERS:	PRESENT	ABSENT
Stephen Anderson, Pharm.D.	x	
Markita Broyles, DPh, MBA	x	
Darlla D. Duniphin, MHS, PA-C	x	
Theresa Garton, M.D.		x
Carla Hardzog-Britt, M.D.	x	
Ashley Huddleston, Pharm.D., BCOP	x	
John Muchmore, M.D., Ph.D.; Chairman	x	
Lee Munoz, D.Ph.	x	
James Osborne, Pharm.D.		x
Paul Louis Preslar, D.O., MBA; Vice Chairman	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	
Sarai Connell, Pharm.D.; MBA; Resident	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	
Brandy Nawaz, Pharm.D.; Clinical Pharmacist	x	
Timothy Pham, Ph.D.; Postdoctoral Research Fellow		x
Leslie Robinson, D.Ph.; PA Coordinator		x
Ashley Teel, Pharm.D.; Clinical Pharmacist		x
Jacquelyn Travers, Pharm.D.; Practice Facilitating Pharmacist	x	
Graduate Students: Michael Nguyen, Pharm.D.	x	
Philip Looper, Pharm.D.	x	
Laura Tidmore, Pharm.D.		x
Corby Thompson, Pharm.D.	x	
Reagan Williams, Pharm.D.	x	
Visiting Pharmacy Student(s): Amaka Anudu	x	

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.; Sr. Director of Pharmacy	x	
Kelli Brodersen, Marketing Coordinator		x
Robert Evans, M.D.; Sr. Medical Director		x
Michael Herndon, D.O.; Chief Medical Officer	x	
Maria Maule, J.D.; Senior Director Legal Services	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	
Kerri Wade, Pharmacy Operations Manager	x	

OTHERS PRESENT:		
Lance Webb, Sanofi Genzyme	Scott Black, Daiichi Sankyo	Dan Doyle, Trividia
Marc Welborn, Intercept Pharm	Marisa Salinas, Dermira	Valerie Ng, Indivior
Rhonda Clark, Indivior	Don Kempin, Novo Nordisk	Charlene Kaiser, Dermira
Megan Loftis, Ultragenx	Dan Doyle, Trividia	Terry McCurren, Otsuka
Evie Knisely, Novartis	John Brunson, Amneal	Jeff Knappen, Spark
Marc Parker, Sunovion	Jim Chapman, AbbVie	Brian Maves, Pfizer
Sean George, Otusuka	Trebla Grant, Kite	Travis Tate, Health Choice
Patrick Harvey, Walgreens	Jason Russell, Bioverativ	

PRESENT FOR PUBLIC COMMENT:	
Marisa Salinas, MD	Dermira
Sean George	Otsuka

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: SEAN GEORGE

2B: AGENDA ITEM NO. 12 SPEAKER: MARISA SALINAS, MD

ACTION: NONE REQUIRED

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

3A: JULY 11, 2018 DUR MINUTES – VOTE

3B: JULY 11, 2018 DUR RECOMMENDATIONS MEMORANDUM

Materials included in agenda packet; presented by Dr. Cothran

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/PROTON PUMP INHIBITOR (PPI) DEPRESCRIBING MAILING UPDATE

4A: MEDICATION COVERAGE ACTIVITY FOR JULY 2018

4B: PHARMACY HELPDESK ACTIVITY FOR JULY 2018

4C: MEDICATION COVERAGE ACTIVITY FOR AUGUST 2018

4D: PHARMACY HELPDESK ACTIVITY FOR AUGUST 2018

4E: PROTON PUMP INHIBITOR (PPI) DEPRESCRIBING MAILING UPDATE

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: VOTE TO PRIOR AUTHORIZE APADAZ® [BENZHYDROCODONE/ ACETAMINOPHEN (APAP)], LUCEMYRA™ (LOFEXIDINE), AND SUBLOCADE™ [BUPRENORPHINE EXTENDED-RELEASE (ER) INJECTION]

5A: INTRODUCTION

5B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Holderread

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: VOTE TO PRIOR AUTHORIZE JYNARQUE™ (TOLVAPTAN)

6A: INTRODUCTION

6B: MARKET NEWS AND UPDATES

6C: COLLEGE OF PHARMACY RECOMMENDATIONS

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

AGENDA ITEM NO. 7: ANNUAL REVIEW OF BREAST CANCER MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE VERZENIO™ (ABEMACICLIB), OGIVRI™ (TRASTUZUMAB-DKST), AND LYNPARZA® (OLAPARIB)

7A: INTRODUCTION
7B: CURRENT PRIOR AUTHORIZATION CRITERIA
7C: UTILIZATION OF BREAST CANCER MEDICATIONS
7D: PRIOR AUTHORIZATION OF BREAST CANCER MEDICATIONS
7E: MARKET NEWS AND UPDATES
7F: PRODUCT SUMMARIES
7G: RECOMMENDATIONS
7H: UTILIZATION DETAILS OF BREAST CANCER MEDICATIONS

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

AGENDA ITEM NO. 8: ANNUAL REVIEW OF SICKLE CELL DISEASE (SCD) MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE NUTRESTORE® (L-GLUTAMINE) AND SIKLOS® (HYDROXYUREA)

8A: CURRENT PRIOR AUTHORIZATION CRITERIA
8B: UTILIZATION OF SCD MEDICATIONS
8C: PRIOR AUTHORIZATION OF SCD MEDICATIONS
8D: MARKET NEWS AND UPDATES
8E: SIKLOS® (HYDROXYUREA) PRODUCT SUMMARY
8F: NUTRESTORE® (L-GLUTAMINE POWDER FOR ORAL SOLUTION) PRODUCT SUMMARY
8G: COLLEGE OF PHARMACY RECOMMENDATIONS
8H: UTILIZATION DETAILS OF SCD MEDICATIONS

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

AGENDA ITEM NO. 9: ANNUAL REVIEW OF PHENYLKETONURIA MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE PALYNZIQ™ (PEGVALIASE-PQPZ)

9A: PHENYLKETONURIA INTRODUCTION
9B: CURRENT PRIOR AUTHORIZATION CRITERIA
9C: UTILIZATION OF PHENYLKETONURIA MEDICATIONS
9D: PRIOR AUTHORIZATION OF PHENYLKETONURIA MEDICATIONS
9E: MARKET NEWS AND UPDATES
9F: PALYNZIQ™ (PEGVALIASE-PQPZ) PRODUCT SUMMARY
9G: COLLEGE OF PHARMACY RECOMMENDATIONS
9H: UTILIZATION DETAILS OF PHENYLKETONURIA MEDICATIONS

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

AGENDA ITEM NO. 10: ANNUAL REVIEW OF SYNAGIS® (PALIVIZUMAB)

10A: CURRENT PRIOR AUTHORIZATION CRITERIA
10B: UTILIZATION OF SYNAGIS® (PALIVIZUMAB)
10C: PRIOR AUTHORIZATION OF SYNAGIS® (PALIVIZUMAB)
10D: SEASON COMPARISON
10E: MARKET NEWS AND UPDATES
10F: COLLEGE OF PHARMACY RECOMMENDATIONS

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

AGENDA ITEM NO. 11: **ANNUAL REVIEW OF FABRY DISEASE MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE GALAFOLD™ (MIGALASTAT)**

11A: INTRODUCTION
11B: CURRENT PRIOR AUTHORIZATION CRITERIA
11C: UTILIZATION OF FABRAZYME® (AGALSIDASE BETA)
11D: PRIOR AUTHORIZATION OF FABRAZYME® (AGALSIDASE BETA)
11E: MARKET NEWS AND UPDATES
11F: GALAFOLD™ (MIGALASTAT) PRODUCT SUMMARY
11G: COLLEGE OF PHARMACY RECOMMENDATIONS
11H: UTILIZATION DETAILS OF FABRAZYME® (AGALSIDASE BETA)

Materials included in agenda packet; presented by Dr. Chandler

ACTION: NONE REQUIRED

AGENDA ITEM NO. 12: **30-DAY NOTICE TO PRIOR AUTHORIZE QBREXZA™ (GLYCOPYRRONIUM)**

12A: HYPERHIDROSIS INTRODUCTION
12B: QBREXZA™ (GLYCOPYRRONIUM) PRODUCT SUMMARY
12C: MARKET NEWS AND UPDATES
12D: COLLEGE OF PHARMACY RECOMMENDATIONS

Dr. Muchmore recommends adding prescribing physician as an option to provide assessment of hyperhidrosis impacting quality of life.

Materials included in agenda packet; presented by Dr. Chandler

ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: **ANNUAL REVIEW OF ANTIHYPERLIPIDEMICS AND 30-DAY NOTICE TO PRIOR AUTHORIZE FLOLIPID® (SIMVASTATIN ORAL SUSPENSION)**

13A: CURRENT PRIOR AUTHORIZATION CRITERIA
13B: UTILIZATION OF ANTIHYPERLIPIDEMICS
13C: PRIOR AUTHORIZATION OF ANTIHYPERLIPIDEMICS
13D: MARKET NEWS AND UPDATES
13E: COLLEGE OF PHARMACY RECOMMENDATIONS
13F: UTILIZATION DETAILS OF ANTIHYPERLIPIDEMICS

Dr. Muchmore recommends that the nicotinic acid trial be removed from the omega-3 fatty acids approval criteria.

Materials included in agenda packet; presented by Dr. Adams

ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: **ANNUAL REVIEW OF PARATHYROID MEDICATIONS**

14A: CURRENT PRIOR AUTHORIZATION CRITERIA
14B: UTILIZATION OF PARATHYROID MEDICATIONS
14C: PRIOR AUTHORIZATION OF PARATHYROID MEDICATIONS
14D: MARKET NEWS AND UPDATES
14E: COLLEGE OF PHARMACY RECOMMENDATIONS
14F: UTILIZATION DETAILS OF CALCIMIMETICS AND VITAMIN D ANALOGS
14G: UTILIZATION DETAILS OF NATPARA® (PARATHYROID HORMONE INJECTION)

Materials included in agenda packet; Non-presentation; Questions only

ACTION: NONE REQUIRED

AGENDA ITEM NO. 15: **ANNUAL REVIEW OF GROWTH HORMONE**

15A: CURRENT PRIOR AUTHORIZATION CRITERIA
15B: UTILIZATION OF GROWTH HORMONE
15C: PRIOR AUTHORIZATION OF GROWTH HORMONE
15D: MARKET NEWS AND UPDATES
15E: COLLEGE OF PHARMACY RECOMMENDATIONS
15F: UTILIZATION DETAILS OF GROWTH HORMONE

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

AGENDA ITEM NO. 16: INDUSTRY NEWS AND UPDATES
16A: INTRODUCTION
16B: NEWS AND UPDATES
Materials included in agenda packet; Non-presentation; Questions only
ACTION: NONE REQUIRED

AGENDA ITEM NO. 17: 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. 18: FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)
18A: TARGETED IMMUNOMODULATOR AGENTS
18B: TOPICAL CORTICOSTEROIDS
18C: CONSTIPATION AND DIARRHEA MEDICATIONS
18D: BLADDER CONTROL MEDICATIONS
18E: ACUTE LYMPHOBLASTIC LEUKEMIA AND CHRONIC MYELOID LEUKEMIA MEDICATIONS
18F: SKIN CANCER MEDICATIONS
18G: GONADOTROPIN-RELEASING HORMONE MEDICATIONS
18H: BUTALBITAL MEDICATIONS
FUTURE BUSINESS SUBJECT TO CHANGE.
Materials included in agenda packet; presented by Dr. Holderread
ACTION: NONE REQUIRED

AGENDA ITEM NO. 19: ADJOURNMENT
The meeting was adjourned at 5:11p.m.

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

Memorandum

Date: September 13, 2018

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

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

Subject: Drug Utilization Review (DUR) Board Recommendations from Meeting of September 12, 2018

Recommendation 1: Proton Pump Inhibitor (PPI) Deprescribing Mailing Update

NO ACTION REQUIRED.

Recommendation 2: Vote to Prior Authorize Apadaz® [Benzhydrocodone/ Acetaminophen (APAP)], Lucemyra™ (Lofexidine), and Sublocade™ [Buprenorphine Extended-Release (ER) Injection]

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following:

1. The placement of Apadaz® (benzhydrocodone/APAP) into Tier-3 of the Opioid Analgesics Product Based Prior Authorization (PBPA) category. Current short-acting Tier-3 criteria will apply.
2. The prior authorization of Lucemyra™ (lofexidine) and Sublocade™ (buprenorphine ER injection) with the following criteria:

Lucemyra™ (Lofexidine) Approval Criteria:

1. An FDA approved indication for mitigation of opioid withdrawal symptoms to facilitate abrupt opioid discontinuation in adults; and
2. Date of opioid discontinuation must be listed on the prior authorization request; and

3. Prescriber must verify member has been screened for hepatic and renal impairment and that dosing is appropriate for the member's degree of hepatic and renal function; and
4. Prescriber must verify member's vital signs have been monitored and that the member is capable of and has been instructed on self-monitoring for hypotension, orthostasis, bradycardia, and associated symptoms; and
5. Member must not have severe coronary insufficiency, a recent myocardial infarction, cerebrovascular disease, chronic renal failure, or marked bradycardia; and
6. Member must not have congenital long QT syndrome; and
7. Prescriber must verify Lucemyra™ will be used in conjunction with a comprehensive management program for the treatment of opioid use disorder; and
8. A patient-specific, clinically significant reason why clonidine tablets or patches cannot be used in place of Lucemyra™ to mitigate opioid withdrawal symptoms must be provided; and
9. Approvals will be for a maximum duration of 14 days; and
10. A quantity limit of 12 tablets daily will apply.

Sublocade™ [Buprenorphine Extended-Release (ER) Injection] Approval Criteria:

1. Sublocade™ must be prescribed by a licensed physician who qualifies for a waiver under the Drug Addiction Treatment Act (DATA) and has notified the Center for Substance Abuse Treatment of the intention to treat addiction patients and has been assigned a Drug Enforcement Agency (DEA) X number; and
2. An FDA approved diagnosis of moderate-to-severe opioid use disorder; and
3. Member must have initiated treatment with a transmucosal buprenorphine-containing product for a minimum of seven days; and
4. Concomitant treatment with opioids (including tramadol) will be denied; and
5. Sublocade™ should only be prepared and administered by a health care provider; and
6. A patient-specific, clinically significant reason why the member cannot use the preferred buprenorphine product(s) (Suboxone®) must be provided; and
7. Approvals will be for the duration of 90 days to allow for concurrent medication monitoring; and
8. A quantity limit of one dose (300mg or 100mg) per 28 days will apply.

General Opioid Analgesics Approval Criteria:

- Tier-1 products are covered with no prior authorization necessary.
- Members with an oncology-related diagnosis are exempt from the prior authorization process, and do not require pain contracts.
- Only one long-acting and one-short acting agent can be used concurrently. Short-acting, solid dosage formulation products are limited to a quantity of four units per day or a quantity of 120 units per 30 days.
- An age restriction applies on oral liquid narcotic analgesic products for all members older than 12 years of age and oral solid dosage forms for all members younger than 10 years of age.
- An age restriction for all tramadol and codeine products (both liquid and solid dosage formulations) for members younger than 12 years of age applies. Members younger than 12 years of age require prior authorization approval for reimbursement of these

products. Authorization requires a patient-specific, clinically significant reason for use of these products despite the medication being contraindicated for the member's age.

Opioid Analgesics Tier-2 Approval Criteria:

1. A documented 30-day trial/titration period with at least one Tier-1 medication within the last 90 days is required for a Tier-2 long-acting medication; or
2. A documented 30-day trial with at least two Tier-1 short-acting medications within the last 90 days is required for a Tier-2 short-acting medication; or
3. A chronic pain diagnosis requiring time-released medication (for long-acting medications).

Opioid Analgesics Tier-3 Approval Criteria:

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

Opioid Analgesics*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
Long-Acting: oxycodone ER 10mg, 15mg, 20mg only (Oxycontin®)◊ **Short-Acting:** ASA/butalbital/caff/cod (Fiorinal with Codeine®) codeine codeine/APAP dihydrocodone/ASA/caff (Synalgos-DC®) hydrocodone/APAP (Norco®) hydrocodone/IBU (Vicoprofen®, Ibudone®, Reprexain™) hydromorphone (Dilaudid®) morphine IR (MSIR®) oxycodone IR (Oxy IR®) oxycodone/APAP (Percocet®) oxycodone/ASA (Percodan®) oxycodone/IBU (Combunox®) tramadol (Ultram®) tramadol/APAP (Ultracet®)	**Long-Acting:** buprenorphine patch (Butrans®) fentanyl patch (Duragesic®) hydrocodone ER (Hysingla® ER) morphine ER tab (MS Contin®) morphine/naltrexone (Embeda®) oxycodone ER 30mg, 40mg, 60mg, 80mg (Oxycontin®)◊ tramadol ER tab (Ultram ER®, Ryzolt®) **Short-Acting:** oxymorphone IR (Opana®) tapentadol IR (Nucynta®)	**Long-Acting:** buprenorphine ER buccal film (Belbuca®) hydrocodone ER (Vantrela™ ER) hydrocodone ER (Zohydro® ER) hydromorphone ER (Exalgo®) methadone (Dolophine®) morphine ER (Arymo® ER) morphine ER (Kadian®) morphine ER (MorphaBond™) morphine/naltrexone (Troxyca® ER) oxycodone ER (Xtampza® ER) tapentadol ER (Nucynta® ER) **Short-Acting:** **benzhydrocodone/APAP (Apadaz®)** dihydrocodeine/APAP/caff (Trezix®) hydrocodone/APAP (Xodol®, Zamicet®, Liquicet®) oxycodone (Oxaydo®) oxycodone (Oxecta®) oxycodone (RoxyBond™) oxycodone/APAP (Primlev™, Xolox®)	**Long-Acting:** oxycodone/APAP ER (Xartemis® XR) tramadol ER cap (ConZip®) **Oncology Only:** fentanyl transmucosal lozenge (Actiq®) fentanyl buccal tab (Fentora®) fentanyl buccal film (Onsolis®) fentanyl SL tab (Abstral®) fentanyl nasal spray (Lazanda®) fentanyl SL spray (Subsys®)

PA = prior authorization; APAP = acetaminophen; ASA = aspirin; IR = immediate-release; ER = extended-release; IBU = ibuprofen; cod = codeine; caff = caffeine; tab = tablet; cap = capsule; SL = sublingual

*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

◊Brand name preferred.

Opioid Analgesics Special Prior Authorization (PA) Approval Criteria:

1. Actiq®, Fentora®, Onsolis®, Abstral®, Lazanda®, and Subsys® are approved for oncology-related diagnoses only.
2. Unique Strengths of Hydrocodone/Acetaminophen (APAP) Approval Criteria:
    a. A patient-specific, clinically significant reason why the member cannot use generic Norco® (hydrocodone/APAP 5/325mg, 7.5/325mg, or 10/325mg).
3. ConZip® [Tramadol Extended-Release (ER) Capsules] Approval Criteria:
    a. A patient-specific, clinically significant reason why the member cannot use the ER tablet formulation. Tier structure rules apply.
4. Xartemis® XR (Oxycodone/APAP ER Tablets) Approval Criteria:
    a. An acute pain condition requiring around-the-clock opioid treatment; and
    b. A patient-specific, clinically significant reason for all of the following:
        i. Why the member cannot use any other opioid medication for treatment of acute pain; and
        ii. Why the member requires a long-acting medication for an acute pain condition; and
        iii. Why the member cannot use Oxycontin® (oxycodone ER) and over-the-counter (OTC) APAP individual products in place of this combination product; and
    c. A quantity limit of four tablets per day will apply with a maximum approval duration of 10 days; and
    d. The member must not exceed 3,250mg of APAP per day from all sources; and
    e. Tier structure rules still apply.

Approval Criteria for Greater than 12 Claims Per Year of Hydrocodone Products:

1. Members may be approved for greater than 12 claims per year of hydrocodone products if the member has a pain contract with a single prescriber. A copy of the pain contract should be submitted with the prior authorization request. Requests outside of the plan outlined in the contract will not be approved.
2. Members with a current oncology-related diagnosis do not require a pain contract for additional approvals.

Suboxone® [Buprenorphine/Naloxone Sublingual (SL) Tablets and Films], Subutex® (Buprenorphine SL Tablets), Zubsolv® (Buprenorphine/Naloxone SL Tablets), and Bunavail® (Buprenorphine/Naloxone Buccal Films) Approval Criteria:

1. Suboxone® is the preferred product. Bunavail® and Zubsolv® authorization requires a patient-specific, clinically significant reason why Suboxone® is not appropriate.
2. Subutex® (buprenorphine) 2mg and 8mg tablets will only be approved if the member is pregnant or has a documented serious allergy or adverse reaction to naloxone.
3. Buprenorphine products FDA approved for a diagnosis of opioid abuse/dependence must be prescribed by a licensed physician who qualifies for a waiver under the Drug Addiction Treatment Act (DATA) and has notified the Center for Substance Abuse Treatment of the intention to treat addiction patients and has been assigned a Drug Enforcement Agency (DEA) X number; and
4. Member must have an FDA approved diagnosis of opioid abuse/dependence; and
5. Concomitant treatment with opioids (including tramadol) will be denied; and

6. Approvals will be for the duration of 90 days to allow for concurrent medication monitoring; and
7. The following limitations will apply:
    a. **Suboxone®** 2mg/0.5mg, 4mg/1mg, and 8mg/2mg SL tablets and films: A quantity limit of 90 SL units per 30 days will apply.
    b. **Suboxone®** 12mg/3mg SL films: A quantity limit of 60 SL films per 30 days will apply.
    c. **Subutex®** 2mg and 8mg SL tablets: A quantity limit of 90 SL tablets per 30 days will apply.
    d. **Zubsolv®** 0.7mg/0.18mg, 1.4mg/0.36mg, 2.9mg/0.71mg, and 5.7mg/1.4mg SL tablets: A quantity limit of 90 SL tablets per 30 days will apply.
    e. **Zubsolv®** 8.6mg/2.1mg SL tablets: A quantity limit of 60 SL tablets per 30 days will apply.
    f. **Zubsolv®** 11.4mg/2.9mg SL tablets: A quantity limit of 30 SL tablets per 30 days will apply.
    g. **Bunavail®** 2.1mg/0.3mg and 4.2mg/0.7mg buccal films: A quantity limit of 90 buccal films per 30 days will apply.
    h. **Bunavail®** 6.3mg/1mg buccal films: A quantity limit of 60 buccal films per 30 days will apply.

High-Dose Buprenorphine Products Approval Criteria:

1. Each request for greater than 24mg bioequivalent buprenorphine per day will be evaluated on a case-by-case basis.
2. A taper schedule, dates of an attempted taper with reason for failure, or a patient-specific, clinically significant reason why a taper schedule or attempt is not appropriate for the member should be documented on the prior authorization request; and
3. Opioid urine drug screens should be submitted with high-dose requests that plan to continue high-dose treatment longer than the duration of one month.
    a. Urine drug screens must show the absence of opioid medications other than buprenorphine products for continued approval; or
    b. Prescriber must document a patient-specific reason the member should continue therapy, reason for opioid use, and document a plan for member to discontinue opioid use; and
4. Symptoms associated with withdrawal at lower doses or symptoms requiring high doses should be listed on the prior authorization request; and
5. Each approval will be for the duration of one month. If urine drug screen and other documentation are submitted indicating high-dose therapy is necessary, an approval can be granted for the duration of three months.
6. Continued high-dose authorization after the three-month approval will require a new (recent) urine drug screen.

Probuphine® (Buprenorphine Implant) Approval Criteria:

1. An FDA approved indication of maintenance treatment of opioid dependence; and
2. Members must be currently on a maintenance dose of 8mg per day or less of a Subutex® or Suboxone® sublingual tablet or its transmucosal buprenorphine product equivalent; and

3. Member must have been stable on current transmucosal buprenorphine dose (of 8mg per day or less) for three months or longer without any need for supplemental dosing or adjustments; and
4. Members must have had no positive urine toxicology results or paid claims for opioids within the last three months. Concomitant treatment with opioids (including tramadol) will be denied; and
5. Probuphine® must be prescribed by a licensed physician who qualifies for a waiver under the Drug Addiction Treatment Act (DATA) and has notified the Center for Substance Abuse Treatment of the intention to treat addiction patients and has been assigned a Drug Enforcement Agency (DEA) X number; and
6. Prescribers must verify they have considered the following factors in determining clinical stability and suitability for Probuphine®:
    a. Period free from illicit opioid drug use
    b. Stability of living environment
    c. Participation in a structured activity/job
    d. Consistency in participation in recommended behavioral therapy/peer support program
    e. Consistency in compliance with clinic visit requirements
    f. Minimal to no desire or need to use illicit opioids
    g. Period without episodes of hospitalizations (addiction or mental health issues), emergency room visits, or crisis interventions
    h. Social support system
7. The prescriber must verify enrollment in the Probuphine® Risk Evaluation and Mitigation Strategy (REMS) program; and
8. Approvals will be for one kit (four implants) per six months. Reauthorizations for an additional six months may be granted if the member does not have ongoing use of supplemental dosing with transmucosal buprenorphine or opioid analgesics while utilizing Probuphine®.

Recommendation 3: Vote to Prior Authorize Jynarque™ (Tolvaptan)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Jynarque™ (tolvaptan) with the following criteria:

Jynarque™ (Tolvaptan) Approval Criteria:

1. An FDA approved indication to slow kidney function decline in adults at risk of rapidly progressing autosomal dominant polycystic kidney disease (ADPKD); and
2. Member must be 18 years of age or older; and
3. Member must not have any contraindications to taking Jynarque™ including the following:
    a. Taking any concomitant strong CYP3A inhibitors (e.g., ketoconazole, itraconazole, lopinavir/ritonavir, indinavir/ritonavir, ritonavir, conivaptan); and
    b. A history of signs or symptoms of significant liver impairment or injury (does not include uncomplicated polycystic liver disease); and
    c. Uncorrected abnormal blood sodium concentrations; and
    d. Unable to sense or respond to thirst; and

e. Hypovolemia; and
f. Hypersensitivity to tolvaptan or any of its components; and
g. Uncorrected urinary outflow obstruction; and
h. Anuria; and

4. Member must not be taking any of the following medications concomitantly with Jynarque™:
    a. Strong CYP3A inhibitors (e.g., ketoconazole, itraconazole, lopinavir/ritonavir, indinavir/ritonavir, ritonavir, conivaptan); and
    b. Strong CYP3A inducers (e.g., rifampin); and
    c. OATP1B1/3 and OAT3 transporter substrates (e.g., statins, bosentan, glyburide, nateglinide, repaglinide, methotrexate, furosemide); and
    d. BCRP transporter substrates (e.g., rosuvastatin); and
    e. V_2-receptor agonists (e.g., desmopressin); and
5. Jynarque™ must be prescribed by a nephrologist or specialist with expertise in the treatment of ADPKD (or be an advanced care practitioner with a supervising physician who is a nephrologist or specialist with expertise in the treatment of ADPKD); and
6. Prescriber must agree to assess ALT, AST, and bilirubin prior to initiation of Jynarque™, at 2 weeks and 4 weeks after initiation, then monthly for 18 months, and every 3 months thereafter; and
7. Female members must not be pregnant and must have a negative pregnancy test prior to therapy initiation; and
8. Prescriber, pharmacy, and member must be enrolled in the Jynarque™ Risk Evaluation and Mitigation Strategy (REMS) program and maintain enrollment throughout therapy.

Recommendation 4: Annual Review of Breast Cancer Medications and 30-Day Notice to Prior Authorize Verzenio™ (Abemaciclib), Ogivri™ (Trastuzumab-dkst), and Lynparza® (Olaparib)

NO ACTION REQUIRED.

Recommendation 5: Annual Review of Sickle Cell Disease (SCD) Medications and 30-Day Notice to Prior Authorize NutreStore® (L-Glutamine) and Siklos® (Hydroxyurea)

NO ACTION REQUIRED.

Recommendation 6: Annual Review of Phenylketonuria Medications and 30-Day Notice to Prior Authorize Palynziq™ (Pegvaliase-pqpz)

NO ACTION REQUIRED.

Recommendation 7: Annual Review of Synagis® (Palivizumab)

NO ACTION REQUIRED.

Recommendation 8: Annual Review of Fabry Disease Medications and 30-Day Notice to Prior Authorize Galafold™ (Migalastat)

NO ACTION REQUIRED.

Recommendation 9: 30-Day Notice to Prior Authorize Qbrexza™ (Glycopyrronium)

NO ACTION REQUIRED.

Recommendation 10: Annual Review of Antihyperlipidemics and 30-Day Notice to Prior Authorize FloLipid® (Simvastatin Oral Suspension)

NO ACTION REQUIRED.

Recommendation 11: Annual Review of Parathyroid Medications

NO ACTION REQUIRED.

Recommendation 12: Annual Review of Growth Hormone

NO ACTION REQUIRED.

Recommendation 13: Industry News and Updates

NO ACTION REQUIRED.

Recommendation 14: U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates

NO ACTION REQUIRED.

Appendix B

2019 Drug Utilization Review Board Meeting Dates

Oklahoma Health Care Authority
October 2018

Meetings are held the second Wednesday of every month at 4:00 PM

January 9, 2019

February 13, 2019

March 13, 2019

April 10, 2019

May 8, 2019

June 12, 2019

July 10, 2019

August 14, 2019

September 11, 2019

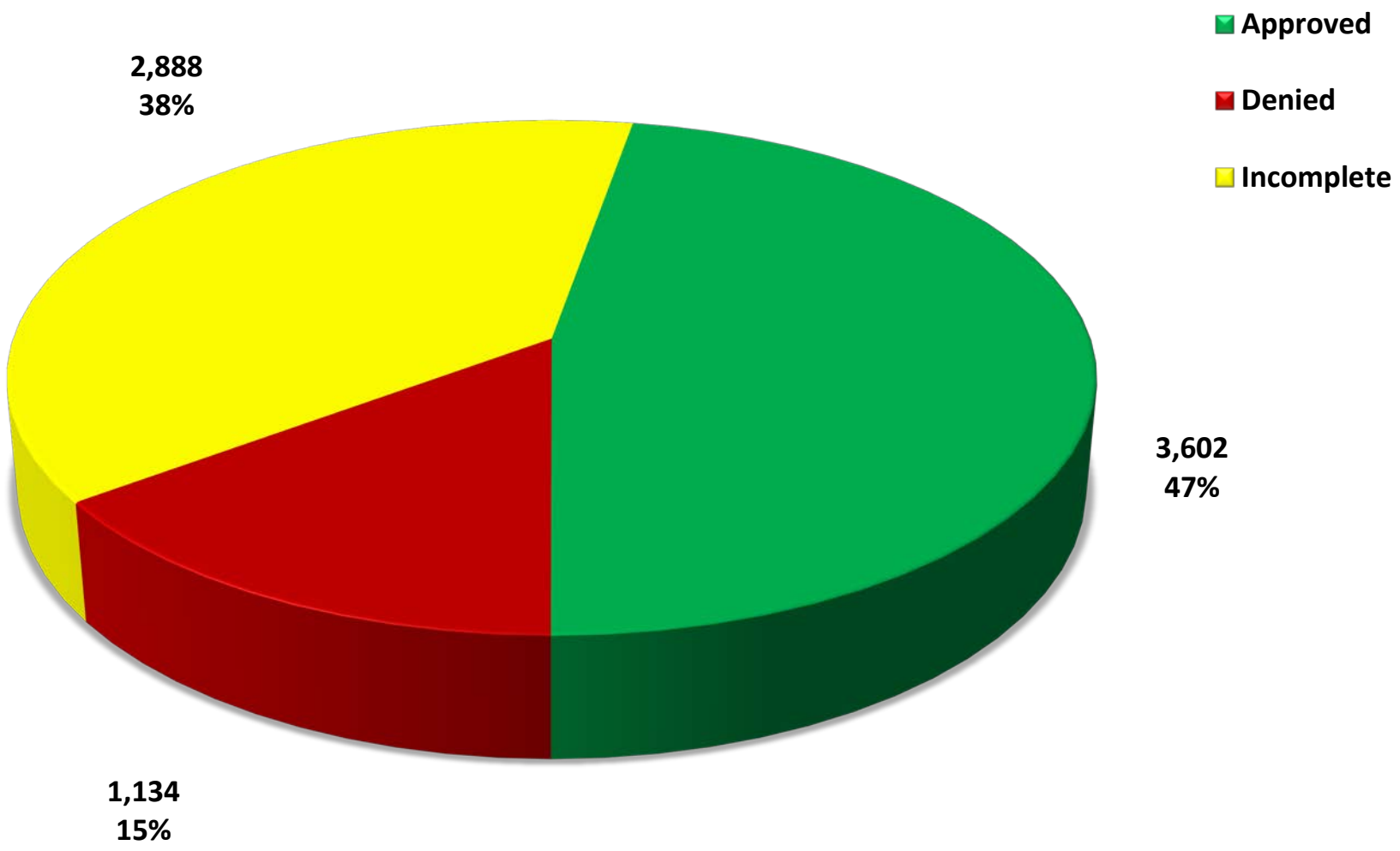
October 9, 2019

November 13, 2019

December 11, 2019

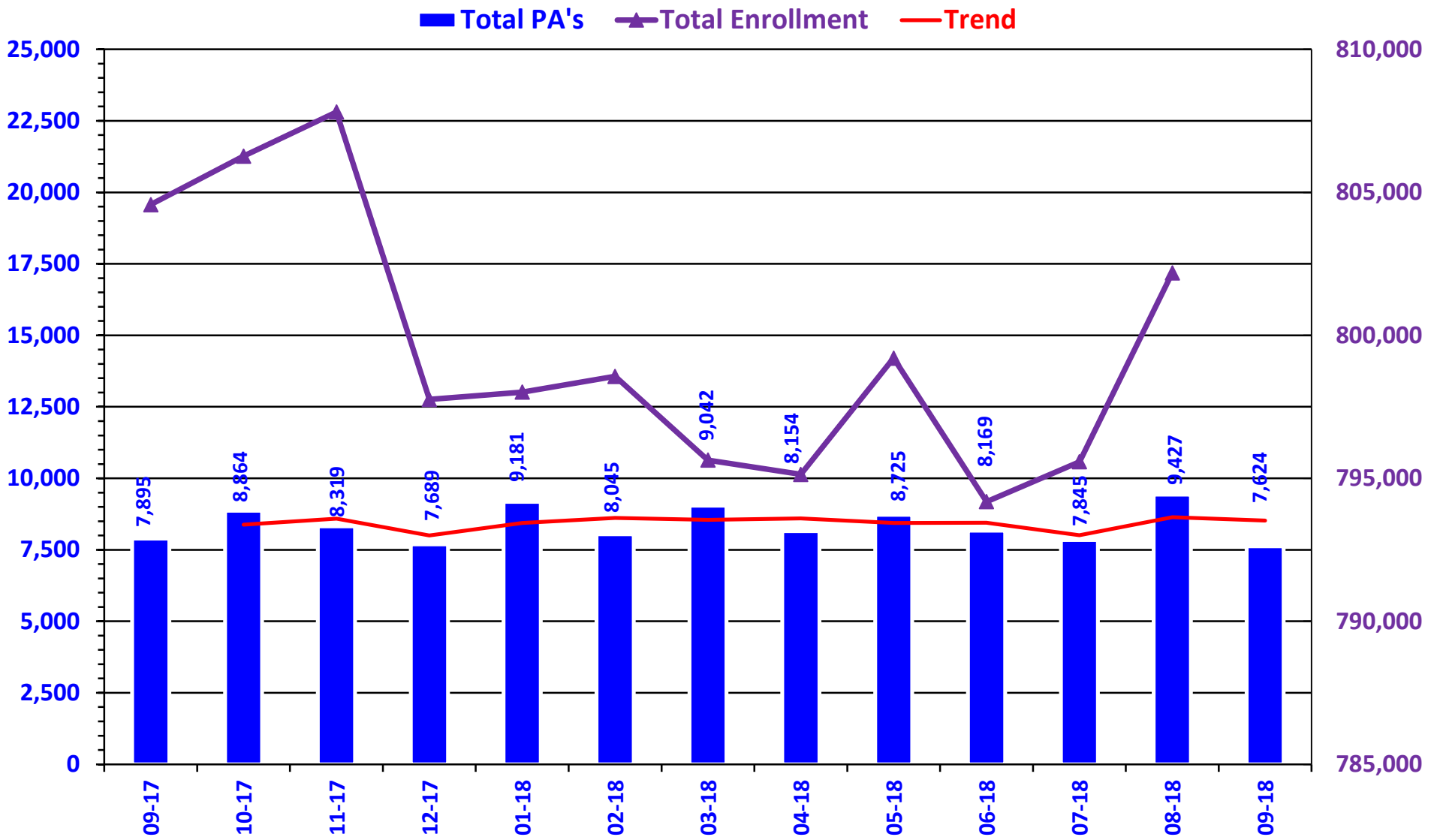
Appendix C

PRIOR AUTHORIZATION ACTIVITY REPORT: SEPTEMBER 2018



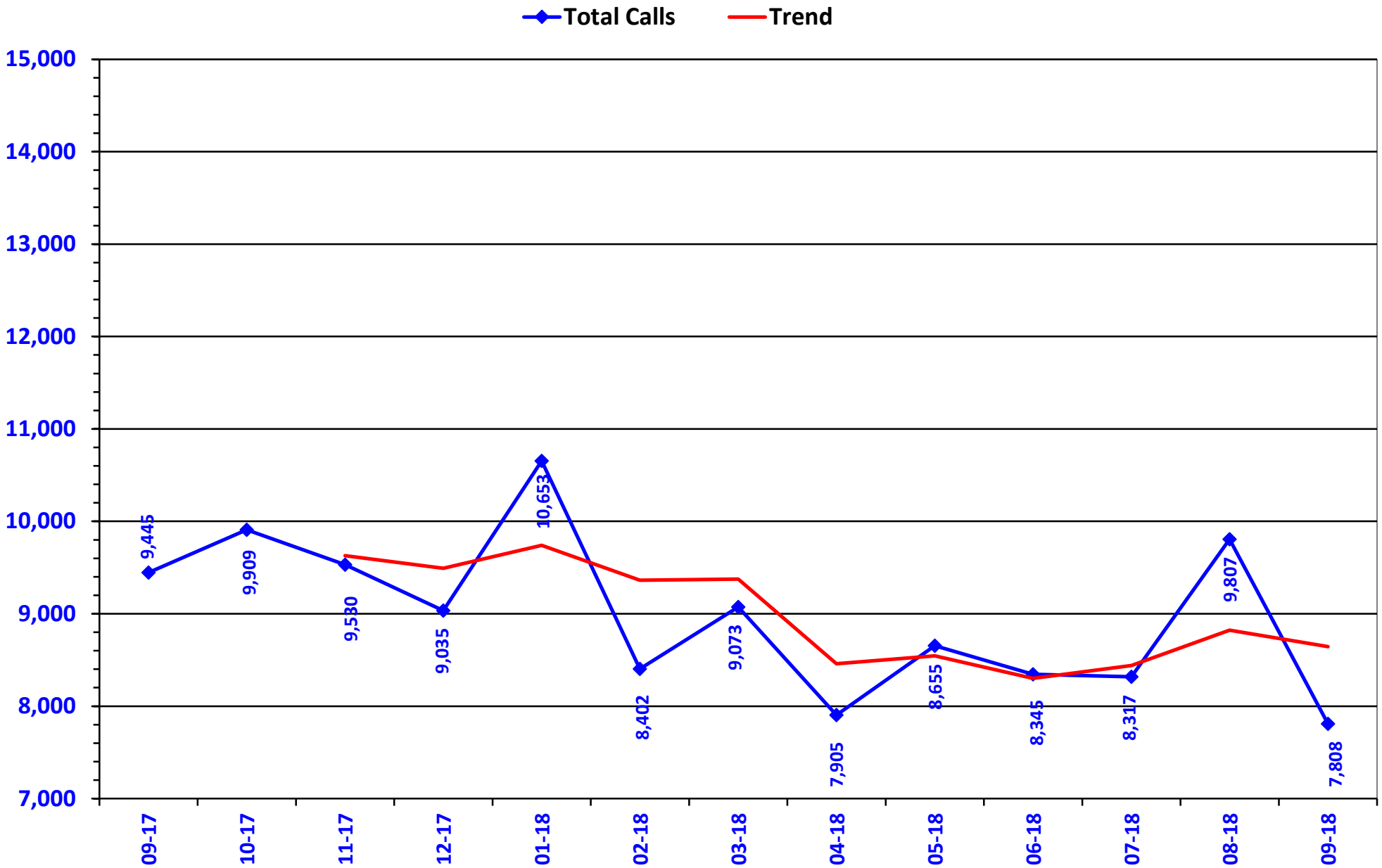
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: SEPTEMBER 2017 – SEPTEMBER 2018



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
SEPTEMBER 2017 – SEPTEMBER 2018



Prior Authorization Activity

9/1/2018 Through 9/30/2018

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	211	15	73	123	350
Analgesic - NonNarcotic	22	0	6	16	0
Analgesic - Narcotic	381	205	32	144	157
Angiotensin Receptor Antagonist	23	4	8	11	221
Antiasthma	57	14	14	29	292
Antibiotic	31	13	4	14	258
Anticonvulsant	107	43	14	50	331
Antidepressant	150	34	30	86	310
Antidiabetic	176	58	29	89	342
Antihistamine	27	8	8	11	290
Antimigraine	38	3	12	23	240
Antineoplastic	108	71	2	35	166
Antiparasitic	14	1	1	12	22
Antiulcers	139	39	45	55	133
Anxiolytic	54	33	3	18	301
Atypical Antipsychotics	221	94	37	90	340
Biologics	91	47	15	29	293
Bladder Control	52	7	20	25	358
Blood Thinners	280	169	11	100	327
Botox	31	22	4	5	326
Buprenorphine Medications	376	273	17	86	78
Cardiovascular	118	61	8	49	336
Cephalosporins	10	2	1	7	6
Chronic Obstructive Pulmonary Disease	158	30	52	76	336
Constipation/Diarrhea Medications	136	22	39	75	209
Contraceptive	11	8	1	2	359
Dermatological	121	14	48	59	181
Diabetic Supplies	420	263	21	136	186
Endocrine & Metabolic Drugs	121	66	10	45	161
Erythropoietin Stimulating Agents	10	4	1	5	69
Fibromyalgia	154	29	71	54	275
Fish Oils	11	1	6	4	358
Gastrointestinal Agents	125	38	19	68	149
Glaucoma	10	3	1	6	248
Growth Hormones	98	65	10	23	146
Hematopoietic Agents	14	4	0	10	157
Hepatitis C	157	99	22	36	8
HFA Rescue Inhalers	48	2	12	34	204
Insomnia	20	1	7	12	358
Insulin	95	36	16	43	290
Multiple Sclerosis	42	20	9	13	184
Muscle Relaxant	41	3	15	23	46
Nasal Allergy	56	8	22	26	190
Neurological Agents	78	25	22	31	180
NSAIDs	140	30	29	81	177
Ocular Allergy	32	7	11	14	164
Osteoporosis	8	6	0	2	358
Other*	292	60	53	179	238
Otic Antibiotic	13	0	2	11	0
Respiratory Agents	27	17	1	9	197

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Statins	12	5	0	7	263
Stimulant	754	367	70	317	345
Synagis	11	0	5	6	0
Testosterone	56	15	16	25	321
Topical Antifungal	31	7	7	17	13
Topical Corticosteroids	71	3	36	32	54
Vitamin	78	21	34	23	151
Pharmacotherapy	47	34	0	13	233
Emergency PAs	1	1	0	0	
Total	**6,216**	**2,530**	**1,062**	**2,624**	
Overrides					
Brand	47	32	3	12	286
Compound	8	7	0	1	114
Diabetic Supplies	11	8	0	3	83
Dosage Change	293	272	0	21	14
High Dose	4	4	0	0	224
Ingredient Duplication	14	10	0	4	7
Lost/Broken Rx	76	72	0	4	17
NDC vs Age	237	145	27	65	263
Nursing Home Issue	51	51	0	0	14
Opioid Quantity	19	14	3	2	171
Other*	60	53	1	6	12
Quantity vs. Days Supply	520	355	31	134	230
STBS/STBSM	24	18	4	2	71
Stolen	8	8	0	0	10
Temporary Unlock	2	2	0	0	1
Third Brand Request	32	20	2	10	14
Wrong D.S. on Previous Rx	2	1	1	0	44
Overrides Total	**1,408**	**1,072**	**72**	**264**	
Total Regular PAs + Overrides	**7,624**	**3,602**	**1,134**	**2,888**	

Denial Reasons	
Unable to verify required trials.	2,235
Does not meet established criteria.	1,167
Lack required information to process request.	613
Other PA Activity	
Duplicate Requests	549
Letters	9,505
No Process	5
Changes to existing PAs	693
Helpdesk Initiated Prior Authorizations	591
PAs Missing Information	14

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

SoonerPsych Program Update

Oklahoma Health Care Authority
October 2018

Prescriber Mailing Summary

The SoonerPsych program is an educational quarterly mailing to prescribers treating members utilizing atypical antipsychotic medications. Each mailing includes a gauge showing prescribers how their practice compares to those of other SoonerCare prescribers of atypical antipsychotic medications regarding potential differences from evidence-based prescribing practices. Each mailing also includes an informational page with evidence-based material related to the mailing topic. Mailing topics are comprised of four modules: polypharmacy, adherence, metabolic monitoring, and diagnosis.

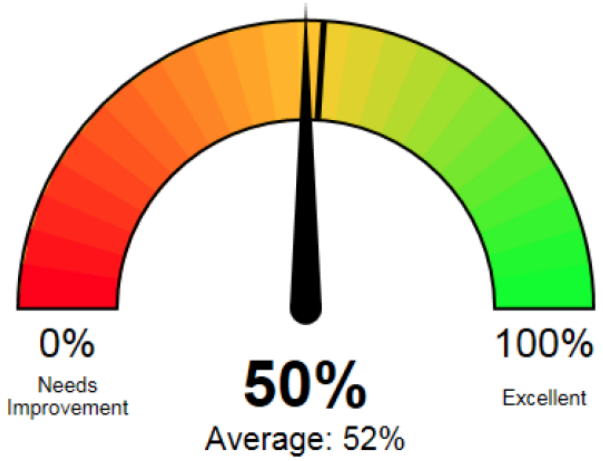
The SoonerPsych program has been using a "report card" format since April 2014. Beginning in April 2016, educational letters were sent to the same group of prescribers with all modules included in each mailing. Included prescribers receive four letters per year to better inform them of their SoonerCare patients using atypical antipsychotic medications and to make it more convenient to track patients and prescribing over time including any improvements or changes. Inclusion criteria requires the prescriber to have five or more SoonerCare patients taking atypical antipsychotic medications. A total of 225 prescribers were selected for inclusion in the 2016, 2017, and January 2018 mailings, and 247 prescribers were selected for inclusion in the April and July 2018 mailings.

Effective January 2017, data collection was expanded from a previous research-based approach to include additional diagnosis fields and monitoring (lipids and glucose) fields in order to provide a more clinically meaningful percentage to send to prescribers. The following list outlines definitions for each module included in the revised SoonerPsych mailing:

- **Polypharmacy:** Polypharmacy defined as members whose pharmacy claims history indicated concurrent use of two or more atypical antipsychotic medications for >90 days.
- **Adherence:** Nonadherence defined as members whose proportion of days covered (PDC) or adherence calculated from pharmacy claims history was <80%.
- **Metabolic Monitoring:** Missing monitoring defined as members whose recent 12-month medical claims history lacked glucose testing. Also includes members with a diagnosis of hyperlipidemia whose recent 12-month medical claims history lacked lipid testing.
- **Diagnosis:** Lack of diagnosis defined as members whose recent 12-month medical claims history lacked a diagnosis with a strong indication for prescribing an antipsychotic medication.

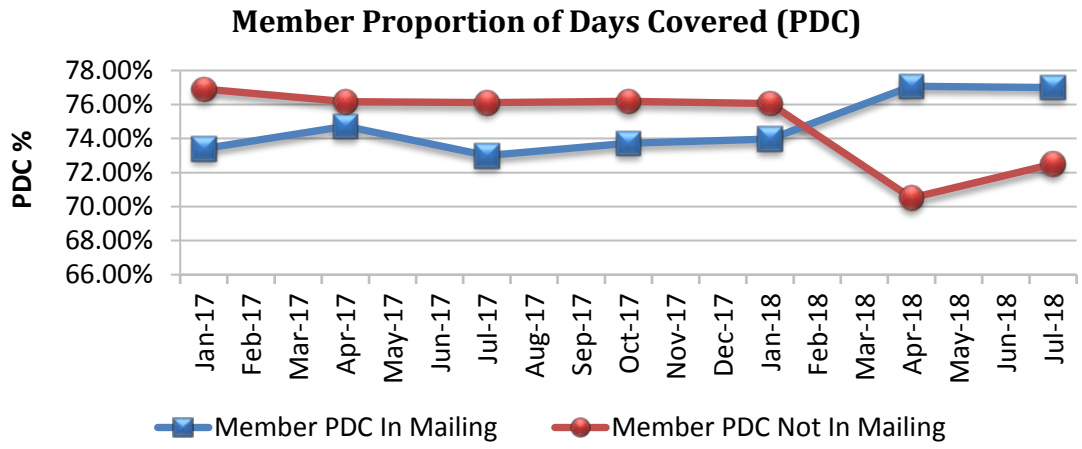
Example Gauge

Each gauge includes the individual prescriber's performance in relation to the specific module as well as the average of other SoonerCare prescribers for comparison. The following is an example gauge included in the mailings.

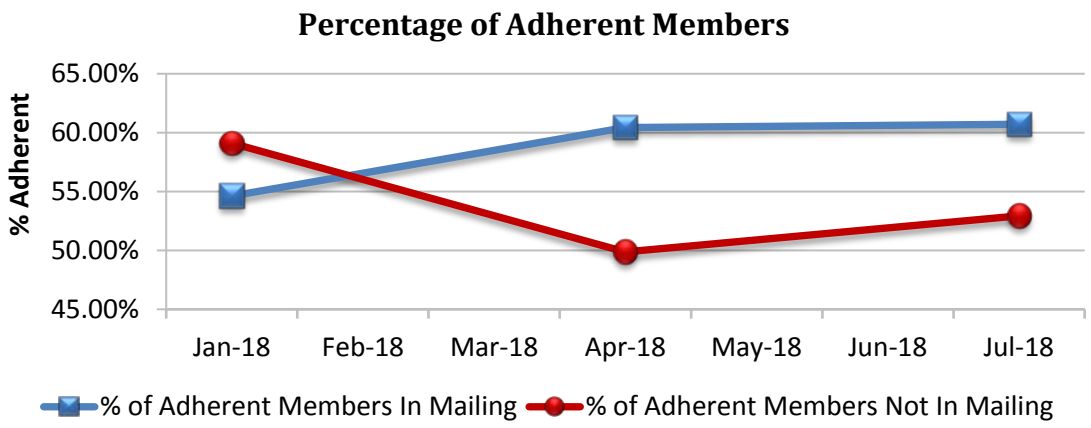


SoonerPsych Trends

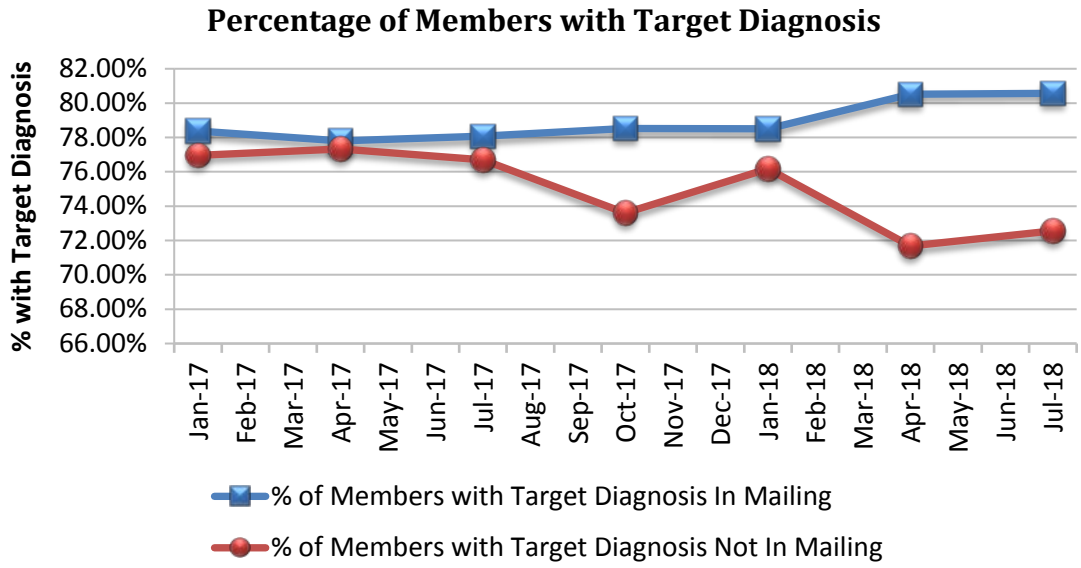
The following graph shows the 2017 and 2018 trends for member PDC. Those members whose prescribers received a mailing are designated separately from those whose prescribers did not. Please note, the vertical axis starts at 66% PDC in order to reflect small changes. It is also important to note that the prescriber mailing list was updated in April 2018 to include a larger number of prescribers and prescribers who were not previously receiving a mailing. Although PDC trends are tracked over time, it may be more meaningful to evaluate April and July 2018 as a new data set.



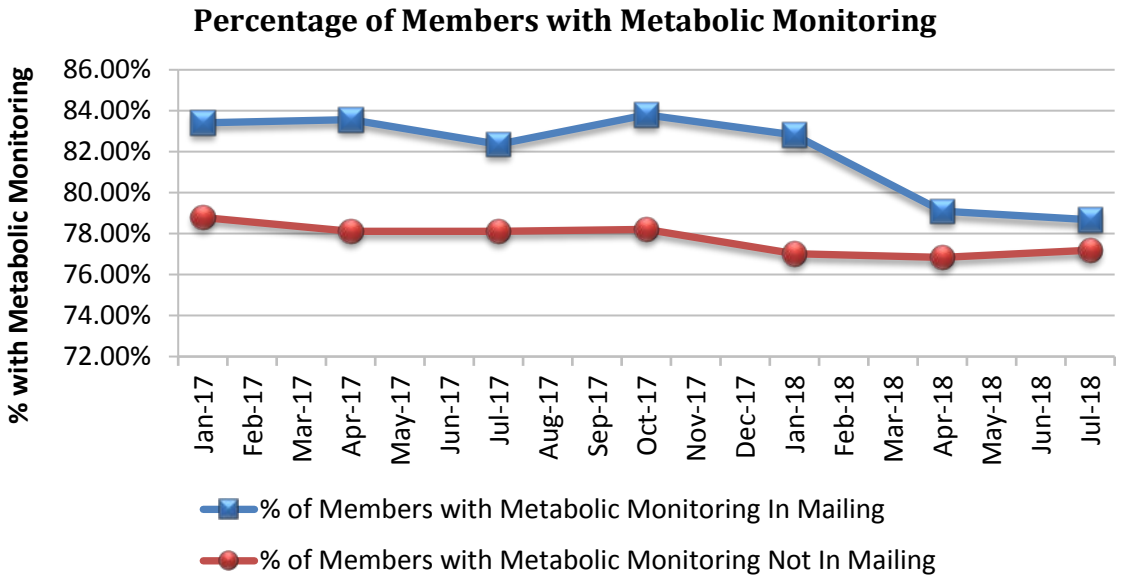
The following graph shows the 2018 trends for the percentage of adherent members. Prescribers who received a mailing are designated separately from those who did not. Please note, the vertical axis starts at 45% of members in order to reflect small changes. This data was included after input from the Drug Utilization Review (DUR) Board in the December 2017 DUR meeting; the DUR Board indicated it would be an important measure for reporting.



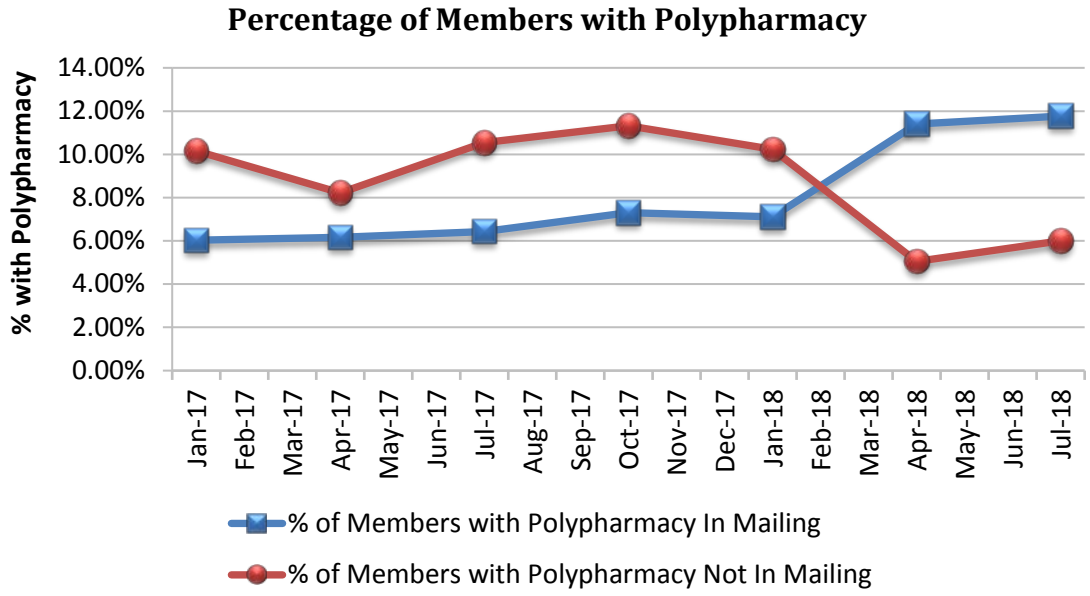
The following graph shows the 2017 and 2018 trends for the percentage of members whose recent 12-month medical claims history had a diagnosis with a strong indication for prescribing an antipsychotic medication. Prescribers who received a mailing are designated separately from those who did not. Please note, the vertical axis starts at 66% of members in order to reflect small changes. It is also important to note that the prescriber mailing list was updated in April 2018 to include a larger number of prescribers and prescribers who were not previously receiving a mailing.



The following graph shows the 2017 and 2018 trends for the percentage of members with appropriate metabolic monitoring while on an antipsychotic medication. Prescribers who received a mailing are designated separately from those who did not. Please note, the vertical axis starts at 72% of members in order to reflect small changes. It is also important to note that the prescriber mailing list was updated in April 2018 to include a larger number of prescribers and prescribers who were not previously receiving a mailing.



The following graph shows the 2017 and 2018 trends for the percentage of members with polypharmacy (concurrent use of two or more atypical antipsychotic medications for more than 90 days). Those prescribers who received a mailing are designated separately from those who did not. Please note, unlike the previous graphs, the vertical axis starts at 0% of members and that a lower percentage is a better outcome (indicates less prescribing of concomitant atypical antipsychotic medications). It is also important to note that the prescriber mailing list was updated in April 2018 to include a larger number of prescribers and prescribers who were not previously receiving a mailing.



Conclusions

Recent 2018 trends indicate improvements in member PDC, the percentage of adherent members, and the percentage of members with a target diagnosis. The percentage of members with appropriate metabolic monitoring is still better for members whose prescribers received a mailing, but a trend towards a similar percentage to those not included in the mailing was seen in 2018. Polypharmacy did not show positive trends in 2018 for those prescribers included in the mailing, but following results of the new prescriber list over time may provide more opportunities to evaluate potential impact of the mailings. These results indicate that consistently receiving evidence-based educational mailings reminds providers of evidence-based practices, and averts some potentially inappropriate prescribing. Recent changes to the mailing format (including all modules in each mailing, mailing to consistent prescribers, and updating the prescriber mailing list), as well as expanding the data collection process, are intended to sustain improvements and reduce waning interventions. The College of Pharmacy will continue to work with the Oklahoma Health Care Authority to improve educational mailings with the goal of improving the quality of care for SoonerCare members utilizing atypical antipsychotic medications. Future results of the combined mailing and the expanded data collection will be reviewed with the DUR Board as they become available.

Appendix D

Vote to Prior Authorize NutreStore® (L-Glutamine) and Siklos® (Hydroxyurea)

Oklahoma Health Care Authority
October 2018

Introduction[1,2,3,4]

- **NutreStore® (L-glutamine powder for oral solution)** is indicated for the treatment of Short Bowel Syndrome (SBS) in patients receiving specialized nutritional support when used in conjunction with a recombinant human growth hormone (rh-GH) that is approved for this indication. Glutamine and rh-GH therapy should be used in conjunction with optimal management of SBS. Optimal management of SBS may include a specialized oral diet (SOD), enteral feedings, parenteral nutrition, and fluid and micronutrient supplements. A SOD may consist of a low-fat, high-carbohydrate diet, adjusted for individual patient preferences and requirements. The Wholesale Acquisition Cost (WAC) of NutreStore® (L-glutamine powder for oral solution) is $5.92 per packet.
    - **L-Glutamine Product Comparison:** L-glutamine is also approved by the U.S. Food and Drug Administration (FDA) as an oral powder formulation (Endari™) to reduce the acute complications of sickle cell disease (SCD) in patients 5 years of age and older. Endari™ is supplied in packets containing 5 grams of L-glutamine powder. The recommended dose is 5g in patients who weigh <30kg, 10g in patients who weigh 30 to 65kg, and 15g in patients who weigh >65kg, each given twice daily. The powder is mixed in 8 ounces of cold or room temperature liquid, such as water, milk, or apple juice, or in 4 to 6 ounces of soft food, such as applesauce or yogurt, and consumed immediately. L-glutamine is also available over-the-counter (OTC) as a dietary supplement. The WAC of Endari™ (L-glutamine oral powder) is $18.50 per packet.
- **Siklos® (hydroxyurea)** is an antimetabolite indicated to reduce the frequency of painful crises and to reduce the need for blood transfusions in pediatric patients 2 years of age and older with sickle cell anemia (SCA) with recurrent, moderate-to-severe, painful crises. This is the first FDA approval of hydroxyurea for use in pediatric patients with SCD. The recommended initial dose is 20mg/kg once daily based on the patient's actual or ideal body weight, whichever is less. The dose may be increased by 5mg/kg/day every 8 weeks, or sooner if a severe painful crisis occurs, until a maximum tolerated dose or 35mg/kg/day is reached (if blood counts are in an acceptable range). The WAC of Siklos® (hydroxyurea) is $5.00 per 100mg tablet.

Recommendations

The College of Pharmacy recommends the prior authorization of Siklos® (hydroxyurea) and NutreStore® (L-glutamine) with the following criteria:

Siklos® (Hydroxyurea Tablets) Approval Criteria:

1. An FDA approved indication of sickle cell anemia; and
2. Member must be 2 years of age or older; and
3. Member must have a history of moderate-to-severe, painful crises; and
4. A trial of hydroxyurea capsules or a patient-specific, clinically significant reason why hydroxyurea capsules are not appropriate for the member; and
5. Prescriber must agree to monitor blood counts every 2 weeks throughout therapy; and
6. Prescriber must agree to monitor the member for the development of secondary malignancies; and
7. Female members must not be pregnant and must have a negative pregnancy test prior to therapy initiation; and
8. Male and female members of reproductive potential must be willing to use effective contraception during and after treatment with Siklos® for at least 6 months after therapy; and
9. Member must not be given live vaccines while on Siklos® therapy; and
10. Initial approvals will be for the duration of 12 months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment.

NutreStore® (L-Glutamine) Approval Criteria [Short Bowel Syndrome (SBS) Diagnosis]:

1. An FDA approved diagnosis of SBS; and
2. NutreStore® must be used in conjunction with a recombinant human growth hormone product that is approved for this indication; and
3. Member must be receiving optimal management of SBS (e.g., specialized oral diet, enteral feedings, parenteral nutrition, fluid and micronutrient supplements); and
4. Approvals will be for up to 16 weeks.

NutreStore® (L-Glutamine) Approval Criteria [Sickle Cell Disease (SCD) Diagnosis]:

1. A diagnosis of SCD; and
2. Member must be 5 years of age or older; and
3. A trial of hydroxyurea or documentation why hydroxyurea is not appropriate for the member; and
4. NutreStore® must be prescribed by, or in consultation with, a hematologist or a specialist with expertise in treatment of SCD (or in consultation with an advanced care practitioner with a supervising physician who is a hematologist or specialist with expertise in treating SCD); and
5. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required.
6. Initial approvals will be for a duration of six months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment.

Additionally, the College of Pharmacy recommends updating the prior authorization criteria for Endari™ (L-glutamine) with the changes noted in red:

Endari™ (L-Glutamine) Approval Criteria:

1. An FDA approved diagnosis of sickle cell disease (SCD); and
2. Member must be 5 years of age or older; and
3. A trial of hydroxyurea or documentation why hydroxyurea is not appropriate for the member; and
4. Endari™ must be prescribed by, or in consultation with, a hematologist or a specialist with expertise in treatment of SCD (or in consultation with an advanced care practitioner with a supervising physician who is a hematologist or specialist with expertise in treating SCD); and
5. A patient-specific, clinically significant reason why NutreStore® (L-glutamine powder for oral solution) cannot be used must be provided; and
6. 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.
7. Initial approvals will be for a duration of six months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment.

---

[1] Ernst D. Siklos Approved for Pediatric Patients With Sickle Cell Anemia. *Monthly Prescribing Reference (MPR)*. Available online at: https://www.empr.com/news/siklos-hydroxyurea-pediatric-sickle-cell-anemia-crises-blood-transfusions/article/720265/. Issued 12/21/2017. Last accessed 09/19/2018.

[2] NutreStore® Prescribing Information. Emmaus Medical, Inc. Available online at: http://www.nutrestore.com/files/NutreStorePI.pdf. Last revised 01/2008. Last accessed 09/19/2018.

[3] L-Glutamine (Endari) for Sickle Cell Disease. *Med Lett Drugs Ther* 2018; 60(1539):21-22.

[4] Siklos® Prescribing Information. Medunik USA. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208843s000lbl.pdf. Last revised 12/2017. Last accessed 09/19/2018.

Appendix E

Vote to Prior Authorize Palynziq™ (Pegvaliase-pqpz)

Oklahoma Health Care Authority
October 2018

Phenylketonuria Pharmacotherapy[1,2,3]

Palynziq™ (pegvaliase-pqpz) is a phenylalanine (Phe)-metabolizing, PEGylated recombinant Phe ammonia lyase (PAL) enzyme indicated to reduce blood Phe concentrations in adult patients with phenylketonuria (PKU) who have uncontrolled blood Phe concentrations >600µmol/L on existing management.

Palynziq™ (pegvaliase-pqpz) is available in single-dose prefilled syringes in the following strengths: 2.5mg/0.5mL, 10mg/0.5mL, and 20mg/mL. Baseline blood Phe concentration should be obtained before initiating treatment with pegvaliase-pqpz. The recommended initial dosage is 2.5mg subcutaneous (sub-Q) once weekly for 4 weeks. The dosage should be titrated in a step-wise manner over at least 5 weeks based on tolerability to achieve a dosage of 20mg sub-Q once daily. The patient should be assessed for tolerability, blood Phe concentration, and dietary protein and Phe intake throughout treatment. Consideration should be given to increasing the dosage to a maximum of 40mg sub-Q once daily in patients who have been on 20mg once daily continuously for at least 24 weeks and who have not achieved either a 20% reduction in blood Phe concentration from pre-treatment baseline or a blood Phe concentration ≤600µmol/L. Palynziq™ should be discontinued in patients who have not achieved at least a 20% reduction in blood Phe concentration from pre-treatment baseline or a blood Phe concentration ≤600µmol/L after 16 weeks of continuous treatment with the maximum dosage of 40mg once daily. The dosage should be reduced and/or dietary protein and Phe intake modified, as needed, to maintain blood Phe concentrations within a clinically acceptable range and >30µmol/L.

Pegvaliase-pqpz has a boxed warning for the risk of anaphylaxis and is only available through the Palynziq™ Risk Evaluation and Mitigation Strategy (REMS) program which requires that patients be prescribed auto-injectable epinephrine with pegvaliase-pqpz. Anaphylaxis occurred in 9% of patients treated with pegvaliase-pqpz in the U.S. Food and Drug Administration (FDA) safety analysis.

The safety and efficacy of pegvaliase-pqpz were established in two clinical studies, PRISM-1 and PRISM-2, in adult patients with PKU with blood Phe concentrations >600µmol/L on existing management. The first study, PRISM-1, was an open-label, randomized, multi-center study of adults with PKU to assess safety and tolerability of self-administered pegvaliase-pqpz in an induction/titration/maintenance regimen with a target maintenance dose of 20mg sub-Q once daily or 40mg sub-Q once daily. Patients previously treated with Kuvan® (sapropterin dihydrochloride) were required to discontinue use at least 14 days prior to the first dose of pegvaliase-pqpz. PRISM-2 was a four-part Phase 3 clinical study that included an open-label continuation of PRISM-1 for up to 13 weeks to assess eligibility for the randomized withdrawal

period. Following this period of up to 13 weeks of additional pegvaliase-pqpz treatment, eligibility for entry into the efficacy assessment period (randomized withdrawal period) was determined by whether a patient achieved ≥20% reduction in blood Phe concentration from pre-treatment baseline (when in previous studies). A total of 86 out of 164 patients (52%) met this response target and continued into the randomized withdrawal period. In the double-blind, placebo-controlled, randomized withdrawal period, patients were randomized in a 2:1 ratio to either continue their maintenance pegvaliase-pqpz dosage or to receive matching placebo for a total of 8 weeks. At week 8 of the randomized withdrawal period, pegvaliase-pqpz-treated patients (20mg once daily or 40mg once daily) maintained their blood Phe concentrations as compared to their randomized withdrawal baseline, whereas patients randomized to matching placebo returned to their pretreatment baseline blood Phe concentrations.

Kuvan® (sapropterin) is a Phe hydroxylase (PAH) activator indicated to reduce blood Phe levels in patients with hyperphenylalaninemia (HPA) due to tetrahydrobiopterin (BH4)-responsive PKU in conjunction with a Phe-restricted diet. Sapropterin was approved by the FDA in December 2007. BH4 is a cofactor required for PAH activity. This pathway accounts for most of Phe catabolism and is responsible for the disposal of approximately 75% of dietary Phe, with the remainder used for protein synthesis. Treatment guidelines recommend that all PKU-diagnosed patients, except for those with two null mutations in *trans*, be offered a trial of sapropterin to determine if the therapy is efficacious in lowering Phe blood levels. In clinical trials, approximately 20 to 56% of PKU patients responded to treatment with sapropterin.

Cost Comparison:

Medication	Cost Per Unit	Cost Per 28 Days	Cost Per Year
Palynziq™ (pegvaliase-pqpz) 2.5mg/0.5mL	**$488.00**	**$1,952.00***	**$25,376.00***
Palynziq™ (pegvaliase-pqpz) 10mg/0.5mL	**$488.00**	**$13,664.00***	**$177,632.00***
Palynziq™ (pegvaliase-pqpz) 20mg/mL	**$488.00**	**$13,664-$27,328***	**$177,632-$355,264.00***
Kuvan® (sapropterin) all strengths/formulations	$36.90-$184.50	$15,498.00¥	$201,474.00¥

Unit = single-dose pre-filled syringe, tablet, or powder for oral solution
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.
*The FDA approved starting dose is 2.5mg sub-Q once weekly for 4 weeks. Dosage should be titrated in a step-wise manner, based on tolerability, over at least 5 weeks, to achieve a dosage of 20mg once daily. Once the 20mg daily dose is maintained over at least 24 weeks, the dose may be increased to a maximum of 40mg daily in patients who have not achieved either a 20% reduction in blood Phe concentration from pre-treatment baseline or a blood Phe concentration ≤600µmol/L.
¥Kuvan® costs based on maximum dose of 20mg/kg once daily for a 75kg patient.

Recommendations

The College of Pharmacy recommends the prior authorization of Palynziq™ (pegvaliase-pqpz) and updating the current prior authorization criteria for Kuvan® (sapropterin). The following criteria would apply (changes noted in red):

Palynziq™ (Pegvaliase-pqpz) Approval Criteria:

1. An FDA approved diagnosis to reduce blood phenylalanine concentrations in patients with phenylketonuria who have uncontrolled blood phenylalanine concentrations >600µmol/L on existing management; and
2. Documentation of active management with a phenylalanine restricted diet; and
3. Baseline phenylalanine concentration must be documented on the prior authorization request and must be drawn within the last 30 days; and
4. Documentation the member's average blood phenylalanine concentration over the last 6 months is >600µmol/L on existing management; and
5. Concomitant use with Kuvan® (sapropterin) will not be approved; and
6. Prescriber, pharmacy, and member must be enrolled in the Palynziq™ Risk Evaluation and Mitigation Strategy (REMS) program and maintain enrollment throughout therapy; and
7. Initial dose must be administered under the supervision of a health care provider equipped to manage anaphylaxis and observe the member for at least 60 minutes following injection; and
8. Member must be prescribed auto-injectable epinephrine and be counseled on its appropriate use; and
9. Initial approvals will be for the duration of 33 weeks to allow for initial titration and for 24 weeks of maintenance treatment with 20mg once daily dosing. Patients should then be assessed for a 20% reduction in blood phenylalanine concentration from pre-treatment baseline or a blood phenylalanine concentration ≤600µmol/L.
    a. If member has not achieved a 20% reduction in blood phenylalanine concentration from pre-treatment baseline or a blood phenylalanine concentration ≤600µmol/L, approvals may be granted for the 40mg once daily dosing for a duration of 16 weeks; or
    b. If member has achieved a 20% reduction in blood phenylalanine concentration from pre-treatment baseline or a blood phenylalanine concentration ≤600µmol/L, subsequent approvals will be for the duration of one year; and
10. Members who do not achieve at least a 20% reduction in blood phenylalanine concentration from pre-treatment baseline or a blood phenylalanine concentration ≤600µmol/L after 16 weeks of continuous treatment with the maximum dosage of 40mg once daily will not be approved for subsequent approvals; and
11. Subsequent approvals will be for the duration of one year.
12. Reauthorization will require the following:
    a. Documentation of active management with a phenylalanine restricted diet; and
    b. Verification from the prescriber of continued response to therapy.

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. Baseline phenylalanine concentration must be documented on the prior authorization request and must be drawn within the last 30 days; and

5. Concomitant use with Palynziq™ (pegvaliase-pqpz) will not be approved; and
6. 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.
7. Subsequent approvals will be for the duration of one year.
8. Reauthorization will require the following:
    a. Documentation of active management with a phenylalanine restricted diet; and
    b. Verification from the prescriber of continued response to therapy.

---

[1] Palynziq™ (pegvaliase-pqpz) Prescribing Information. BioMarin Pharmaceutical Inc. Available online at: https://www.palynziq.com/prescribinginformation.pdf. Last revised 05/2018. Last accessed 09/24/2018.

[2] BioMarin Pharmaceutical Inc. BioMarin Announces FDA Approval for Kuvan First Specific Drug Therapy Approved for the Treatment of PKU. Available online at: http://investors.biomarin.com/2007-12-13-BioMarin-Announces-FDA-Approval-for-Kuvan. Issued 12/2007. Last accessed 09/24/2018.

[3] Page J. New Drug Evaluation: Pegvaliase-pqpz Injection, Subcutaneous. Oregon State University College of Pharmacy. Available online at: http://www.orpdl.org/durm/meetings/meetingdocs/2018_09_27/finals/Pegvaliase_NDE.pdf. Issued 09/2018. Last accessed 09/27/2018.

Appendix F

Vote to Prior Authorize Galafold™ (Migalastat)

Oklahoma Health Care Authority
October 2018

Introduction[1,2]

Galafold™ (migalastat) is an alpha-galactosidase A (alpha-Gal A) pharmacological chaperone indicated for the treatment of adults with a confirmed diagnosis of Fabry disease and an amenable *GLA* gene variant based on in vitro assay data. Treatment is indicated for patients with an amenable *GLA* variant that is interpreted by a clinical genetics professional as causing Fabry disease in the clinical context of the patient. Consultation with a clinical genetics professional is strongly recommended in cases where the amenable *GLA* variant is of uncertain clinical significance or may be benign (not causing Fabry disease). Certain *GLA* mutations causing Fabry disease result in the production of abnormally folded and less stable forms of the alpha-Gal A protein which retain enzymatic activity. Migalastat reversibly binds to the active site of the alpha-Gal A protein in amenable *GLA* variants and stabilizes it. This allows trafficking into the lysosome. In the lysosome, migalastat dissociates from alpha-Gal A allowing it to break down globotriaosyl-ceramide (GL-3).

In a 6-month randomized, double-blind, placebo-controlled phase (stage 1) followed by a 6-month open-label, treatment phase (stage 2), migalastat was found to reduce the number of GL-3 inclusions per kidney interstitial capillary (KIC) at 6 months. In stage 1 (6-month) post hoc analysis and stage 2 (12-month) pre-specified analysis in 45 patients with suitable mutant alpha-Gal A, 6 months of migalastat was associated with a significantly greater reduction in the mean number of GL-3 inclusions per KIC than placebo (−0.25±0.10 vs. 0.07±0.13; P=0.008). The reduction in KIC GL-3 at 6 months remained stable after an additional 6 months of treatment. A significant reduction in the mean number of GL-3 inclusions per KIC was observed at 12 months in patients who switched from placebo to migalastat at 6 months (−0.33±0.15; P=0.01). Patients included in the study were 16 to 74 years of age, had a mutation in the *GLA* gene resulting in a mutant protein that would respond to migalastat as determined by preliminary assay, and had an estimated glomerular filtration rate (eGFR) >30mL/min/1.73m^2.

Migalastat is supplied as 123mg capsules packaged in a 14-capsule wallet pack for a 4-week supply. The recommended dosing regimen of migalastat is 123mg orally once every other day at the same time of day. Migalastat should be taken on an empty stomach, with no food for at least two hours before and two hours after administration.

Cost Comparison:

Medication	Cost Per Unit*	Cost Per 28 Days of Therapy	Cost Per Year
Galafold™ (migalastat) 123mg	**$1,732.14**	**$24,249.96**	**$315,249.48**
Fabrazyme® (agalsidase beta) 35mg	$5,894.00	$23,576.00$^{\Delta}$	$306,488.00$^{\Delta}$

Costs do not reflect rebated price or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
*Unit = capsule or vial
$^{\Delta}$Cost for Fabrazyme® based on 1mg/kg given every two weeks for a 70kg patient.

Recommendations

The College of Pharmacy recommends the prior authorization of Galafold™ (migalastat) with the following criteria [the criteria shown in red on line 4 has been added due to current lack of evidence for efficacy using Galafold™ (migalastat) with enzyme replacement therapy]:

Galafold™ (Migalastat) Approval Criteria:

1. An FDA approved diagnosis of Fabry disease with a confirmed amenable *GLA* gene variant based on in vitro assay data; and
2. Galafold™ must be prescribed in consultation with a geneticist or an advanced care practitioner with a supervising physician who is a geneticist; and
3. Member must have an estimated glomerular filtration rate (eGFR) of at least 30mL/min/1.73m^2; and
4. Galafold™ will not be approved for concomitant use with enzyme replacement therapy (ERT); and
5. Galafold™ will initially be approved for six months. After that time, compliance will be required for continued authorization; and
6. A quantity limit of 14 capsules per 28 days will apply.

[1] Galafold™ Prescribing Information. Amicus Therapeutics, Inc. Available online at: https://www.amicusrx.com/pi/galafold.pdf. Last revised 08/2018. Last accessed 09/14/2018.

[2] Germain DP, Hughes DA, Nicholls K, et al. Treatment of Fabry's Disease with the Pharmacologic Chaperone Migalastat. *N Engl J Med* 2016; 375:545-555.

Appendix G

Vote to Prior Authorize Qbrexza™ (Glycopyrronium)

Oklahoma Health Care Authority
October 2018

Introduction[1]

Qbrexza™ (glycopyrronium) is an anticholinergic indicated for the topical treatment of primary axillary hyperhidrosis in adults and pediatric patients 9 years of age and older. Glycopyrronium is a competitive inhibitor of acetylcholine receptors that are located on certain peripheral tissues, including sweat glands. In hyperhidrosis, glycopyrronium inhibits the action of acetylcholine on sweat glands, thereby reducing sweating.

Efficacy of glycopyrronium was determined in two randomized, vehicle-controlled, multicenter trials, Trial 1 and Trial 2, in patients with primary axillary hyperhidrosis. Patients were randomized to receive either glycopyrronium 2.4% or vehicle applied once daily to each axilla. The co-primary endpoints were the proportion of patients having at least a 4-point improvement from baseline in the weekly mean Axillary Sweating Daily Diary (ASDD) Item 2 score at week 4 and the mean absolute change from baseline in measured sweat production at week 4. The ASDD is designed to measure the severity and impact of any underarm sweating experienced by the patient within the previous 24 hours, including nighttime hours. The question from Item 2 is "During the past 24 hours, how would you rate your underarm sweating at its worst?" and is scored from 0 (no sweating) to 10 (worst possible sweating). The ASDD Item 2 responder rate was significantly greater for glycopyrronium-treated (GT) patients than for vehicle-treated patients in Trial 1 and Trial 2 ($P<0.001$). For Trial 1, the GT group had a greater reduction in gravimetrically measured sweat production than the vehicle group (-96.2mg/5min vs. -90.6mg/5min, respectively; $P=0.001$). For Trial 2, a difference favoring glycopyrronium over the vehicle for mean absolute change from baseline in sweat production was seen (-110.3mg/5min vs. -92.2mg/5min, respectively; $P<0.001$).

Qbrexza™ is supplied in a carton containing 30 pouches. Each pouch contains a single-use cloth pre-moistened with 2.4% glycopyrronium solution. Glycopyrronium 2.4% cloth is for topical use in the underarm area only and not for use in other body areas. It is to be applied once every 24 hours to clean, dry skin in the underarm area. A single cloth should be used for both underarms. Since glycopyrronium may cause temporary dilation of the pupils and blurred vision if it comes in contact with the eyes, washing hands immediately with soap and water after applying and discarding the glycopyrronium cloth is recommended. Glycopyrronium may also cause worsening of urinary retention and lack of sweating in high ambient temperatures leading to heat illness. Overuse of glycopyrronium may increase the incidence of these anticholinergic effects.

Cost Comparison:

Medication	Cost Per Unit*	Cost Per 30 Days of Therapy or 60mL Bottle
Qbrexza™ (glycopyrronium 2.4%)	**$18.33**	**$549.90**
Drysol™ (aluminum chloride 20%)	$0.16	$9.60
Xerac AC® (aluminum chloride 6.25%)	$0.14	$8.40

Cost does not reflect rebated price or net cost. Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
*Unit = cloth or milliliter

Specialist Recommendations: The College of Pharmacy received input from an Oklahoma Health Care Authority staffed physician regarding the coverage of Qbrexza™ (glycopyrronium). It was recommended that Qbrexza™ only be covered for children with hyperhidrosis where a licensed behavioral health specialist has done a paper assessment and determined the hyperhidrosis is causing social anxiety, depression, or other mental health-related issues. Additionally, it was recommended that a failed trial of Drysol™ (20% aluminum chloride) be required prior to Qbrexza™ approval consideration.

Recommendations

The College of Pharmacy recommends the prior authorization of Qbrexza™ (glycopyrronium) with the following criteria [the criteria shown in red on line 2 has been updated based on the Drug Utilization Review (DUR) Board recommendation, and additional criteria has been added on line 4 to ensure safe product use]:

Qbrexza™ (Glycopyrronium) Approval Criteria:

1. An FDA approved diagnosis of primary axillary hyperhidrosis in pediatric patients 9 years of age to 20 years of age; and
2. Documentation of assessment by a licensed behavior specialist or the prescribing physician indicating the member's hyperhidrosis is causing social anxiety, depression, or similar mental health-related issues that impact the member's ability to function in day-to-day living must be provided; and
3. Member must have failed a trial of Drysol™ (20% aluminum chloride) at least three weeks in duration; and
4. Prescriber must verify that the member has received counseling on the safe and proper use of Qbrexza™; and
5. A quantity limit of one box (30 cloths) per 30 days will apply.

[1] Dermira, Inc. Qbrexza™ Prescribing Information. Available online at: http://pi.dermira.com/QbrexzaPI.pdf. Last revised 06/2018. Last accessed 09/18/2018.

Appendix H

Vote to Prior Authorize FloLipid® (Simvastatin Oral Suspension) and Update the Prior Authorization Criteria for Antihyperlipidemics

Oklahoma Health Care Authority
October 2018

Introduction[1,2,3,4,5,6]

- **FloLipid® (simvastatin oral suspension)** was approved by the U.S. Food and Drug Administration (FDA) in April 2016 and is available as a 20mg/5mL and 40mg/5mL strawberry-flavored oral suspension. Each bottle of oral suspension contains 150mL and should be used within one month of opening. FloLipid® is bioequivalent to Zocor® (simvastatin tablets). FloLipid® recently became available on the market, and the Wholesale Acquisition Cost (WAC) of FloLipid® 40mg/5mL is $1.66 per milliliter, resulting in a monthly cost of $249.00 at a dose of 40mg per day. In comparison, the National Average Drug Acquisition Cost (NADAC) of generic simvastatin 40mg tablet is $0.04 per tablet, resulting in a monthly cost of $1.20 at a dose of 40mg per day.
- **Repatha® (evolocumab)** was approved by the FDA in December 2017 for the prevention of heart attacks, strokes, and coronary revascularization in adults with established cardiovascular (CV) disease. In the Repatha® CV outcomes study (FOURIER), Repatha® reduced the risk of heart attack by 27%, the risk of stroke by 21%, and the risk of coronary revascularization by 22%. The FDA also approved Repatha® to be used as an adjunct to diet, alone or in combination with other lipid-lowering therapies, such as statins, for the treatment of adults with primary hyperlipidemia to reduce low density lipoprotein cholesterol (LDL-C). Repatha® was first FDA approved in 2015 as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic CV disease, who require additional lowering of LDL-C, and as an adjunct to diet and other LDL-lowering therapies (e.g., statins, ezetimibe, LDL apheresis) in patients 13 years of age or older with homozygous familial hypercholesterolemia (HoFH) who require additional lowering of LDL-C.

Recommendations

The College of Pharmacy recommends the following changes to the Statin Medications and Ezetimibe Product Based Prior Authorization (PBPA) category (changes noted in red):

1. Placement of FloLipid® (simvastatin oral suspension) into the Special Prior Authorization (PA) Tier:
   a. Use of FloLipid® will require a patient-specific, clinically significant reason why the member cannot use simvastatin oral tablets, even when the tablets are crushed.
2. Moving ezetimibe to Tier-1 based on generic availability and low net cost.

Statin Medications and Ezetimibe*	
Tier-1	**Special PA**
atorvastatin (Lipitor®)	fluvastatin (Lescol® & Lescol® XL)
ezetimibe (Zetia®)	lovastatin (Altoprev®)
lovastatin (Mevacor®)	pitavastatin calcium (Livalo®)
pravastatin (Pravachol®)	pitavastatin magnesium (Zypitamag™)
rosuvastatin (Crestor®)	pitavastatin sodium (Nikita™)
simvastatin (Zocor®)	**simvastatin suspension (FloLipid®)**
	simvastatin/ezetimibe (Vytorin®)

*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

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

1. Use of any Special PA medication will require a patient-specific, clinically significant reason why lower tiered medications with similar or higher LDL reduction cannot be used; and
2. Use of FloLipid® (simvastatin oral suspension) will require a patient specific, clinically significant reason why the member cannot use simvastatin oral tablets, even when the tablets are crushed.

Additionally, the College of Pharmacy recommends removing the prior authorization from omega-3-acid ethyl esters (generic Lovaza®), based on low net cost, as well as removing the nicotinic acid trial requirement from the current omega-3 fatty acids approval criteria, based on recommendations from the Drug Utilization Review (DUR) Board (changes noted in red):

Omega-3 Fatty Acids Approval Criteria:

1. Laboratory documentation of severe hypertriglyceridemia (fasting triglycerides ≥500mg/dL) and controlled diabetes (fasting glucose <150mg/dL at the time of triglycerides measurement and HgA1c <7.5%); and
2. Previous failure with ~~both nicotinic acid and~~ fibric acid medications; and
3. Use of Vascepa® or Epanova® requires a previous failure of or a patient-specific, clinically significant reason why the member cannot use omega-3-acid ethyl esters (generic Lovaza®), which is available without prior authorization; and
4. Use of Vascepa® 0.5 gram requires a patient-specific, clinically significant reason why the member cannot use Vascepa® 1 gram.

Furthermore, the College of Pharmacy recommends the following updates to the current Juxtapid® and Kynamro® Approval Criteria, based on net costs (changes noted in red):

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

1. An FDA approved diagnosis of homozygous familial hypercholesterolemia (HoFH) defined by the presence of at least one of the following criteria:
    a. A documented functional mutation(s) in both LDL receptor alleles or alleles known to affect LDL receptor functionality via genetic testing; or
    b. An untreated total cholesterol >500mg/dL and triglycerides <300mg/dL and at least one of the following:

i. Documentation that both parents have untreated total cholesterol >250mg/dL; or
ii. Presence of tendinous/cutaneous xanthoma prior to age 10 years; and

2. Documented ~~failure~~ trial of high dose statin therapy (LDL reduction capability equivalent to ~~atorvastatin 80mg or higher~~ rosuvastatin 40mg) or maximally tolerated statin therapy at least 12 weeks in duration; and
3. Documented trial of Repatha® (evolocumab) at least 12 weeks in duration; and
4. Member requires additional lowering of LDL-C (baseline, current, and goal LDL-C levels must be provided); and
5. Prescriber must be certified with Juxtapid® or Kynamro® REMS program.

Lastly, the College of Pharmacy recommends the following updates to the current PCSK9 Inhibitors Approval Criteria, based on the new FDA approved indications for Repatha® (changes noted in red):

PCSK9 Inhibitors Approval Criteria:

1. **For Repatha® (evolocumab):**
   a. An FDA approved diagnosis of homozygous familial hypercholesterolemia (HoFH) defined by the presence of at least one of the following:
      i. Documented functional mutation(s) in both LDL receptor alleles or alleles known to affect LDL receptor functionality via genetic testing; or
      ii. An untreated total cholesterol >500mg/dL and at least one of the following:
         1. Documented evidence of definite heterozygous familial hypercholesterolemia (HeFH) in both parents; or
         2. Presence of tendinous/cutaneous xanthoma prior to age 10 years; or
   b. An FDA approved diagnosis of primary hyperlipidemia; or
   c. An FDA approved indication to reduce the risk of myocardial infarction, stroke, and coronary revascularization in adults with established cardiovascular disease (CVD); and
      i. Documentation of established CVD; and
         1. Supporting diagnoses/conditions and dates of occurrence signifying established CVD; or
2. **For Praluent® (alirocumab):**
   a. An FDA approved diagnosis of HeFH defined by the presence of one of the following criteria:
      i. Documented functional mutation(s) in the LDL receptor (LDLR) gene or other HeFH-related genes via genetic testing; or
      ii. Definite HeFH using either the Simon Broome Register criteria or the Dutch Lipid Network criteria; or
   b. An FDA approved diagnosis of clinical atherosclerotic cardiovascular disease defined by the presence of one of the following criteria:
      i. High cardiovascular risk confirmed by Framingham risk score; and
         1. Supporting diagnoses/conditions signifying this risk level; or
      ii. Documented history of Coronary Heart Disease (CHD); and

1. Supporting diagnoses/conditions and dates of occurrence signifying history of CHD; and

3. Member must be 13 years of age or older for the diagnosis of HoFH or must be 18 years of age or older for all other FDA-approved diagnoses or indications; and
4. Member must be on high dose statin therapy (LDL reduction capability equivalent to rosuvastatin 40mg) or on maximally tolerated statin therapy; and
    a. Statin trials must be at least 12 weeks in duration (dosing, dates, duration of treatment, and reason for discontinuation must be provided); and
    b. LDL-cholesterol (LDL-C) levels should be included following at least 12 weeks of treatment with each statin medication; and
    c. For statin intolerance due to myalgia, creatine kinase (CK) labs verifying rhabdomyolysis must be provided; and
    d. Tier structure rules still apply; and
5. Member requires additional lowering of LDL-C (baseline, current, and goal LDL-C levels must be provided); and
6. Prescriber must verify that member has been counseled on appropriate use, storage of the medication, and administration technique; and
7. A quantity limit of two syringes or pens per 28 days will apply for Praluent®. A quantity limit of two syringes or autoinjectors per 28 days will apply for Repatha® 140mg and a quantity limit of one autoinjector per 28 days for Repatha® 420mg. Patients requesting Repatha® 420mg strength will not be approved for multiple 140mg syringes or autoinjectors but instead should use one 420mg autoinjector.
8. Initial approvals will be for the duration of three months. Continued authorization at that time will require the prescriber to provide recent LDL-C levels to demonstrate the effectiveness of this medication, and compliance will be checked at that time and every six months thereafter for continued approval.

---

[1] U.S. Food and Drug Administration (FDA). NDA Approval: FloLipid® (Simvastatin Oral Suspension). Available online at: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=BasicSearch.process. Issued 04/21/2016. Last accessed 09/18/2018.

[2] FloLipid® (Simvastatin Oral Suspension) Prescribing Information. Salerno Pharma. Available online at: http://www.salernopharma.com/wp-content/uploads/2017/10/FloLipid-Insert.pdf. Last revised 07/2017. Last accessed 09/18/2018.

[3] FloLipid® (Simvastatin Oral Suspension) Package Insert. MedLibrary.org. Available online at: https://medlibrary.org/lib/rx/meds/flolipid-1/. Last revised 10/12/2017. Last accessed 09/18/2018.

[4] Amgen News Release: FDA Approves Amgen's Repatha® (Evolocumab) to Prevent Heart Attack and Stroke. Available online at: https://www.amgen.com/media/news-releases/2017/12/fda-approves-amgens-repatha-evolocumab-to-prevent-heart-attack-and-stroke/. Issued 12/01/2017. Last accessed 09/18/2018.

[5] Repatha® (Evolocumab) Prescribing Information. Amgen. Available online at: http://pi.amgen.com/united_states/repatha/repatha_pi_hcp_english.pdf. Last revised 12/2017. Last accessed 09/18/2018.

[6] Repatha® (Evolocumab) Package Insert. MedLibrary.org. Available online at: https://medlibrary.org/lib/rx/meds/repatha/. Last revised 12/01/2017. Last accessed 09/18/2018.

Appendix I

Vote to Prior Authorize Verzenio™ (Abemaciclib), Ogivri™ (Trastuzumab-dkst), and Lynparza® (Olaparib)

Oklahoma Health Care Authority
October 2018

Introduction[1,2,3]

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

- **September 2017:** The FDA approved Verzenio™ (abemaciclib) in combination with fulvestrant for women with hormone receptor (HR)-positive, human epidermal receptor 2 (HER2)-negative, advanced or metastatic breast cancer with disease progression following endocrine therapy.
- **December 2017:** Perjeta® (pertuzumab) was granted regular approval by the FDA for use in combination with Herceptin® (trastuzumab) and chemotherapy as adjuvant treatment of patients with HER2-positive early breast cancer at high risk of recurrence.
- **December 2017:** The FDA approved Ogivri™ (trastuzumab-dkst) as a biosimilar to Herceptin® (trastuzumab) for the treatment of patients with HER2-overexpressing breast cancer or metastatic stomach cancer (gastric or gastroesophageal junction adenocarcinoma).
- **January 2018:** The FDA granted regular approval to Lynparza® (olaparib), a poly (ADP-ribose) polymerase (PARP) inhibitor, for the treatment of patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm), HER2-negative, metastatic breast cancer who have been treated with chemotherapy either in the neoadjuvant, adjuvant, or metastatic setting. Lynparza® was previously approved for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer.
- **February 2018:** The FDA approved Verzenio™ (abemaciclib) for use in combination with an aromatase inhibitor as initial endocrine-based therapy for postmenopausal women with HR-positive, HER2-negative, advanced or metastatic breast cancer.
- **April 2018:** The FDA approved Afinitor® (everolimus) tablets for oral suspension for the adjunctive treatment of adult and pediatric patients 2 years of age and older with tuberous sclerosis complex (TSC)-associated partial-onset seizures. Everolimus was previously approved for two other manifestations of TSC: TSC-associated subependymal giant cell astrocytoma (SEGA) and TSC-associated renal angiomyolipoma.
- **July 2018:** The FDA expanded the indication for Kisqali® (ribociclib) for use in combination with an aromatase inhibitor for pre/perimenopausal women with HR-positive, HER2-negative, advanced or metastatic breast cancer, as initial endocrine-based therapy.

Guideline Updates:

- **Perjeta® (Pertuzumab):** Perjeta® received additional recommendations to be used as adjuvant, systemic therapy for patients with node positive, HER2-positive tumors or for patients with high-risk, node negative breast cancer.
- **Afinitor® (Everolimus):** Afinitor® received additional recommendations to be used in combination with exemestane, fulvestrant, or tamoxifen for the treatment of HER2-negative, HR-positive, advanced breast cancer.

Product Summaries[4,5,6]

Lynparza® (Olaparib):

- **Therapeutic Class:** PARP inhibitor
- **Indication(s):**
  - For the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer, who are in complete or partial response to platinum-based chemotherapy
  - For the treatment of adult patients with deleterious or suspected deleterious gBRCAm, advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy
  - In patients with deleterious or suspected deleterious gBRCAm, HER2-negative, metastatic breast cancer who have been treated with chemotherapy in the neoadjuvant, adjuvant, or metastatic setting; patients with HR-positive breast cancer should have been treated with a prior endocrine therapy or be considered inappropriate for endocrine therapy
- **How Supplied:** 100mg and 150mg oral tablets
- **Dose:** 300mg orally twice daily with or without food
- **Cost:** $115.72 per tablet; 300mg twice daily for 30 days (120 tablets): $13,886.40

Ogivri™ (Trastuzumab-dkst):

- **Therapeutic Class:** HER2/neu receptor antagonist; biosimilar to Herceptin® (trastuzumab)
- **Indication(s):**
  - Treatment of HER2-overexpressing breast cancer
  - Treatment of HER2-overexpressing, metastatic gastric or gastroesophageal junction adenocarcinoma
- **How Supplied:** 420mg lyophilized powder in a multiple-dose vial for reconstitution
- **Dose:**
  - Adjuvant Treatment of HER2-Overexpressing Breast Cancer:
    - Recommended initial dose of 4mg/kg over 90 minutes via intravenous (IV) infusion, then 2mg/kg over 30 minutes weekly for 12 weeks (with paclitaxel or docetaxel) or 18 weeks (with docetaxel/carboplatin); 1 week after the last weekly dose of trastuzumab-dkst, 6mg/kg should be administered as an IV infusion over 30 to 90 minutes every 3 weeks to complete a total of 52 weeks of therapy; or

    - Recommended initial dose of 8mg/kg over 90 minutes via IV infusion, then 6mg/kg over 30 to 90 minutes via IV infusion every 3 weeks for 52 weeks
  - Metastatic HER2-Overexpressing Breast Cancer:
    - Initial dose of 4mg/kg as a 90 minute IV infusion, followed by subsequent weekly doses of 2mg/kg as 30 minute IV infusions
  - Metastatic HER2-Overexpressing Gastric Cancer:
    - Initial dose of 8mg/kg over 90 minutes via IV infusion, followed by 6mg/kg over 30 to 90 minutes via IV infusion every 3 weeks
- **Cost:** Cost information for Ogivri™ is not yet available

Verzenio™ (Abemaciclib):

- **Therapeutic Class:** Kinase inhibitor
- **Indication(s):**
  - In combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of postmenopausal women with HR-positive, HER2-negative, advanced or metastatic breast cancer
  - In combination with fulvestrant for the treatment of women with HR-positive, HER2-negative, advanced or metastatic breast cancer with disease progression following endocrine therapy
  - As monotherapy for the treatment of adult patients with HR-positive, HER2-negative, advanced or metastatic breast cancer with disease progression following endocrine therapy and prior chemotherapy in the metastatic setting
- **How Supplied:** 50mg, 100mg, 150mg, and 200mg oral tablets
- **Dose:** The recommended starting dose when used in combination with fulvestrant or an aromatase inhibitor is 150mg twice daily. The recommended starting dose when used as monotherapy is 200mg twice daily. Dosing interruption and/or dose reductions may be required based on individual safety and tolerability.
- **Cost:** $201.45 per tablet; $12,087 per month based on recommended dose of 1 tablet twice daily

Recommendations

Afinitor® (Everolimus) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of advanced breast cancer; and
2. Negative expression of human epidermal receptor type 2 (HER2); and
3. Hormone receptor positive; and
4. Used in combination with exemestane, fulvestrant, or tamoxifen; and
5. Member must have failed treatment with, have a contraindication to, or be intolerant to letrozole or anastrozole.

Afinitor® (Everolimus) Approval Criteria [Tuberous Sclerosis Complex (TSC)-Associated Partial-Onset Seizures Diagnosis]:

1. An FDA approved diagnosis of TSC-associated partial-onset seizures; and
2. Initial prescription must be written by a neurologist or neuro-oncologist; and

3. Member must have failed therapy with at least three other medications commonly used for seizures; and
4. Afinitor® must be used as adjunctive treatment; and
5. The member must not be taking any P-gp and strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, ritonavir, clarithromycin) concurrently with Afinitor®; and
6. The member must not be taking St. John's wort concurrently with Afinitor®; and
7. The prescriber must verify that Afinitor® trough levels and adverse reactions (e.g., non-infectious pneumonitis, stomatitis, hyperglycemia, dyslipidemia, thrombocytopenia, neutropenia, febrile neutropenia) will be monitored, and dosing changes or discontinuations will correspond with recommendations in the drug labeling; and
8. Verification from the prescriber that female members will use contraception while receiving Afinitor® therapy and for eight weeks after the last dose of Afinitor® and that male members with female partners of reproductive potential will use contraception while receiving Afinitor® therapy and for four weeks after the last dose of Afinitor®; and
9. The member's recent body surface area (BSA) must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling.
10. Initial approvals will be for the duration of three months. For continuation, the prescriber must include information regarding improved response/effectiveness of the medication.

Kisqali® (Ribociclib) Approval Criteria [Breast Cancer Diagnosis]:

~~1. A patient-specific, clinically significant reason why the member cannot use the co-packaged formulation with letrozole; and~~
~~2. A diagnosis of advanced or metastatic breast cancer, initial therapy; and~~
3. Member must be hormone receptor positive; and
4. Member must be human epidermal receptor type 2 (HER2)-negative; and
5. If used in combination with an aromatase inhibitor:
    a. Diagnosis of advanced or metastatic breast cancer, initial therapy; or
6. If used in combination with fulvestrant:
    a. Diagnosis of advanced or metastatic breast cancer, as initial endocrine based therapy or following disease progression on endocrine therapy; and
    b. Must be used in postmenopausal women only.

~~7. Ribociclib must be given in combination with an aromatase inhibitor; and~~
~~8. Ribociclib must be used in postmenopausal women only.~~

Kisqali® Femara® Co-Pack (Ribociclib/Letrozole) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of advanced or metastatic breast cancer, initial therapy; and
2. Member must be hormone receptor positive; and
3. Member must be human epidermal receptor type 2 (HER2)-negative.~~; and~~
~~4. Ribociclib must be used in postmenopausal women only.~~

Lynparza® (Olaparib) Approval Criteria [Ovarian Cancer Diagnosis]:

1. Diagnosis of deleterious or suspected deleterious germline BRCA mutated (gBRCAm), advanced ovarian cancer; and

2. The member must have been treated with three or more prior lines of chemotherapy. Prior chemotherapy regimens should be documented on the prior authorization request; and
3. A quantity limit based on FDA approved dosing will apply.

Lynparza® (Olaparib) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of metastatic breast cancer; and
2. Member must have shown progression on previous chemotherapy in any setting; and
3. Human epidermal receptor 2 (HER2)-negative; and
4. Positive test for a germline BRCA-mutation (gBRCAm); and
5. Members with hormone receptor positive disease must have failed prior endocrine therapy or are considered to not be a candidate for endocrine therapy.

Ogivri™ (Trastuzumab-dkst) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of human epidermal receptor 2 (HER2)-overexpressing breast cancer; and
2. A patient-specific, clinically significant reason why the member cannot use Herceptin® (trastuzumab).

Ogivri™ (Trastuzumab-dkst) Approval Criteria [Metastatic Gastric or Gastroesophageal Junction Adenocarcinoma Diagnosis]:

1. Diagnosis of human epidermal receptor 2 (HER2)-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma; and
2. A patient-specific, clinically significant reason why the member cannot use Herceptin® (trastuzumab).

Perjeta® (Pertuzumab) Approval Criteria [Breast Cancer Diagnosis]:

1. Positive expression of human epidermal receptor type 2 (HER2); and
2. Used in one of the following settings:
    a. Metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease:
        i. Used in combination with trastuzumab and docetaxel; or
    b. Neoadjuvant treatment of members with locally advanced, inflammatory, or early stage breast cancer (either >2cm in diameter or node positive):
        i. Used in combination with trastuzumab and docetaxel (neoadjuvant treatment may also contain other agents in addition to trastuzumab and docetaxel); or
    c. Adjuvant systemic therapy for patients with node positive, HER2-positive tumors or high-risk node negative members [tumor >1cm; tumor 0.5 to 1cm with histologic or nuclear grade 3; estrogen receptor (ER)/progesterone receptor (PR) negative; or age <35]:
        i. Used in combination with trastuzumab and paclitaxel following AC (doxorubicin/cyclophosphamide); or
        ii. Used in combination with trastuzumab and docetaxel following AC; or
        iii. Used in combination with TCH (docetaxel/carboplatin/trastuzumab).

Verzenio™ (Abemaciclib) Approval Criteria [Breast Cancer Diagnosis]:

1. Used in one of the following settings:
    a. In combination with an aromatase inhibitor as initial endocrine-based therapy for postmenopausal women; or
    b. In combination with fulvestrant with disease progression following endocrine therapy in advanced or metastatic breast cancer; or
    c. As monotherapy for disease progression following endocrine therapy and prior chemotherapy in metastatic breast cancer; and
2. All the following criteria must be present:
    a. Advanced or metastatic breast cancer; and
    b. Progressed after endocrine therapy when used with fulvestrant or as initial therapy in combination with an aromatase inhibitor; and
    c. Hormone receptor positive; and
    d. Human epidermal receptor 2 (HER2)-negative.

---

[1] U.S. Food and Drug Administration (FDA). Hematology/Oncology (Cancer) Approvals & Safety Notifications. Available online at: https://www.fda.gov/drugs/informationondrugs/approveddrugs/ucm279174.htm. Last revised 09/24/2018. Last accessed 09/27/2018.

[2] Von Minckwitz G, Procter MJ, De Azambuja E, et al. Adjuvant Pertuzumab and Trastuzumab in Early HER2-Positive Breast Cancer. *N Engl J Med* 2017; 377:122-131.

[3] Kornblum N, Zhao F, Manola J, et al. Randomized Phase II Trial of Fulvestrant Plus Everolimus or Placebo in Postmenopausal Women With Hormone Receptor–Positive, Human Epidermal Growth Factor Receptor 2–Negative Metastatic Breast Cancer Resistant to Aromatase Inhibitor Therapy: Results of PrE0102. *JCO* 2018; 36(16):1556-1563.

[4] Verzenio™ (abemaciclib) Prescribing Information. Eli Lilly and Company. Available online at: http://uspl.lilly.com/verzenio/verzenio.html#pi. Last revised 02/2018. Last accessed 09/27/2018.

[5] Ogivri™ (trastuzumab-dkst) Prescribing Information. Mylan. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/761074s000lbl.pdf. Last revised 12/2017. Last accessed 09/27/2018.

[6] Lynparza® (olaparib) Prescribing Information. AstraZeneca Pharmaceuticals. Available online at: https://www.azpicentral.com/lynparza_tb/pi_lynparza_tb.pdf#page=1. Last revised 01/2018. Last accessed 09/27/2018.

Appendix J

Fiscal Year 2018 Annual Review of Acute Lymphoblastic Leukemia (ALL) and Chronic Myeloid Leukemia (CML) Medications and 30-Day Notice to Prior Authorize Yescarta® (Axicabtagene)

Oklahoma Health Care Authority
October 2018

Introduction[1,2,3,4]

Leukemia is an abnormal and autonomous proliferation of one or more blood-forming elements with infiltrations of the bone marrow and other organs. Leukemia is a heterogeneous group of neoplasms arising from the malignant transformation of hematopoietic cells that eventually replace the normal marrow, leading to the signs and symptoms of leukemia. Approximately 60,300 new cases of leukemia are expected to be diagnosed in 2018 and approximately 24,370 deaths from leukemia are expected in 2018.

Chronic myeloid leukemia (CML) is a slowly progressing blood and bone marrow disease that usually occurs during or after middle age and rarely occurs in children. CML occurs due to a genetic mutation called the Philadelphia chromosome (Ph) resulting in the bone marrow making an enzyme called tyrosine kinase that causes too many stem cells to become white blood cells (blasts). A piece of chromosome 9 and a piece of chromosome 22 break off and trade places forming the BCR-ABL gene. CML treatment changed dramatically with the approval of imatinib in 2001, a targeted therapy that inhibits the BCR-ABL tyrosine kinase. Currently there are several tyrosine kinase inhibitors (TKIs) approved to treat CML including imatinib, nilotinib, dasatinib, and ponatinib; these are the mainstays of treatment for CML.

Acute lymphoblastic leukemia (ALL) is the most common type of cancer in children, but can also be seen in adults. It is estimated that there will be 5,960 new cases of ALL in 2018 and 1,470 estimated deaths from ALL in 2018. The majority of patients with ALL are between 15 and 39 years of age. Adolescent and young adult (AYA) patients are treated similar to pediatric patients receiving aggressive chemotherapy including induction, consolidation, and maintenance for 1 to 3 years. Adults can be treated similar to AYA patients or with multi-agent chemotherapy. Some patients with ALL, typically adults, have Philadelphia chromosome positive (Ph+) disease and can be treated with BCR-ABL TKIs in addition to chemotherapy.

Current Prior Authorization Criteria

Blincyto® (Blinatumomab) Approval Criteria:

1. Blincyto® should be used as a single-agent only; and
2. Member must have one of the following:
    a. Relapsed/refractory Philadelphia chromosome negative (Ph-) acute lymphoblastic leukemia (ALL); or

b. Relapsed/refractory Philadelphia chromosome positive (Ph+) ALL after failure of two tyrosine kinase inhibitors (TKIs); or
c. Ph- ALL as consolidation in adolescent/young adult or members younger than 65 years of age without substantial comorbidity with persistent or late clearance minimal residual disease positive (MRD+) following a complete response to induction.

Besponsa® (Inotuzumab Ozogamicin) Approval Criteria:

1. Besponsa® must be used as a single-agent only; and
2. Member must have one of the following:
   a. Relapsed/refractory Philadelphia chromosome negative (Ph-) acute lymphoblastic leukemia (ALL); or
   b. Relapsed/refractory Philadelphia chromosome positive (Ph+) ALL who are intolerant/refractory to two or more tyrosine kinase inhibitors (TKIs).

Bosulif® (Bosutinib) Approval Criteria [Philadelphia Chromosome Positive (Ph+) Acute Lymphoblastic Leukemia (ALL) Diagnosis]:

1. Bosulif® may be authorized for relapsed/refractory ALL either as:
   a. Single-agent; or
   b. In combination with an induction regimen not previously given; and
2. Bosulif® must be used only in members with E255K/V, F317L/VI/C, F359V/C/I, T315A, or Y253H mutations.

Bosulif® (Bosutinib) Approval Criteria [Chronic Myeloid Leukemia (CML) Diagnosis]:

1. Members with chronic, accelerated, or blast phase CML with resistance or intolerance after primary treatment with either: dasatinib, imatinib, or nilotinib with the following BCR-ABL1 transcript levels:
   a. 0.01% to 1% at >12 months; or
   b. >1% to 10% at ≥12 months; or
   c. >10% at any milestone.

Gleevec® (Imatinib) Approval Criteria [Philadelphia Chromosome Positive (Ph+) Acute Lymphoblastic Leukemia (ALL) Diagnosis]:

1. Gleevec® may be approved for one of the following indications:
   a. Upfront therapy (including induction and consolidation) in combination with multi-agent chemotherapy or as a single-agent; or
   b. Maintenance therapy including:
      i. In combination with vincristine and prednisone, with or without methotrexate and mercaptopurine; or
      ii. Post-hematopoietic stem cell transplant; or
   c. In relapsed/refractory ALL and as a single-agent or in combination with multi-agent chemotherapy.

Gleevec® (Imatinib) Approval Criteria [Bone Cancer – Chordoma Diagnosis]:

1. Single-agent therapy or in combination with cisplatin or sirolimus for the treatment of recurrent disease.

Gleevec® (Imatinib) Approval Criteria [Chronic Myeloid Leukemia (CML) Diagnosis]:

1. Member must have one of the following:
    a. Newly diagnosed chronic, accelerated, or blast phase CML; or
    b. Post-hematopoietic stem cell transplant.

Gleevec® (Imatinib) Approval Criteria [Melanoma Diagnosis]:

1. Member must meet all of the following criteria:
    a. Gleevec® must be used as a single-agent; and
    b. Second-line or subsequent therapy for disease progression or after maximum clinical benefit from BRAF targeted therapy; and
    c. Metastatic or unresectable tumors; and
    d. Activating mutations of C-KIT.

Gleevec® (Imatinib) Approval Criteria [Myelodysplastic Syndrome (MDS) Diagnosis]:

1. Chronic myelomonocytic leukemia (CMML) for 5q31-33 translocations and/or PDGFRβ gene rearrangements.

Gleevec® (Imatinib) Approval Criteria [Non-Melanoma Skin Cancers – Dermatofibrosarcoma Protuberans (DFSP) Diagnosis]:

1. Tumors with t(17;22) translocation; and
2. Member must have one of the following:
    a. Adjuvant therapy for positive surgical margins following excision; or
    b. Recurrent disease if disease is unresectable or if additional resection would lead to unacceptable functional or cosmetic outcomes; or
    c. For metastatic disease.

Gleevec® (Imatinib) Approval Criteria [Soft Tissue Sarcoma – Desmoid Tumors (Aggressive Fibromatosis) Diagnosis]:

1. Primary, recurrent, or progressive disease with one of the following:
    a. Initial treatment for resectable disease; or
    b. Adjuvant treatment for gross residual disease; or
    c. Initial treatment for unresectable disease or for disease for which surgery would be unacceptably morbid.

Gleevec® (Imatinib) Approval Criteria [Soft Tissue Sarcoma – Gastrointestinal Stromal Tumors (GIST) Diagnosis]:

1. Primary/preoperative treatment for members with documented GIST with one of the following:
    a. Resectable with risk of significant morbidity; or
    b. Unresectable; or
    c. Recurrent; or
    d. Metastatic; or

2. Postoperative treatment with one of the following:
    a. Complete resection of primary GIST; or
    b. Persistent gross residual disease; or
3. Continued treatment for one of the following:
    a. Limited progression; or
    b. Generalized progression.

Gleevec® (Imatinib) Approval Criteria [Soft Tissue Sarcoma – Pigmented Villonodular Synovitis/Tenosynovial Giant Cell Tumor Diagnosis]:

1. Gleevec® must be used as a single-agent only.

Iclusig® (Ponatinib) Approval Criteria [Philadelphia Chromosome Positive (Ph+) Acute Lymphoblastic Leukemia (ALL) Diagnosis]:

1. Member must have one of the following:
    a. Induction/consolidation with HyperCVAD; or
    b. Maintenance therapy in combination with vincristine and prednisone, with or without methotrexate and mercaptopurine; or
    c. Maintenance therapy post-hematopoietic stem cell transplant; or
    d. Relapsed/refractory disease either as a single-agent, in combination with chemotherapy not previously given, or in members with T315I mutations.

Iclusig® (Ponatinib) Approval Criteria [Chronic Myeloid Leukemia (CML) Diagnosis]:

1. Member must have one of the following:
    a. In members with a T315I mutation; or
    b. Intolerant or resistant to all other tyrosine kinase inhibitors (TKIs); or
    c. Post-hematopoietic stem cell transplantation in members with prior accelerated or blast phase prior to transplant or who have relapsed.

Kymriah® (Tisagenlecleucel) Approval Criteria [Acute Lymphoblastic Leukemia (ALL) Diagnosis]:

1. All of the following must be met for approval:
    a. B-cell precursor acute ALL; and
    b. Member must be 25 years of age or younger; and
    c. Refractory or in second or later relapse:
        i. Philadelphia chromosome negative (Ph-) ALL: must be refractory or with ≥2 relapses; or
        ii. Philadelphia chromosome positive (Ph+) ALL: must have failed ≥2 tyrosine kinase inhibitors (TKIs); and
    d. Therapies to consider prior to tisagenlecleucel if appropriate: clinical trial, multi-agent chemotherapy with or without hematopoietic cell transplantation (HCT), blinatumomab (category 1 recommendation), and inotuzumab (category 1 recommendation).
2. Health care facilities must be on the certified list to administer CAR T-cells and must be trained in the management of cytokine release syndrome (CRS), neurologic toxicities, and comply with the REMS requirements.

Synribo® (Omacetaxine) Approval Criteria [Chronic Myeloid Leukemia (CML) Diagnosis]:

1. Synribo® must be used as a single-agent only; and
2. Member must have one of the following:
    a. Primary treatment of advanced phase CML with disease progression to accelerated phase; or
    b. Post-hematopoietic stem cell transplant in members who have relapsed; or
    c. In members with a T315I mutation; or
    d. Members who are intolerant or resistant to two or more tyrosine kinase inhibitors (TKIs).

Sprycel® (Dasatinib) Approval Criteria [Philadelphia Chromosome Positive (Ph+) Acute Lymphoblastic Leukemia (ALL) Diagnosis]:

1. Member must have one of the following:
    a. Upfront therapy (including induction and consolidation) in combination with multi-agent chemotherapy or as a single-agent; or
    b. Maintenance therapy including:
        i. In combination with vincristine and prednisone, with or without methotrexate and mercaptopurine; or
        ii. Post-hematopoietic stem cell transplant; or
    c. Relapsed/refractory as a single-agent or in combination with multi-agent chemotherapy.

Sprycel® (Dasatinib) Approval Criteria [Chronic Myeloid Leukemia (CML) Diagnosis]:

1. Member must have one of the following:
    a. Newly diagnosed chronic, accelerated, or blast phase CML; or
    b. Post-hematopoietic stem cell transplant.

Sprycel® (Dasatinib) Approval Criteria [Soft Tissue Sarcoma – Gastrointestinal Stromal Tumor (GIST) Diagnosis]:

1. Member must have all of the following:
    a. Progressive disease and failed imatinib, sunitinib, or regorafenib; and
    b. PDGFRA D842V mutation.

Tasigna® (Nilotinib) Approval Criteria [Philadelphia Chromosome Positive (Ph+) Acute Lymphoblastic Leukemia (ALL) Diagnosis]:

1. Member must have one of the following:
    a. Upfront therapy (including induction and consolidation) in combination with multi-agent chemotherapy or as a single-agent; or
    b. Maintenance therapy including:
        i. In combination with vincristine and prednisone, with or without methotrexate and mercaptopurine; or
        ii. Post-hematopoietic stem cell transplant; or
    c. Relapsed/refractory as a single-agent or in combination with multi-agent chemotherapy.

Tasigna® (Nilotinib) Approval Criteria [Chronic Myeloid Leukemia (CML) Diagnosis]:

1. Member must have one of the following:
    a. Newly diagnosed chronic, accelerated, or blast phase CML; or
    b. Post-hematopoietic stem cell transplant.

Tasigna® (Nilotinib) Approval Criteria [Soft Tissue Sarcoma – Gastrointestinal Stromal Tumor (GIST) Diagnosis]:

1. Member must have progressive disease and failed imatinib, sunitinib, or regorafenib.

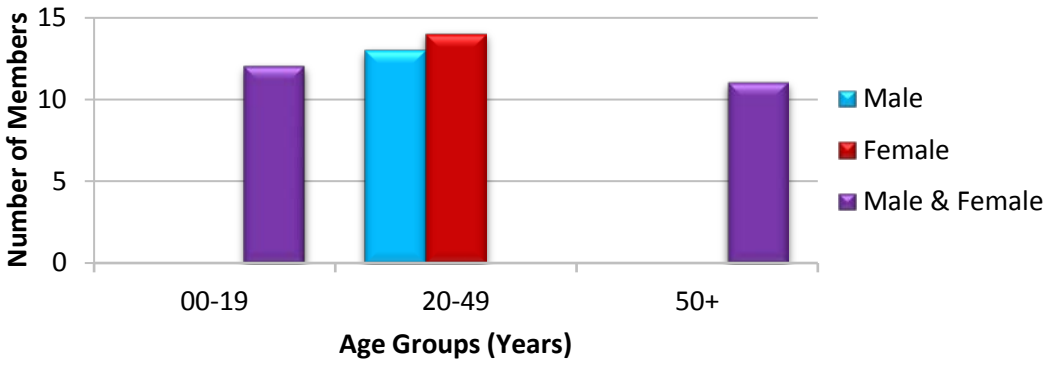
Utilization of ALL/CML Medications: Fiscal Year 2018

Comparison of Fiscal Years

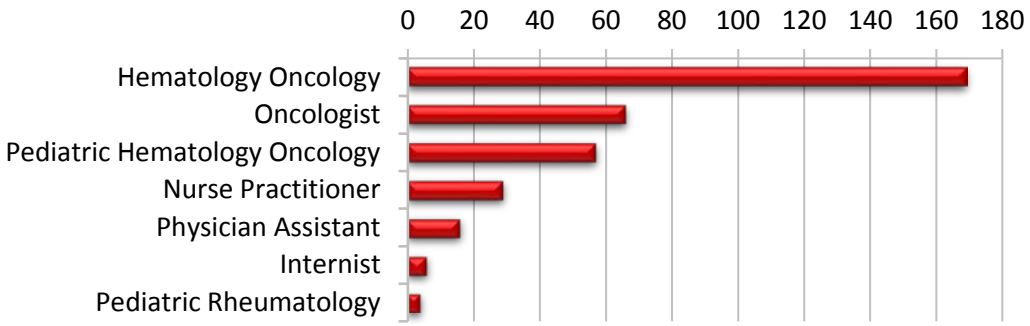
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2017	49	354	$3,626,596.07	$10,244.62	$342.49	39,056	10,589
2018	50	347	$2,729,784.31	$7,866.81	$261.60	18,771	10,435
% Change	**2.00%**	**-2.00%**	**-24.70%**	**-23.20%**	**-23.60%**	**-51.90%**	**-1.50%**
Change	**1**	**-7**	**-$896,811.76**	**-$2,377.81**	**-$80.89**	**-20,285**	**-154**

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

Demographics of Members Utilizing ALL/CML Medications: Pharmacy Claims

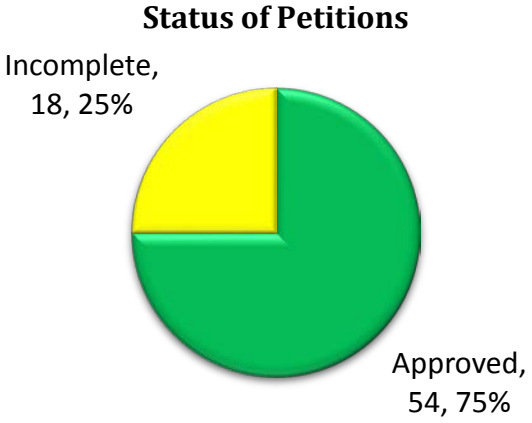


Top Prescriber Specialties of ALL/CML Medications By Number of Claims: Pharmacy Claims



Prior Authorization of ALL/CML Medications

There were 72 prior authorization requests submitted for 41 unique members for ALL/CML medications during fiscal year 2018. The following chart shows the status of the submitted petitions for fiscal year 2018.



Market News and Updates[5,6,7]

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

- **October 2017:** The FDA granted regular approval to Yescarta® (axicabtagene) for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high-grade B-cell lymphoma, and DLBCL arising from follicular lymphoma (FL). Although axicabtagene is not an ALL or CML therapy, it will be reviewed with this class to allow for both chimeric antigen receptor T-cell therapies (CAR T) to be reviewed together [i.e., Kymriah® (tisagenlecleucel), Yescarta® (axicabtagene)].

New Indication(s) and Label Update(s):

- **November 2017:** The FDA granted regular approval to Sprycel® (dasatinib) for the treatment of pediatric patients with Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in the chronic phase (CP).
- **December 2017:** The FDA granted accelerated approval to Bosulif® (bosutinib) for the treatment of patients with newly-diagnosed Ph+ CML-CP.
- **December 2017:** The FDA updated the label for Tasigna® (nilotinib) to include information on nilotinib discontinuation, post-discontinuation monitoring criteria, and guidance for treatment re-initiation in patients taking nilotinib for Ph+ CML who have achieved a sustained molecular response.
- **March 2018:** The FDA granted accelerated approval to Blincyto® (blinatumomab) for the treatment of adult and pediatric patients with B-cell precursor acute lymphoblastic leukemia (ALL) in first or second complete remission with minimal residual disease (MRD) ≥0.1%.

- **March 2018:** The FDA approved Tasigna® (nilotinib) for pediatric patients 1 year of age and older with newly diagnosed Ph+ CML-CP or Ph+ CML-CP resistant or intolerant to prior TKI therapy.
- **May 2018:** The FDA approved Kymriah® (tisagenlecleucel), a CD19-directed genetically modified autologous T-cell immunotherapy, for adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy including DLBCL not otherwise specified, high grade B-cell lymphoma and DLBCL arising from FL. Kymriah® was previously approved for the treatment of B-cell precursor ALL that is refractory or in second or later relapse.

Institute for Clinical and Economic Review (ICER):

- **March 2018:** ICER released a final evidence report on CAR T therapies for B-cell cancers. ICER is an independent, non-profit research organization that evaluates medical evidence and convenes public deliberative bodies to help stakeholders interpret and apply evidence to improve patient outcomes and control costs. An independent panel voted on key questions related to the systematic review of clinical evidence and economic analysis of CAR T therapies. The following are panel voting results regarding efficacy and cost-effectiveness of CAR T therapies:
  - **Pediatric B-Cell ALL:**
    - The panel voted 10 to 3 in favor of Kymriah® (tisagenlecleucel) adequately demonstrating a net health benefit for pediatric B-cell ALL versus treatment with clofarabine or comparable immunotherapy or chemotherapy (e.g., blinatumomab, multi-agent chemotherapy including clofarabine).
    - The majority of panel members (7 votes) judged tisagenlecleucel to represent "intermediate" long-term value for money for the treatment of pediatric B-cell ALL.
  - **Adult Aggressive B-Cell Lymphoma:**
    - The panel voted 11 to 2 in favor of Yescarta® (axicabtagene) adequately demonstrating a net health benefit for adult aggressive B-cell lymphoma versus treatment with regimens used in the SCHOLAR-1 trial.
    - A total of 13 out of 13 panel members voted there was not adequate evidence to distinguish a net health benefit between tisagenlecleucel and axicabtagene.
    - The vote was split (low: 5; intermediate: 5) regarding the long-term value for money of treatment with axicabtagene versus treatment with the regimens assessed in the SCHOLAR-1 trial.

Pipeline:

- **December 2018:** The FDA is set to make its decision on the supplemental Biologics License Application (sBLA) for Sprycel® (dasatinib) for expanded approval into Ph+ ALL in the pediatric population. Dasatinib was previously approved for the treatment of pediatric patients with Ph+ CML-CP in November 2017.

Yescarta® (Axicabtagene) Product Summary[8]

Yescarta® (Axicabtagene):

- **Therapeutic Class:** CD19-directed genetically modified autologous T-cell immunotherapy
- **Indication(s):** For the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including DLBCL not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from FL
- **How Supplied:** Suspension for infusion comprised of 2×10^6 CAR-positive viable T-cells per kilogram (kg) of body weight, with a maximum of 2×10^8 CAR-positive viable T-cells in approximately 68mL
- **Dose:**
  - Dosing is based on the number of CAR-positive viable T-cells
  - The target dose is 2×10^6 CAR-positive viable T-cells per kg body weight, with a maximum of 2×10^8 CAR-positive viable T-cells
- **Cost:** Wholesale Acquisition Cost (WAC) of $373,000 per one-time dose

Recommendations

- Update the prior authorization criteria to reflect new FDA approved indications and guideline recommendations. Changes can be seen in the following criteria listed in red (only criteria with updates listed).
- The prior authorization of Yescarta® (axicabtagene) with the following criteria listed in red.

Yescarta® (Axicabtagene) Approval Criteria:

1. All of the following must be met for approval:
   a. Large B-cell lymphoma [including diffuse large B cell lymphoma (DLBCL), high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma (FL)]; and
   b. Member must be 18 years of age or older; and
   c. Relapsed/refractory after two or more lines of therapy; and
   d. Member must not have primary central nervous system lymphoma; and
2. Health care facilities must be on the certified list to administer CAR T-cells and must be trained in the management of cytokine release syndrome (CRS), neurologic toxicities, and comply with the REMS requirements.

Bosulif® (Bosutinib) Approval Criteria [Chronic Myeloid Leukemia (CML) Diagnosis]:

1. Members with chronic, accelerated, or blast phase CML; and ~~with resistance or intolerance after primary treatment with either: dasatinib, imatinib, or nilotinib with the following BCR-ABL1 transcript levels:~~
   ~~a. 0.01% to 1% at >12 months; or~~
   ~~b. >1% to 10% at ≥12 months; or~~
   ~~c. >10% at any milestone.~~
2. Newly diagnosed or resistant/intolerant to other tyrosine kinase inhibitors (TKIs).

Kymriah® (Tisagenlecleucel) Approval Criteria [Lymphoma Diagnosis]:

1. All of the following must be met for approval:
   a. Large B-cell lymphoma [including diffuse large B-cell lymphoma (DLBCL), high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma (FL)]; and
   b. Relapsed or refractory disease; and
   c. Member must be 18 years of age or older; and
   d. Member must have had two or more lines of therapy; and
2. Health care facilities must be on the certified list to administer CAR T-cells and must be trained in the management of cytokine release syndrome (CRS), neurologic toxicities, and comply with the REMS requirements.

Utilization Details of ALL/CML Medications: Fiscal Year 2018

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
IMATINIB PRODUCTS					
IMATINIB MES TAB 400MG	114	18	$383,156.53	6.33	$3,361.02
IMATINIB MES TAB 100MG	37	6	$131,204.66	6.17	$3,546.07
SUBTOTAL	**151**	**21**	**$514,361.19**	**7.19**	**$3,406.37**
DASATINIB PRODUCTS					
SPRYCEL TAB 100MG	87	12	$1,137,647.31	7.25	$13,076.41
SPRYCEL TAB 50MG	36	7	$244,649.88	5.14	$6,795.83
SPRYCEL TAB 70MG	9	1	$76,093.94	9	$8,454.88
SPRYCEL TAB 20MG	6	2	$49,749.58	3	$8,291.60
SPRYCEL TAB 140MG	4	2	$48,340.76	2	$12,085.19
SUBTOTAL	**142**	**21**	**$1,556,481.47**	**6.76**	**$10,961.14**
NILOTINIB PRODUCTS					
TASIGNA CAP 150MG	20	4	$201,819.57	5	$10,090.98
TASIGNA CAP 200MG	17	2	$194,717.09	8.5	$11,453.95
SUBTOTAL	**37**	**6**	**$396,536.66**	**6.17**	**$10,717.21**
BLINATUMOMAB PRODUCTS					
BLINCYTO INJ 35MCG	8	3	$113,281.04	2.67	$14,160.13
SUBTOTAL	**8**	**3**	**$113,281.04**	**2.67**	**$14,160.13**
PONATINIB PRODUCTS					
ICLUSIG TAB 15MG	5	1	$82,837.75	5	$16,567.55
ICLUSIG TAB 45MG	4	1	$66,286.20	4	$16,571.55
SUBTOTAL	**9**	**2**	**$149,123.95**	**4.5**	**$16,569.33**
TOTAL	**347**	**50***	**$2,729,784.31**	**6.94**	**$7,866.81**

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

[1] Howlader N, Noone AM, Krapcho M, Miller D, Bishop K, Kosary CL, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER Cancer Statistics Review, 1975-2014, National Cancer Institute. Bethesda, MD. Available online at: https://seer.cancer.gov/csr/1975_2014/. Based on November 2016 SEER data submission, posted to the SEER web site, April 2017. Last accessed 09/2018.

[2] Arber DA, Orazi A, Hasserjian R, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. *Blood* 2016; 127:2391.

[3] Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2017. *CA Cancer J Clin* 2017; 67:7.

[4] Höglund M, Sandin F, Hellström K, et al. Tyrosine kinase inhibitor usage, treatment outcome, and prognostic scores in CML: report from the population-based Swedish CML registry. *Blood* 2013; 122:1284.

[5] U.S. Food and Drug Administration (FDA). Hematology/Oncology (Cancer) Approvals & Safety Notifications. Available online at: https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm279174.htm. Last revised 09/13/2018. Last accessed 09/17/2018.

[6] Institute for Clinical and Economic Review (ICER). Chimeric Antigen Receptor T-Cell Therapy for B-Cell Cancers: Effectiveness and Value: Final Evidence Report. Available online at: https://icer-review.org/wp-content/uploads/2017/07/ICER_CAR_T_Final_Evidence_Report_032318.pdf. Issued 03/23/2018. Last accessed 09/17/2018.

[7] Broderick JM. FDA Accepts Application for Dasatinib for Pediatric Ph+ ALL. *OncLive*. Available online at: https://www.onclive.com/web-exclusives/fda-accepts-application-for-dasatinib-for-pediatric-ph-all. Issued 08/30/2018. Last accessed 09/25/2018.

[8] Yescarta® (axicabtagene) Prescribing Information. Kite Pharma, Inc. Available online at: https://www.yescarta.com/files/yescarta-pi.pdf. Last accessed 09/26/2018.

Appendix K

Fiscal Year 2018 Annual Review of Skin Cancer Medications and 30-Day Notice to Prior Authorize Braftovi™ (Encorafenib), Mektovi® (Binimetinib), and Libtayo® (Cemiplimab-rwlc)

Oklahoma Health Care Authority
October 2018

Introduction[1,2,3,4,5,6,7,8,9,10,11,12,13,14]

Skin cancers are commonly divided into two different types: nonmelanoma skin cancer (NMSC) and melanoma skin cancer. In general, NMSC are far more common than melanomas but result in lower mortality. Basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) are the most common forms of NMSC. BCC is the most common cancer diagnosed in the United States, occurring in over 2 million people annually, and the incidence of BCC continues to be on the incline. More people are diagnosed with BCC than all other cancers combined. The incidence of SCC is approximately half of BCC. Because NMSC rarely metastasizes, treatment is largely focused on localized therapies including different surgical approaches and topical agents. Systemic therapy is reserved for the select number of advanced and metastatic cases.

According to the National Cancer Institute, in 2018, an estimated 91,270 new cases of melanoma skin cancer were diagnosed in the United States, resulting in 9,320 deaths from the disease. The average lifetime risk of developing melanoma in the United States is 1 in 34 for women and 1 in 53 for men. While the incidence of melanoma is far lower than NMSC, melanomas behave much more aggressively and have high rates of metastases leading to poor survival outcomes in advanced cases. Survival rates vary based on the clinical stage of the disease at diagnosis, with 5-year survival ranging from 15 to 60% in patients with distant and local metastases, respectively. Traditional cytotoxic chemotherapy has failed to provide successful treatment outcomes in this patient population and has a very small role in treating patients with melanoma. Surgery, immunotherapy, molecularly targeted agents, and radiation are the cornerstones to the treatment of melanoma. Over the past 10 years, drug developers have focused on agents that target various immune checkpoints, specifically cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) and the programmed death 1/programmed death ligand 1 (PD-1/PD-L1) pathway, which result in a tumor-specific immune response in a subset of patients. Additionally, the development of molecularly targeted therapy began after it was found that activating BRAF mutations occur in half of all melanomas. BRAF mutations lead to activation of the mitogen-activated protein kinase (MAPK) pathway and promote tumor development. Research in these areas has led to U.S. Food and Drug Administration (FDA) approval for the following agents in the last 5 years: ipilimumab, vemurafenib, pembrolizumab, dabrafenib, trametinib, cobimetinib, and nivolumab. The National Comprehensive Cancer Network (NCCN) guidelines for melanoma treatment recommend all of these agents, some as monotherapy and others in combination, as first-line therapy. Use of these agents has also expanded into the adjuvant setting. Development of these new drugs has produced an increase in response rates and modest improvements in survival in some melanoma cases. The cost

associated with treating skin cancer, approximately $8.1 billion, increased 5 times faster than treatments for any other cancer between 2002 and 2011.

Current Prior Authorization Criteria

Bavencio® (Avelumab) Approval Criteria [Merkel Cell Carcinoma (MCC) Diagnosis]:

1. Diagnosis of metastatic MCC; and
2. Member must be 12 years of age or older.

Bavencio® (Avelumab) Approval Criteria [Urothelial Carcinoma Diagnosis]:

1. Diagnosis of locally advanced or metastatic urothelial carcinoma; and
2. Disease has progressed during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy.

Cotellic® (Cobimetinib) Approval Criteria [Melanoma Diagnosis]:

1. Diagnosis of unresectable or metastatic melanoma; and
2. BRAF V600E or V600K mutation; and
    a. Cobimetinib is not indicated for wild-type BRAF melanoma.
3. Member meets one of the following:
    a. Used as first-line therapy in combination with vemurafenib; or
    b. Used as second-line therapy or subsequent therapy with vemurafenib.

Erivedge® (Vismodegib) Approval Criteria [Basal Cell Carcinoma (BCC) Diagnosis]:

1. Diagnosis of locally advanced BCC that has either:
    a. Recurred following surgery or radiation therapy; or
    b. Surgery or radiation is contraindicated; or
2. Diagnosis of metastatic BCC.

Imlygic® (Talimogene Laherparepvec) Approval Criteria [Melanoma Diagnosis]:

1. Member has unresectable cutaneous, subcutaneous, or nodal lesions that are recurrent after initial surgery; and
    a. Talimogene laherparepvec is not indicated in members with visceral metastases.
2. The member is not immunocompromised or pregnant.

Keytruda® (Pembrolizumab) Approval Criteria [Melanoma Diagnosis]:

1. Diagnosis of unresectable or metastatic melanoma; and
2. Pembrolizumab must be used as a single-agent; and
3. Member meets one of the following:
    a. Pembrolizumab is being used as first-line therapy; or
    b. Pembrolizumab is being used as second-line therapy or subsequent therapy for disease progression if not previously used; and
4. The member has not previously failed other PD-1 inhibitors [e.g., Opdivo® (nivolumab)].

Keytruda® (Pembrolizumab) Approval Criteria [Hodgkin Lymphoma Diagnosis]:

1. Diagnosis of relapsed or refractory classical Hodgkin lymphoma; and
    a. Exception: lymphocyte-predominant Hodgkin lymphoma

2. Pembrolizumab must be used as a single-agent; and
3. The member has not previously failed other PD-1 inhibitors [e.g., Opdivo® (nivolumab)].

Keytruda® (Pembrolizumab) Approval Criteria [Non-Small Cell Lung Cancer (NSCLC) Diagnosis]:

1. Diagnosis of metastatic NSCLC; and
2. Tumors proportion scores for PD-L1 expression as follows:
    a. Single-agent, first-line: ≥50%; or
    b. First-line in combination with carboplatin and pemetrexed: no expression required; or
    c. Single-agent, second-line: ≥1%; and
3. Member meets one of the following:
    a. Previously untreated metastatic non-squamous NSCLC in combination with pemetrexed and carboplatin; or
    b. New diagnosis as first-line therapy (member has not received chemotherapy to treat disease) if:
        i. Tumor does not express sensitizing Epidermal Growth Factor Receptor (EGFR) mutations or Anaplastic Lymphoma Kinase (ALK) translocations; or
    c. Single-agent for disease progression on or after platinum-containing chemotherapy (i.e., cisplatin, carboplatin):
        i. Members with EGFR mutation-positive tumors should have disease progression on an FDA-approved therapy for these aberrations prior to receiving pembrolizumab. *This does not apply if tumors do not have these mutations*; and
            1. *Examples of drugs for EGFR-mutation-positive tumors: osimertinib, erlotinib, afatinib, or gefitinib*
        ii. Members with ALK genomic tumor aberrations should have disease progression on an FDA-approved therapy for these aberrations prior to receiving pembrolizumab. *This does not apply if tumors do not have these mutations*; and
            1. *Examples of drugs for ALK-mutation-positive tumors: crizotinib, ceritinib, or alectinib*
4. The member has not previously failed other PD-1 inhibitors [e.g., Opdivo® (nivolumab)].

Keytruda® (Pembrolizumab) Approval Criteria [Head and Neck Cancer Diagnosis]:

1. Diagnosis of recurrent or metastatic disease; and
2. Squamous cell histology; and
3. Member has received a prior platinum containing regimen (i.e., cisplatin, carboplatin); and
4. The member has not previously failed other PD-1 inhibitors [e.g., Opdivo® (nivolumab)].
5. Dose does not exceed 200mg every three weeks.

Keytruda® (Pembrolizumab) Approval Criteria [Urothelial Carcinoma Diagnosis]:

1. Member must have one of the following:

a. Locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy; or
b. Within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy; or
c. Frontline pembrolizumab for members with locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing chemotherapy; and
    i. Cisplatin ineligibility is defined by at least one of the following: baseline creatinine clearance of <60mL/min, an ECOG performance status of 2, Class III heart failure, grade 2 or greater peripheral neuropathy, or grade 2 or greater hearing loss.

2. The member has not previously failed other PD-1 inhibitors [e.g., Opdivo® (nivolumab)].

Keytruda® (Pembrolizumab) Approval Criteria [Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumor (Tissue/Site-Agnostic) Diagnosis]:

1. The member has not previously failed other PD-1 inhibitors [e.g., Opdivo® (nivolumab)]; and
2. Member must have one of the following:
    a. MSI-H or dMMR solid tumors that have progressed following prior treatment with no satisfactory alternative treatment options; or
    b. MSI-H or dMMR colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.

Keytruda® (Pembrolizumab) Approval Criteria [Gastric or Gastroesophageal Junction Tumor Diagnosis]:

1. Recurrent, locally advanced or metastatic gastric or gastroesophageal junction adenocarcinoma; and
2. Tumors must express PD-L1; and
3. The member has not previously failed other PD-1 inhibitors [e.g., Opdivo® (nivolumab)]; and
4. Disease progression on or after two or more prior systemic therapies (including fluoropyrimidine- and platinum-containing chemotherapy, and if appropriate, HER2/neu-targeted therapy).

Keytruda® (Pembrolizumab) Approval Criteria [Cervical Cancer Diagnosis]:

1. A diagnosis of recurrent or metastatic cervical cancer; and
2. Member has had disease progression on or after chemotherapy; and
3. Tumors must express PD-L1 [Combined Positive Score (CPS) ≥1]; and
4. The member has not previously failed other PD-1 inhibitors [e.g., Opdivo® (nivolumab)].

Keytruda® (Pembrolizumab) Approval Criteria [Primary Mediastinal Large B-cell Lymphoma (PMBCL) Diagnosis]:

1. A diagnosis of PMBCL in adult or pediatric members; and
2. Member must have refractory disease or pembrolizumab must be used in members who have relapsed after two or more prior lines of therapy; and

3. Authorizations will not be granted for members who require urgent cytoreduction; and
4. The member has not previously failed other PD-1 inhibitors [e.g., Opdivo® (nivolumab)].

Mekinist® (Trametinib) Approval Criteria [Melanoma Diagnosis]:

1. Diagnosis of unresectable or metastatic melanoma; and
2. BRAF V600E or V600K mutation; and
    a. Trametinib is not indicated for wild-type BRAF melanoma.
3. Member meets one of the following:
    a. Used as first-line therapy in combination with dabrafenib; or
    b. Used as second-line therapy or subsequent therapy with dabrafenib; or
    c. Used as second-line therapy or subsequent therapy as a single-agent if:
        i. Member was intolerant to prior BRAF inhibitor therapy (i.e., dabrafenib, vemurafenib); and
        ii. No evidence of disease progression on prior BRAF inhibitor therapy (i.e., dabrafenib, vemurafenib).

Mekinist® (Trametinib) Approval Criteria [Non-Small Cell Lung Cancer (NSCLC) Diagnosis]:

1. BRAF V600E or V600K mutation; and
    a. Trametinib is not indicated for wild-type BRAF NSCLC.
2. Diagnosis of refractory or metastatic disease; and
3. Trametinib must be used in combination with dabrafenib.

Odomzo® (Sonidegib) Approval Criteria [Basal Cell Carcinoma (BCC) Diagnosis]:

1. Diagnosis of locally advanced BCC that has either:
    a. Recurred following surgery or radiation therapy; or
    b. Surgery or radiation is contraindicated; or
2. Diagnosis of metastatic BCC.

Opdivo® (Nivolumab) Approval Criteria [Melanoma Diagnosis]:

1. Diagnosis of unresectable or metastatic melanoma; and
2. Nivolumab must be used as a single-agent or in combination with ipilimumab:
    a. As first-line therapy for untreated melanoma; or
    b. As second-line or subsequent therapy for documented disease progression while receiving or since completing most recent therapy:
        i. If the member has not previously failed other PD-1 inhibitors [e.g., Keytruda® (pembrolizumab)]; and
3. Dose as follows:
    a. Single-agent: 240mg every two weeks or 480mg every four weeks; or
    b. In combination with ipilimumab: nivolumab 1mg/kg, followed by ipilimumab on the same day, every three weeks for four doses, then 240mg every two weeks or 480mg every four weeks.

Opdivo® (Nivolumab) Approval Criteria [Adjuvant Treatment of Melanoma Diagnosis]:

1. Member has complete resection of melanoma; and
2. Diagnosis of stage IIIB/C melanoma following complete resection; and

3. The member has not previously failed other PD-1 inhibitors [e.g., Keytruda® (pembrolizumab)]; and
4. Nivolumab must be used as a single-agent; and
5. Dose as follows:
    a. Single-agent: 240mg every two weeks or 480mg every four weeks; and
    b. Maximum duration of one year.

Opdivo® (Nivolumab) Approval Criteria [Non-Small Cell Lung Cancer (NSCLC) Diagnosis]:

1. Diagnosis of metastatic NSCLC; and
2. Tumor histology is one of the following:
    a. Adenocarcinoma; or
    b. Squamous cell; or
    c. Large cell; and
3. Disease progression on or after platinum-containing chemotherapy (i.e., cisplatin, carboplatin); and
4. The member has not previously failed other PD-1 inhibitors [e.g., Keytruda® (pembrolizumab)]; and
5. Nivolumab must be used as a single-agent; and
6. Dose as follows: 240mg every two weeks or 480mg every four weeks.

Opdivo® (Nivolumab) Approval Criteria [Small Cell Lung Cancer (SCLC) Diagnosis]:

1. One of the following criteria is met:
    a. Disease relapsed within six months of initial chemotherapy; or
    b. Disease is progressive on initial chemotherapy; and
2. Nivolumab must be used as a single-agent or in combination with ipilimumab; and
3. The member has not previously failed other PD-1 inhibitors [e.g., Keytruda® (pembrolizumab)].

Opdivo® (Nivolumab) Approval Criteria [Hodgkin Lymphoma Diagnosis]:

1. Diagnosis of relapsed or refractory classical Hodgkin lymphoma; and
    a. Exception: lymphocyte-predominant Hodgkin lymphoma
2. Nivolumab must be used as a single-agent; and
3. The member has not previously failed other PD-1 inhibitors [e.g., Keytruda® (pembrolizumab)].

Opdivo® (Nivolumab) Approval Criteria [Renal Cell Cancer (RCC) Diagnosis]:

1. For nivolumab monotherapy:
    a. Diagnosis of relapsed or surgically unresectable stage IV disease; and
    b. Failed prior therapy with one of the following medications:
        i. Sunitinib; or
        ii. Sorafenib; or
        iii. Pazopanib; or
        iv. Axitinib; or
2. For nivolumab use in combination with ipilimumab:

    a. Diagnosis of relapsed or surgically unresectable stage IV disease in the initial treatment of members with intermediate or poor risk, previously untreated, advanced RCC; and
3. The member has not previously failed other PD-1 inhibitors [e.g., Keytruda® (pembrolizumab)]; and
4. Dose as follows:
    a. Single-agent: 240mg every two weeks or 480mg every four weeks; or
    b. In combination with ipilimumab: nivolumab 3mg/kg followed by ipilimumab 1mg/kg on the same day, every three weeks for a maximum of four doses, then nivolumab 240mg every two weeks or 480mg every four weeks.

Opdivo® (Nivolumab) Approval Criteria [Head and Neck Cancer Diagnosis]:

1. A diagnosis of recurrent or metastatic head and neck cancer; and
2. Squamous cell histology; and
3. Member has received prior platinum-containing regimen (i.e., cisplatin, carboplatin); and
4. The member has not previously failed other PD-1 inhibitors [e.g., Keytruda® (pembrolizumab)]; and
5. Dose as follows: 240mg every two weeks or 480mg every four weeks.

Opdivo® (Nivolumab) Approval Criteria [Urothelial Bladder Cancer]:

1. A diagnosis of metastatic or unresectable locally advanced cancer; and
2. Used as second-line or greater therapy; and
3. The member has not previously failed other PD-1 inhibitors [e.g., Keytruda® (pembrolizumab)]; and
4. Member has failed a platinum containing regimen.

Opdivo® (Nivolumab) Approval Criteria [Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Metastatic Colorectal Cancer Diagnosis]:

1. A diagnosis of MSI-H or dMMR metastatic colorectal cancer; and
2. The member has not previously failed other PD-1 inhibitors [e.g., Keytruda® (pembrolizumab)]; and
3. Progression following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.

Opdivo® (Nivolumab) Approval Criteria [Hepatocellular Carcinoma (HCC) Diagnosis]:

1. Relapsed or progressive disease; and
2. The member has not previously failed other PD-1 inhibitors [e.g., Keytruda® (pembrolizumab)]; and
3. Member must have been previously treated with sorafenib.

Tafinlar® (Dabrafenib) Approval Criteria [Melanoma Diagnosis]:

1. Diagnosis of unresectable or metastatic melanoma; and
2. BRAF V600E or V600K mutation; and
    a. Dabrafenib is not indicated for wild-type BRAF melanoma.

3. Dabrafenib must be used as a single-agent or in combination with trametinib (Mekinist®); and
4. One of the following is met:
    a. Used as first-line therapy; or
    b. Used as second-line therapy or subsequent therapy.

Tafinlar® (Dabrafenib) Approval Criteria [Non-Small Cell Lung Cancer (NSCLC) Diagnosis]:

1. BRAF V600E or V600K mutation; and
    a. Dabrafenib is not indicated for wild-type BRAF NSCLC.
2. Diagnosis of refractory or metastatic disease; and
3. Dabrafenib must be used as a single-agent or in combination with trametinib (Mekinist®).

Yervoy® (Ipilimumab) Approval Criteria [Unresectable or Metastatic Melanoma Diagnosis]:

1. Ipilimumab is used in combination with nivolumab as:
    a. First-line therapy; or
    b. Second-line or subsequent therapy for disease progression if nivolumab was not previously used; or
2. Ipilimumab is used as a single-agent for one of the following:
    a. First-line therapy as a single course of four treatments; or
    b. Second-line or subsequent lines of therapy as a single course of four treatments; or
    c. Retreatment, consisting of a 4-dose limit, for an individual who had no significant systemic toxicity during prior ipilimumab therapy, and whose disease progressed after being stable >6 months following completion of a prior course of ipilimumab, and for whom no intervening therapy has been administered; and
3. Maximum dose of 3mg/kg will apply.

Yervoy® (Ipilimumab) Approval Criteria [Adjuvant Treatment of Melanoma]:

1. Member has complete resection of melanoma with lymphadenectomy; and
2. Member has stage III disease with regional nodes of >1mm and no in-transit metastasis; and
3. Ipilimumab must be used as a single-agent; and
4. Maximum dose of 10mg/kg will apply.

Yervoy® (Ipilimumab) Approval Criteria [Small Cell Lung Cancer (SCLC) Diagnosis]:

1. One of the following criteria is met:
    a. Disease relapsed within six months of initial chemotherapy; or
    b. Disease is progressive on initial chemotherapy; and
2. Used in combination with nivolumab.

Yervoy® (Ipilimumab) Approval Criteria [Renal Cell Carcinoma (RCC) Diagnosis]:

1. A diagnosis of relapsed or surgically unresectable stage IV disease in the initial treatment of members with intermediate or poor risk, previously untreated, advanced RCC; and
2. Ipilimumab must be used in combination with nivolumab; and

3. The member has not failed previous PD-1 inhibitors [e.g., Keytruda® (pembrolizumab)]; and
4. Dose as follows: nivolumab 3mg/kg followed by ipilimumab 1mg/kg on the same day, every three weeks for a maximum of four doses, then nivolumab 240mg every two weeks or 480mg every four weeks.

Zelboraf® (Vemurafenib) Approval Criteria [Melanoma Diagnosis]:

1. Diagnosis of unresectable or metastatic melanoma; and
2. BRAF V600E or V600K mutation; and
   a. Vemurafenib is not indicated for wild-type BRAF melanoma.
3. Vemurafenib must be used as a single-agent or in combination with cobimetinib; and
4. One of the following is met:
   a. Used as first-line therapy; or
   b. Used as second-line or subsequent therapy.

Zelboraf® (Vemurafenib) Approval Criteria [Non-Small Cell Lung Cancer (NSCLC) Diagnosis]:

1. BRAF V600E or V600K mutation; and
   a. Vemurafenib is not indicated for wild-type BRAF NSCLC.
2. Diagnosis of refractory or metastatic disease; and
3. Vemurafenib must be used as a single-agent.

Zelboraf® (Vemurafenib) Approval Criteria [Hairy-Cell Leukemia Diagnosis]:

1. Vemurafenib must be used as a single-agent; and
2. Vemurafenib is being used to treat disease progression following failure of purine analog therapy (i.e., pentostatin, cladribine).

Utilization of Skin Cancer Medications: Fiscal Year 2018

Comparison of Fiscal Years: Skin Cancer Medications (Pharmacy Claims)

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2017	11	55	$514,455.38	$9,353.73	$319.93	6,042	1,608
2018	18	117	$1,006,456.73	$8,602.19	$294.80	9,536	3,414
% Change	**63.60%**	**112.70%**	**95.60%**	**-8.00%**	**-7.90%**	**57.80%**	**112.30%**
Change	**7**	**62**	**$492,001.35**	**-$751.54**	**-$25.13**	**3,494**	**1,806**

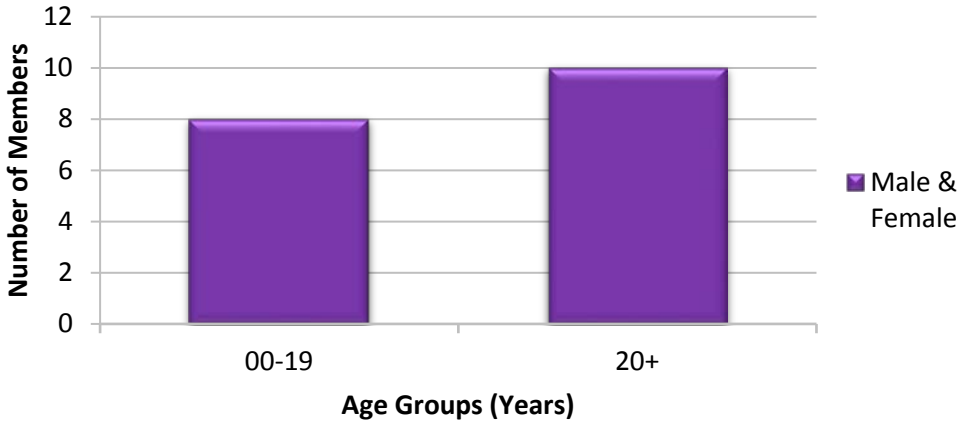
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

Comparison of Fiscal Years: Skin Cancer Medications (Medical Claims)

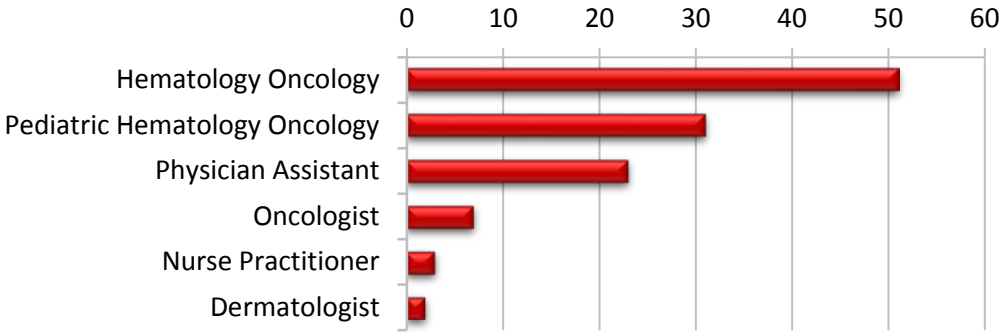
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/Claim	Total Units
2017	77	385	$2,730,238.57	$7,091.53	92,243
2018	97	519	$4,655,347.33	$8,969.84	129,439
% Change	**25.97%**	**34.81%**	**70.51%**	**26.49%**	**40.32%**
Change	**20**	**134**	**$1,925,108.76**	**$1,878.31**	**37,196**

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

Demographics of Members Utilizing Skin Cancer Medications: Pharmacy Claims



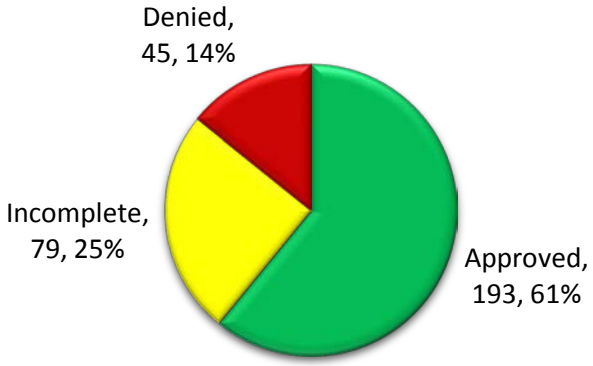
Top Prescriber Specialties of Skin Cancer Medications By Number of Claims: Pharmacy Claims



Prior Authorization of Skin Cancer Medications

There were 317 prior authorization requests submitted for 155 unique members for skin cancer medications during fiscal year 2018. The following chart shows the status of the submitted petitions for fiscal year 2018.

Status of Petitions



Market News and Updates[15,16,17]

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

- **June 2018:** The FDA approved Braftovi™ (encorafenib) and Mektovi® (binimetinib) for use in combination in patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation.

New Indication(s) and Label Update(s):

- **November 2017:** The FDA granted regular approval to Zelboraf® (vemurafenib) for the treatment of patients with Erdheim-Chester Disease (ECD) with a BRAF V600 mutation. Vemurafenib was previously approved for the treatment of patients with hairy-cell leukemia, non-small cell lung cancer (NSCLC), and melanoma.
- **April 2018:** The FDA granted approvals to Opdivo® (nivolumab) and Yervoy® (ipilimumab) in combination for the treatment of intermediate or poor risk, previously untreated, advanced renal cell carcinoma (RCC).
- **April 2018:** The FDA granted regular approval to Tafinlar® (dabrafenib) and Mekinist® (trametinib) for use in combination for the adjuvant treatment of patients with melanoma with a BRAF V600E or V600K mutation and involvement of lymph node(s), following complete resection.
- **May 2018:** The FDA approved Tafinlar® (dabrafenib) in combination with Mekinist® (trametinib) for the treatment of anaplastic thyroid cancer (ATC) with a BRAF V600E mutation.
- **July 2018:** The FDA granted accelerated approval to Yervoy® (ipilimumab) for use in combination with Opdivo® (nivolumab) for the treatment of patients 12 years of age and older with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer (mCRC) that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.
- **August 2018:** The FDA granted accelerated approval to Opdivo® (nivolumab) for the treatment of patients with metastatic small cell lung cancer (SCLC) with progression after platinum-based chemotherapy and at least one other line of therapy.
- **August 2018:** The FDA updated the prescribing information for Keytruda® (pembrolizumab) and Tecentriq® (atezolizumab) to require the use of an FDA-approved companion diagnostic test to determine programmed death-ligand 1 (PD-L1) levels in tumor tissue from patients with locally advanced or metastatic urothelial cancer who are cisplatin-ineligible. The FDA approved two different companion diagnostic tests, one for use with pembrolizumab and one for use with atezolizumab.
- **August 2018:** The FDA approved Keytruda® (pembrolizumab) for use in combination with Alimta® (pemetrexed) and platinum as first-line treatment of patients with metastatic, non-squamous non-small cell lung cancer (NSqNSCLC), with no EGFR or ALK genomic tumor aberrations.
- **September 2018:** The FDA approved Libtayo® (cemiplimab-rwlc) for the treatment of patients with metastatic cutaneous squamous cell carcinoma (CSCC) or locally advanced CSCC who are not candidates for curative surgery or curative radiation.

Pipeline:

- There are currently no skin cancer medications scheduled to be reviewed by the FDA in 2018.

Product Summaries[18,19,20]

Braftovi™ (Encorafenib):

- **Therapeutic Class:** Kinase inhibitor
- **Indication(s):** For use in combination with Mektovi® (binimetinib) for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation
- **How Supplied:** 50mg and 75mg oral capsules
- **Dose:** 450mg by mouth once daily
- **Cost:** Wholesale Acquisition Cost (WAC) of $60.98 per 75mg capsule or $365.88 per 450mg dose, resulting in a monthly cost of $10,976.40

Mektovi® (Binimetinib):

- **Therapeutic Class:** Kinase inhibitor
- **Indication(s):** For use in combination with Braftovi™ (encorafenib) for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation
- **How Supplied:** 15mg oral tablets
- **Dose:** 45mg by mouth twice daily
- **Cost:** WAC of $60.98 per 15mg tablet or $182.94 per 45mg dose, resulting in a monthly cost of $10,976.40

Libtayo® (Cemiplimab-rwlc):

- **Therapeutic Class:** Programmed death receptor-1 (PD-1) blocking antibody
- **Indication(s):** For the treatment of patients with metastatic CSCC or locally advanced CSCC who are not candidates for curative surgery or curative radiation
- **How Supplied:** 350mg/7mL (50mg/mL) solution in a single-dose vial
- **Dose:** 350mg via intravenous (IV) infusion over 30 minutes every 3 weeks
- **Cost:** Not available

Recommendations

- Update the prior authorization criteria to reflect new FDA approved indications and guideline recommendations. Changes can be seen in the following criteria listed in red (only criteria with updates listed).
- The prior authorization of Braftovi™ (encorafenib), Mektovi® (binimetinib), and Libtayo® (cemiplimab-rwlc) with the following criteria listed in red.

Braftovi™ (Encorafenib) Approval Criteria [Melanoma Diagnosis]:

1. Diagnosis of unresectable or metastatic melanoma; and
2. BRAF V600E or V600K mutation; and
3. Used in combination with binimetinib.

Mektovi® (Binimetinib) Approval Criteria [Melanoma Diagnosis]:

1. Diagnosis of unresectable or metastatic melanoma; and
2. BRAF V600E or V600K mutation; and
3. Used in combination with encorafenib.

Libtayo® (Cemiplimab-rwlc) Approval Criteria [Cutaneous Squamous Cell Carcinoma (CSCC) Diagnosis]:

1. Diagnosis of metastatic or locally advanced CSCC; and
2. Member is not eligible for curative surgery or radiation; and
3. Member has not received prior immunotherapy agent(s) [e.g., Keytruda® (pembrolizumab), Opdivo® (nivolumab), Yervoy® (ipilimumab)].

Opdivo® (Nivolumab) Approval Criteria [Metastatic Colorectal Cancer (mCRC) Diagnosis]:

1. Diagnosis of mCRC; and
2. Disease has progressed on treatment with 5-FU, oxaliplatin, and irinotecan; and
3. Tumor possesses high microsatellite-instability or mismatch repair deficiency; and
4. Used as a single-agent or in combination with ipilimumab.

Yervoy® (Ipilimumab) Approval Criteria [Metastatic Colorectal Cancer (mCRC) Diagnosis]:

1. Diagnosis of mCRC; and
2. Disease has progressed on treatment with 5-FU, oxaliplatin, and irinotecan; and
3. Tumor possesses microsatellite instability-high or mismatch repair deficiency; and
4. Used in combination with nivolumab.

Mekinist® (Trametinib) Approval Criteria [Anaplastic Thyroid Cancer (ATC) Diagnosis]:

1. Diagnosis of anaplastic thyroid cancer (ATC); and
2. Locally advanced or metastatic disease; and
3. BRAF V600E mutation; and
4. No satisfactory locoregional treatment options.

Tafinlar® (Dabrafenib) Approval Criteria [Anaplastic Thyroid Cancer (ATC) Diagnosis]:

1. Diagnosis of anaplastic thyroid cancer (ATC); and
2. Locally advanced or metastatic disease; and
3. BRAF V600E mutation; and
4. No satisfactory locoregional treatment options.

Zelboraf® (Vemurafenib) Approval Criteria [Erdheim-Chester Disease (ECD)]:

1. BRAF V600E or V600K mutation; and
2. Vemurafenib must be used as a single-agent.

Utilization Details of Skin Cancer Medications: Fiscal Year 2018

Pharmacy Claims: Fiscal Year 2018

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
TRAMETINIB PRODUCTS					
MEKINIST TAB 0.5MG	29	6	$162,060.44	4.83	$5,588.29
MEKINIST TAB 2MG	28	5	$297,332.28	5.6	$10,619.01
SUBTOTAL	**57**	**10**	**$459,392.72**	**5.7**	**$8,059.52**
VEMURAFENIB PRODUCTS					
ZELBORAF TAB 240MG	24	4	$220,254.94	6	$9,177.29
SUBTOTAL	**24**	**4**	**$220,254.94**	**6**	**$9,177.29**
VISMODEGIB PRODUCTS					
ERIVEDGE CAP 150MG	15	4	$161,616.20	3.75	$10,774.41
SUBTOTAL	**15**	**4**	**$161,616.20**	**3.75**	**$10,774.41**
COBIMETINIB PRODUCTS					
COTELLIC TAB 20MG	13	3	$86,221.91	4.33	$6,632.45
SUBTOTAL	**13**	**3**	**$86,221.91**	**4.33**	**$6,632.45**
DABRAFENIB PRODUCTS					
TAFINLAR CAP 75MG	8	2	$78,970.96	4	$9,871.37
SUBTOTAL	**8**	**2**	**$78,970.96**	**4**	**$9,871.37**
TOTAL	**117**	**18***	**$1,006,456.73**	**6.5**	**$8,602.19**

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

Medical Claims: Fiscal Year 2018

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM
J9299 NIVOLUMAB INJECTION	350	60	$2,408,873.78	$6,882.50
J9271 PEMBROLIZUMAB INJECTION	168	38	$1,684,936.40	$10,029.38
J9228 IPILIMUMAB INJECTION	18	9	$513,411.15	$28,522.84
J9023 AVELUMAB INJECTION	3	1	$48,126.00	$16,042.00
TOTAL	**519+**	**97***	**$4,655,347.33**	**$8,969.84**

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

[1] National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology (Basal Cell Skin Cancer). Available online at: https://www.nccn.org/professionals/physician_gls/pdf/nmsc.pdf. Last accessed 09/22/2018.
[2] National Cancer Institute. SEER Cancer Statistics. Available online at: http://www.cancer.gov/about-cancer/what-is-cancer/statistics. Last accessed 09/22/2018.
[3] NCCN. NCCN Clinical Practice Guidelines in Oncology (Melanoma). Available online at: https://www.nccn.org/professionals/physician_gls/pdf/melanoma.pdf. Last accessed 09/22/2018.
[4] American Cancer Society. Key Statistics for Melanoma Skin Cancer. Available online at: https://www.cancer.org/cancer/melanoma-skin-cancer/about/key-statistics.html. Last accessed 09/22/2018.
[5] Davies H, Bignell GR, Cox C, et al. Mutations of the BRAF gene in human cancer. *Nature* 2002; 417(6892):949-954.
[6] Hodi FS, O'Day SJ, McDermott DF, et al. Improved survival with Ipilimumab in patients with metastatic melanoma. *N Engl J Med* 2010; 363(8):711-723.
[7] Robert C, Thomas L, Bondarenko I, et al. Ipilimumab plus Dacarbazine for previously untreated metastatic melanoma. *N Engl J Med* 2011; 364(26):2517-2526.
[8] McArthur GA, Chapman PB, Robert C, et al. Safety and efficacy of vemurafenib in BRAFV600E and BRAFV600K mutation-positive melanoma (BRIM-3): extended follow-up of a phase 3, randomised, open-label study. *Lancet Oncol* 2014; 15(3):323-332.
[9] Hamid O, Robert C, Daud A, et al. Safety and tumor responses with Lambrolizumab (Anti–PD-1) in melanoma. *N Engl J Med* 2013; 369(2):134-144.
[10] Hauschild A, Grob J-J, Demidov LV, et al. Dabrafenib in BRAF-mutated metastatic melanoma: a multicenter, open-label, phase 3 randomised controlled trial. *Lancet* 2012; 380(9839):358-365.
[11] Flaherty KT, Robert C, Hersey P, et al. Improved survival with MEK inhibition in BRAF-mutated melanoma. *N Engl J Med* 2012; 367(2):107-114.
[12] Larkin J, Ascierto PA, Dréno B, et al. Combined vemurafenib and cobimetinib in BRAF-mutated melanoma. *N Engl J Med* 2014; 371(20):1867-1876.
[13] Topalian SL, Sznol M, McDermott DF, et al. Survival, durable tumor remission, and long-term safety in patients with advanced melanoma receiving Nivolumab. *J Clin Oncol* 2014; 32(10):1020-1030.
[14] Guy GP, Machlin S, Ekwueme DU, Yabroff KR. Prevalence and costs of skin cancer treatment in the US, 2002-2006 and 2007-2011. *Am J Prev Med* 2014.
[15] U.S. Food and Drug Administration (FDA). Hematology/Oncology (Cancer) Approvals & Safety Notifications. Available online at: https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm279174.htm. Last revised 09/13/2018. Last accessed 09/17/2018.
[16] FDA. FDA updates prescribing information for Keytruda and Tecentriq. Available online at: https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm617378.htm. Issued 08/16/2018. Last accessed 09/17/2018.
[17] Regeneron Pharmaceuticals, Inc. FDA Approves Libtayo® (cemiplimab-rwlc) as First and Only Treatment for Advanced Cutaneous Squamous Cell Carcinoma. Available online at: https://newsroom.regeneron.com/news-releases/news-release-details/fda-approves-libtayor-cemiplimab-rwlc-first-and-only-treatment. Issued 09/28/2018. Last accessed 10/01/2018.
[18] Braftovi™ Prescribing Information. Array Biopharma. Available online at: http://www.arraybiopharma.com/documents/Braftovi_Prescribing_information.pdf. Last revised 06/2018. Last accessed 09/17/2018.
[19] Mektovi® Prescribing Information. Array Biopharma. Available online at: http://www.arraybiopharma.com/documents/Mektovi_Prescribing_information.pdf. Last revised 06/2018. Last accessed 09/17/2018.
[20] Libtayo® (cemiplimab-rwlc) Prescribing Information. Regeneron Pharmaceuticals, Inc. Available online at: https://www.regeneron.com/sites/default/files/Libtayo_FPI.pdf. Last revised 09/2018. Last accessed 10/01/2018.

Appendix L

Fiscal Year 2018 Annual Review of Targeted Immunomodulator Agents and 30-Day Notice to Prior Authorize Ilumya™ (Tildrakizumab-asmn) and Olumiant® (Baricitinib)

Oklahoma Health Care Authority
October 2018

Current Prior Authorization Criteria

Targeted Immunomodulator Agents*±		
Tier-1 (DMARDs appropriate to disease state)	**Tier-2***	**Tier-3**
6-mercaptopurine	adalimumab (Humira®)	abatacept (Orencia®)
azathioprine	etanercept (Enbrel®)	adalimumab-adbm (Cyltezo™)
hydroxychloroquine		adalimumab-atto (Amjevita™)
leflunomide		alefacept (Amevive®)
mesalamine		anakinra (Kineret®)
methotrexate		apremilast (Otezla®)
minocycline		brodalumab (Siliq™)
NSAIDs		canakinumab (Ilaris®)[¥]
oral corticosteroids		certolizumab pegol (Cimzia®)
		etanercept-szzs (Erelzi™)
		golimumab (Simponi® & Simponi® Aria™)
		guselkumab (Tremfya™)
		infliximab (Remicade®)
		infliximab-abda (Renflexis™)
		infliximab-dyyb (Inflectra™)
		ixekizumab (Taltz®)
		rituximab (Rituxan®)
		sarilumab (Kevzara®)
		secukinumab (Cosentyx®)[Ω]
		tocilizumab (Actemra®)[π]
		tofacitinib (Xeljanz® & Xeljanz® XR)
		ustekinumab (Stelara®)
		vedolizumab (Entyvio™)

DMARDs = disease modifying antirheumatic drugs; NSAIDs = nonsteroidal anti-inflammatory drugs

*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC) if NADAC unavailable. Tier-2 drugs subject to move to Tier-3. Appropriate laboratory monitoring must be verified by the prescriber prior to approval.

[±]Biosimilars or reference products preferred based on lowest net cost product. Authorization of higher net cost biosimilars or reference products requires a patient-specific, clinically significant reason why the member could not use the preferred formulation.

[+]Unique criteria applies for a diagnosis of hidradenitis suppurativa (HS) and noninfectious intermediate and posterior uveitis and panuveitis.

[Δ]If the net cost of Xeljanz® XR (tofacitinib extended-release) and Orencia® ClickJect™ (abatacept autoinjector) is determined to be greater than the net cost of the immediate-release formulation of Xeljanz® or the prefilled syringe formulation of Orencia® authorization would also require a patient-specific, clinically significant reason why the member cannot use the immediate-release formulation of Xeljanz® or the prefilled syringe formulation of Orencia®.

[¥]Unique criteria applies for a diagnosis of Cryopyrin-Associated Periodic Syndromes (CAPS), Tumor Necrosis Factor Receptor-Associated Periodic Syndrome (TRAPS), Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD), or Familial Mediterranean Fever (FMF).

[Ω]For Cosentyx™ (secukinumab), only a trial of Humira® from the available Tier-2 medications will be required (based on supplemental rebate participation).

[π]Unique criteria applies for a diagnosis of giant cell arteritis (GCA) and chimeric antigen receptor T (CAR T) cell-induced cytokine release syndrome (CRS).

- Current tier trial requirements can be found in the recommendations section at the end of this report.

Utilization of Targeted Immunomodulator Agents: Fiscal Year 2018

Targeted Immunomodulator Agent Fiscal Year Comparison: Pharmacy Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2017	828	5,189	$26,888,698.46	$5,181.87	$177.76	74,179	151,264
2018	816	5,535	$30,121,216.08	$5,441.95	$184.08	62,039	163,631
% Change	**-1.40%**	**6.70%**	**12.00%**	**5.00%**	**3.60%**	**-16.40%**	**8.20%**
Change	**-12**	**346**	**$3,232,517.62**	**$260.08**	**$6.32**	**-12,140**	**12,367**

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

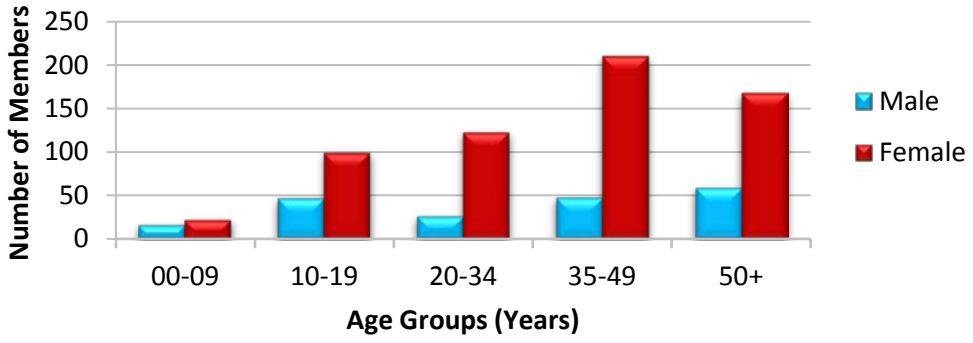
- There was a significant increase in cost while utilization remained relatively flat. It is important to note that several of these products are in their waning patent stages and will soon face or are facing biosimilar competition; typically when a product is close to the end of its patent life the manufacturer will raise the price. The consumer price index (CPI) penalty of the federal rebate is designed to keep Medicaid net cost relatively flat despite price increases. The cost increase in the table does not reflect the net cost increase. Additionally, the majority of utilization was seen in Tier-2 medications which are supplementally rebated medications. The supplementally rebated prices are also not reflected in the fiscal year comparison table.

Targeted Immunomodulator Agent Fiscal Year Comparison: Medical Claims

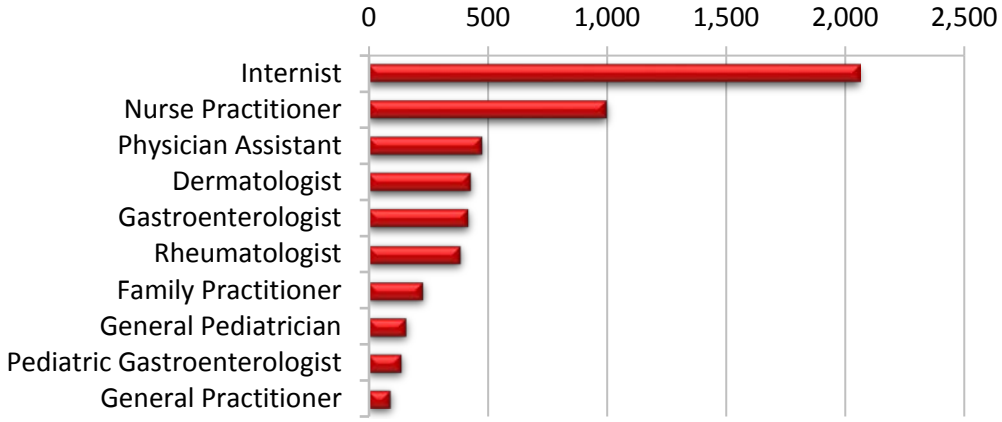
Fiscal Year	*Total Members	+Total Claims	Total Cost	Cost/Claim	Total Units
2017	165	563	$2,616,196.42	$4,646.89	32,859
2018	198	715	$3,521,237.28	$4,924.81	98,489
% Change	**20.00%**	**27.00%**	**34.59%**	**5.98%**	**199.73%**
Change	**33**	**152**	**$905,040.86**	**$277.92**	**65,630**

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

Demographics of Members Utilizing Targeted Immunomodulator Agents: Pharmacy Claims



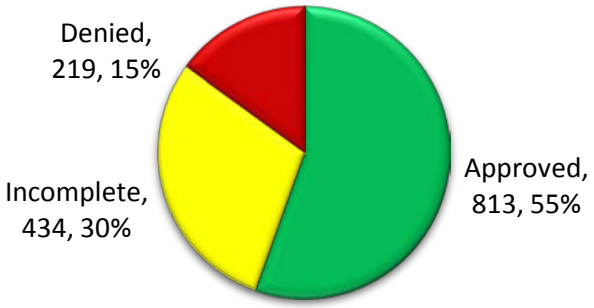
Top Prescriber Specialties of Targeted Immunomodulator Agents by Number of Claims: Pharmacy Claims



Prior Authorization of Targeted Immunomodulator Agents

There were 1,466 prior authorization requests submitted for targeted immunomodulator agents during fiscal year 2018. Computer edits are in place to detect lower tiered medications in a member's claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions for fiscal year 2018.

Status of Petitions



Market News and Updates[1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26]

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

- **November 2017:** Enbrel Mini™ with AutoTouch™ (etanercept)
- **December 2017:** Ixifi™ (infliximab-qbtx)
- **March 2018:** Ilumya™ (tildrakizumab-asmn)
- **June 2018:** Olumiant® (baricitinib)

New Indication(s):

- **October 2017:** The FDA approved an expanded indication for Stelara® (ustekinumab) for the treatment of moderate-to-severe plaque psoriasis (PsO) in adolescents 12 years of age and older. Ustekinumab was previously approved for the treatment of PsO in adults, active psoriatic arthritis (PsA), and Crohn's disease (CD).
- **October 2017:** The FDA approved expanded indications for Simponi Aria® (golimumab) for the treatment of adults with active PsA or active ankylosing spondylitis (AS). Golimumab was previously approved for the treatment of rheumatoid arthritis (RA).

- **December 2017:** The FDA approved an expanded indication for Taltz® (ixekizumab) for the treatment of adults with active PsA. Ixekizumab was previously approved for PsO.
- **December 2017:** The FDA approved an expanded indication for Xeljanz® (tofacitinib) and Xeljanz® XR (tofacitinib extended-release) for the treatment of active PsA. Tofacitinib was previously approved for the treatment of RA.
- **March 2018:** The FDA approved an expanded indication for Xeljanz® (tofacitinib) for the treatment of moderately-to-severely active ulcerative colitis (UC). Tofacitinib was previously approved for the treatment of RA and PsA.
- **May 2018**: The FDA approved an expanded indication for Cimzia® (certolizumab) for the treatment of adults with moderate-to-severe PsO. Certolizumab was previously approved for the treatment of RA, PsA, and AS.
- **June 2018:** The FDA approved Rituxan® (rituximab) for the treatment of adults with moderate-to-severe pemphigus vulgaris (PV), an autoimmune blistering disease that affects the skin and mucous membranes. Rituxan® was previously approved for the treatment of non-Hodgkin's lymphoma, chronic lymphocytic leukemia, RA, granulomatosis with polyangiitis (GPA), and microscopic polyangiitis.

News:

- **September 2017:** The FDA announced they are evaluating the need for regulatory action regarding Actemra® (tocilizumab) intravenous (IV) and subcutaneous (sub-Q) and the potential risk of pancreatitis and hepatotoxicity.
- **December 2017:** Despite FDA approval of Ixifi™ (infliximab-qbtx), a biosimilar to Remicade® (infliximab), the manufacturer of Ixifi™, Pfizer, announced that the company will not launch Ixifi™ in the United States. Pfizer already has another Remicade® biosimilar on the market known as Inflectra® (infliximab-dyyb). One other Remicade® biosimilar is also FDA approved: Merck and Samsung Bioepis' Renflexis® (infliximab-abda).
- **February 2018:** The Pediatric Dermatology Research Alliance (PeDRA) and the National Psoriasis Foundation developed guidelines for the treatment of pediatric PsO. The document included consensus recommendations regarding pediatric PsO patients with comorbid conditions including the following: obesity, type 2 diabetes mellitus, dyslipidemia, hypertension, nonalcoholic fatty liver disease, polycystic ovarian syndrome, gastrointestinal (GI) diseases, arthritis, uveitis, mood disorders, and substance abuse.
- **March 2018:** UCB announced that the FDA approved an update to the Cimzia® (certolizumab) labeling to include new data regarding the transfer of drug through the placenta and breast milk from mother to infant. Findings from pharmacokinetic studies indicated negligible to low transfer of certolizumab through the placenta as well as minimal transfer to breast milk.
- **April 2018:** The American College of Gastroenterology (ACG) updated its clinical guideline for the management of CD in adults. A strong recommendation from the guideline included the use of fecal calprotectin to help differentiate inflammatory bowel disease (IBD) from irritable bowel syndrome (IBS). Graded recommendations were also issued for therapeutic options [e.g., sulfasalazine, corticosteroids, anti-tumor necrosis factor (TNFα) agents] by severity of disease.

- **August 2018:** The Institute for Clinical and Economic Review (ICER) published a final evidence report regarding targeted immunomodulatory agents for the treatment of moderate-to-severe PsO. ICER results found quality-of-life (QOL) improvements to be similar across agents, but treatment initiation with the interleukin-17 (IL-17) medications or Taltz® (guselkumab) led to the greatest improvement in quality adjusted life years (QALYs). Initiation with Otezla® (apremilast), Enbrel® (etanercept), or Remicade® (infliximab) were considered the least effective. In contrast, initiation with the IL-17 drugs, guselkumab, or Cimzia® (certolizumab) generally led to the highest total cost, while initiation with apremilast, etanercept, or infliximab led to lower total costs.

Pipeline Update(s):

- **Truxima™ (rituximab biosimilar):** In February 2017, Truxima™ became the first biosimilar to rituximab approved by the European Medicines Agency. Celltrion, the maker of Truxima™ received a complete response letter (CRL) from the FDA in April 2018. The FDA cited poor aseptic practices at Celltrion's manufacturing plant. No timeline on a resubmission has been released.
- **Rixathon® (rituximab biosimilar):** In June 2017, Sandoz received approval in Europe for Rixathon®, a biosimilar to rituximab. In May 2018, the FDA issued a CRL to Sandoz for Rixathon®. Sandoz has indicated it will work with the FDA to resubmit; however, no timeline was provided.
- **Upadacitinib:** In April 2018, AbbVie announced positive results from a Phase 3 trial of upadacitinib, an investigational Janus Kinase-1 (JAK-1) inhibitor, for the treatment of RA. After 12 weeks of treatment, 71% of patients receiving an oral once-daily dose of upadacitinib 15mg achieved a 20% reduction in symptoms, compared with 36% of patients receiving placebo.
- **Risankizumab:** In April 2018, AbbVie announced the submission of a Biologics License Application (BLA) to the FDA for risankizumab, an investigational IL-23 inhibitor being studied for the treatment of moderate-to-severe PsO. Phase 3 trials of risankizumab in PsO and CD are ongoing, and it is also being investigated to treat PsA.
- **Olumiant® (baricitinib):** In June 2018, data presented at the European League Against Rheumatism (EULAR) Congress revealed once-daily, oral baricitinib 4mg was associated with significant clinical improvements compared to placebo in patients with systemic lupus erythematosus (SLE). In a 24-week double-blind study, a significantly greater percentage of patients in the baricitinib 4mg group achieved resolution of arthritis or rash compared with placebo (67% vs. 53%; $P<0.05$).

Ilumya™ (Tildrakizumab-asmn) Product Summary[27]

Indication(s): Ilumya™ (tildrakizumab-asmn) is an IL-23 antagonist indicated for the treatment of adults with moderate-to-severe PsO who are candidates for systemic or phototherapy.

Dosing:

- Ilumya™ is supplied as 100mg/mL single-dose, pre-filled syringes. The syringes must be refrigerated and removed from refrigeration 30 minutes prior to injection. Syringes must be used within 30 days of being removed from refrigeration.

- The recommended dose of tildrakizumab is 100mg via sub-Q injection at weeks 0, 4, and every 12 weeks thereafter.
- Tildrakizumab should only be administered by a health care provider.
- Injections may be given in the abdomen (at least 2 inches from the navel), thigh, or upper arm.

Mechanism of Action: Tildrakizumab is a humanized IgG1/k monoclonal antibody that selectively binds to the p19 subunit of IL-23 and inhibits its interaction with the IL-23 receptor. IL-23 is a naturally occurring cytokine that is involved in inflammatory and immune responses. Tildrakizumab inhibits the release of proinflammatory cytokines and chemokines.

Contraindication(s): Tildrakizumab is contraindicated in patients with a previous serious hypersensitivity reaction to tildrakizumab or to any of the excipients in the product formulation.

Warnings and Precautions:

- Hypersensitivity: Cases of angioedema and urticaria occurred in tildrakizumab-treated patients in clinical trials. If a serious hypersensitivity reaction occurs, tildrakizumab should be discontinued immediately and appropriate therapy initiated.
- Infections: Tildrakizumab may increase the risk of infection. Although infections were slightly more common in the tildrakizumab group (23%) in clinical studies, the difference in frequency of infections between the tildrakizumab group and the placebo group was <1% during the placebo-controlled period. However, subjects with active infections or a history of recurrent infections were not included in clinical trials. The rates of serious infections for the tildrakizumab group and the placebo group were ≤0.3%.
- Pretreatment Evaluation for Tuberculosis (TB): Patients should be evaluated for TB infection prior to initiating treatment with tildrakizumab, and treatment of latent TB should be administered prior to administering tildrakizumab.
- Immunizations: Prior to initiating therapy with tildrakizumab, consideration should be given to completion of all age appropriate immunizations according to current immunization guidelines. The use of live vaccines should be avoided in patients treated with tildrakizumab.

Efficacy: The efficacy of tildrakizumab was assessed in two multi-center, randomized, double-blind, placebo-controlled trials (Trial 2 and Trial 3). The trials included 926 adult patients treated with tildrakizumab 100mg (N=616) or placebo (N=310). Included patients had a Physician Global Assessment (PGA) score of ≥3 (moderate) on a 5-point scale of overall disease severity, Psoriasis Area and Severity Index (PASI) score ≥12, and a minimum body surface area (BSA) involvement of 10%. In both trials, patients were randomized to either placebo or tildrakizumab [100mg at week 0, week 4, and every twelve weeks thereafter (Q12W)] for up to 64 weeks. Trials 2 and 3 assessed the changes from baseline to Week 12 in the two co-primary endpoints: PASI 75, the proportion of subjects who achieved at least a 75% reduction in the PASI composite score; and the proportion of patients with a PGA of 0 (“cleared”) or 1 (“minimal”) and at least a 2-point improvement. At baseline, these patients had a median affected BSA of 27%, a median PASI score of 17.8, and approximately 33% had a PGA score of 4

("marked") or 5 ("severe"). Approximately 34% had received prior phototherapy, 39% had received prior conventional systemic therapy, and 18% had received prior biologic therapy for the treatment of PsO. The results of Trial 2 and Trial 3 are presented in the following table.

Table 1: Tildrakizumab Results at Week 12

	Trial 2		Trial 3	
	Tildrakizumab 100mg (N=309) n (%)	Placebo (N=154) n (%)	Tildrakizumab 100mg (N=307) n (%)	Placebo (N=156) n (%)
PGA of 0 or 1	179 (58)	11 (7)	168 (55)	7 (4)
PASI 75	197 (64)	9 (6)	188 (61)	9 (6)
PASI 90	107 (35)	4 (3)	119 (39)	2 (1)
PASI 100	43 (14)	2 (1)	38 (12)	0 (0)

PGA = physician global assessment; PASI = Psoriasis Area and Severity Index; PASI # = proportion of patients who achieved at least a #% reduction in the PASI composite score; N = number; % = percentage

Cost Comparison:

Medication	Cost Per Unit	Cost for 24 Weeks of Therapy
Ilumya™ (tildrakizumab-asmn) 100mg/mL syringe	**$13,256.00**	**$26,512.00**
Enbrel® (etanercept) 50mg/mL SureClick® autoinjector	$1,185.25*	$28,446.00*
Humira® (adalimumab) 40mg/0.8mL pen	$1,899.12*	$22,789.44*
Stelara® (ustekinumab) 45mg/0.5mL syringe	$9,908.26	$19,816.51

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 Costs (SMAC) if NADAC unavailable.
Unit = pen, syringe, or autoinjector
*Supplementally rebatated products
Dosing based on recommended treatment doses for PsO in a 75kg adult patient.
Cost for 24 weeks of therapy based on maintenance treatment dosing after initial dosing is complete.

Olumiant® (Baricitinib) Product Summary[28,29,30]

Indication(s): Olumiant® (baricitinib) is a JAK inhibitor indicated for the treatment of adult patients with moderately-to-severely active RA who have had an inadequate response to one or more TNF antagonist therapies.

- Limitation of Use: Use of baricitinib in combination with other JAK inhibitors, biologic disease-modifying antirheumatic drugs (DMARDs), or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended.

Dosing:

- Olumiant® is supplied as 2mg oral tablets.
- The recommended dose of baricitinib is 2mg by mouth once daily.
- Baricitinib may be used as monotherapy or in combination with methotrexate or other DMARDs.
- Baricitinib initiation is not recommended in patients with an absolute lymphocyte count (ALC) <500cells/mm^3, absolute neutrophil count (ANC) <1,000cells/mm^3, or hemoglobin (Hgb) level <8g/dL.

- Baricitinib use should be avoided in patients with active, serious infection(s), including localized infections.
- Baricitinib is not recommended for use in patients with an estimated glomerular filtration rate (eGFR) <60mL/min/1.73 m^2.
- Baricitinib is not recommended for use in patients with severe hepatic impairment.

Boxed Warning: Serious Infections, Malignancy, and Thrombosis

- Serious infections leading to hospitalization or death, including TB and bacterial, invasive fungal, viral, and other opportunistic infections, have occurred in patients receiving baricitinib.
  - If a serious infection develops, baricitinib should be interrupted until the infection is controlled.
  - Prior to starting baricitinib, a test for latent TB should be performed; if it is positive, treatment for TB should be initiated prior to starting baricitinib.
  - All patients should be monitored for active TB during treatment, even if the initial latent TB test is negative.
- Lymphoma and other malignancies have been observed in patients treated with baricitinib.
- Thrombosis, including deep venous thrombosis (DVT), pulmonary embolism (PE), and arterial thrombosis, some fatal, have occurred in patients treated with baricitinib. Patients with symptoms of thrombosis should be evaluated promptly.

Mechanism of Action: Baricitinib is a JAK inhibitor. JAKs are intracellular enzymes which transmit signals arising from cytokine or growth factor-receptor interactions on the cellular membrane to influence cellular processes of hematopoiesis and immune cell function. Within the signaling pathway, JAKs phosphorylate and activate signal transducers and activators of transcription (STATs) which modulate intracellular activity including gene expression. Baricitinib modulates the signaling pathway at the point of JAKs, preventing the phosphorylation and activation of STATs.

Contraindication(s): None

Warnings and Precautions:

- Serious Infections: Serious and sometimes fatal infections due to bacterial, mycobacterial, invasive fungal, viral, or other opportunistic pathogens have been reported in RA patients receiving baricitinib. The most common serious infections reported with baricitinib included pneumonia, herpes zoster, and urinary tract infection. Baricitinib use should be avoided in patients with an active, serious infection, including localized infections. Patients should be evaluated and tested for latent or active TB infection prior to administration of baricitinib. Patients with latent TB should be treated with standard antimycobacterial therapy before initiating baricitinib.
- Malignancy and Lymphoproliferative Disorders: The risks and benefits of baricitinib treatment should be considered prior to initiating therapy in patients with a known malignancy other than a successfully treated nonmelanoma skin cancer (NMSC) or when considering continuing baricitinib in patients who develop a malignancy. NMSCs have

been reported in patients treated with baricitinib. Periodic skin examination is recommended for patients who are at increased risk for skin cancer.

- Thrombosis: Thrombosis, including DVT and PE, has been observed at an increased incidence in patients treated with baricitinib compared to placebo. In addition, arterial thrombosis events in the extremities have been reported in clinical studies with baricitinib. Many of these adverse events were serious and some resulted in death. There was no clear relationship between platelet count elevations and thrombotic events. Baricitinib should be used with caution in patients who may be at increased risk of thrombosis. If clinical features of DVT/PE or arterial thrombosis occur, patients should be evaluated promptly and treated appropriately.
- GI Perforations: Events of GI perforation have been reported in clinical studies with baricitinib, although the role of JAK inhibition in these events is not known. Baricitinib should be used with caution in patients who may be at increased risk for GI perforation (e.g., patients with a history of diverticulitis). Patients presenting with new onset abdominal symptoms should be evaluated promptly for early identification of GI perforation.
- Laboratory Abnormalities:
  - Neutropenia: Treatment with baricitinib was associated with an increased incidence of neutropenia (ANC <1,000cells/mm^3) compared to placebo. Initiation should be avoided or treatment should be interrupted in patients with an ANC <1,000cells/mm^3.
  - Lymphopenia: ALC <500cells/mm^3 were reported in baricitinib clinical trials. Initiation should be avoided or treatment should be interrupted in patients with an ALC <500cells/mm^3.
  - Anemia: Decreases in Hgb levels to <8g/dL were reported in baricitinib clinical trials. Initiation should be avoided or treatment should be interrupted in patients with Hgb <8g/dL.
  - Liver Enzyme Elevations: Treatment with baricitinib was associated with increased incidence of liver enzyme elevation compared to placebo. Increases to ≥5 times and ≥10 times the upper limit of normal (ULN) were observed for both ALT and AST in patients in baricitinib clinical trials. If increases in ALT or AST are observed and drug-induced liver injury is suspected, baricitinib should be interrupted.
  - Lipid Elevations: Treatment with baricitinib was associated with increases in lipid parameters, including total cholesterol, low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein (HDL) cholesterol.
- Vaccinations: Use of live vaccines should be avoided in patients treated with baricitinib. Immunizations should be updated in agreement with current guidelines prior to initiating baricitinib therapy.

Efficacy: The efficacy and safety of baricitinib 2mg once daily was assessed in two 24-week randomized, double-blind, multicenter Phase 3 trials (Study 3 and Study 4) including adult patients with moderately-to-severely active RA. Eligible patients had at least six tender and six swollen joints at baseline.

- Study 3 assessed 684 patients with moderately-to-severely active RA who had an inadequate response or intolerance to conventional DMARDs (cDMARDs). Patients

received baricitinib 2mg once daily or placebo added to existing background cDMARD treatment. The primary endpoint was the proportion of patients who achieved an American College of Rheumatology (ACR20) at week 12. ACR20 is defined as a 20% improvement in the number of tender and swollen joints, and a 20% improvement in three of the following five criteria: patient global assessment, PGA, functional ability measure [most often Health Assessment Questionnaire (HAQ)], visual analog pain scale, and erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP). Disease activity score (DAS) 28 was assessed as a secondary endpoint. DAS28 is a composite score intended to measure RA activity; the score is composed of the number of swollen joints (out of the 28 assessed), the number of tender joints (out of the 28 assessed), the ESR or CRP, and the patient global assessment of health. A DAS28 of >5.1 implies active disease, <3.2 low disease activity, and <2.6 remission.

- Study 4 assessed 527 patients with moderately-to-severely active RA who had an inadequate response or intolerance to one or more TNF inhibitor therapies with or without other biologic DMARDs. Patients received baricitinib 2mg or placebo added to background cDMARD treatment. The primary endpoint was the proportion of patients who achieved an ACR20 response at week 12. DAS28 was assessed as a secondary endpoint.
- Results of Study 3 and Study 4 are presented in the following table.

Table 2: Baricitinib Results at Week 24

	Study 3		Study 4	
	Placebo + cDMARDs (N=228)	**Baricitinib + cDMARDs N=229 Δ (95% CI)**	**Placebo + cDMARDs (N=176)**	**Baricitinib + cDMARDs (N=174) Δ (95% CI)**
ACR 20 Week 24 % of patients	42	61 19 (10, 28)	27	45 18 (8, 27)
ACR 50 Week 24 % of patients	21	41 20 (12, 28)	13	23 10 (2, 18)
ACR 70 Week 24 % of patients	8	25 17 (11, 24)	3	13 10 (4, 16)
DAS28-CRP <2.6	11	31 (13, 27)	6	11 (-1, 11)

cDMARDs = conventional disease-modifying anti-rheumatic drugs; ACR# = #% improvement in the number of tender and swollen joints, and a 20% improvement in three of the five prespecified criteria; DAS28-CRP = disease activity score with c-reactive protein (a score of <2.6 indicates RA remission); N = number

Δ = 95% confidence interval (CI) for the difference (Δ) in response rate between baricitinib treatment and placebo

Cost Comparison:

Medication	Cost Per Unit	Cost for 24 Weeks of Therapy
Olumiant® (baricitinib) 2mg tablet	**$1,750.01**	**$21,000.06**
Enbrel® (etanercept) 50mg/mL SureClick® autoinjector	$1,185.25	$28,446.00
Humira® (adalimumab) 40mg/0.8mL pen	$1,899.12	$22,789.44
Xeljanz® (tofacitinib) 5mg tablet	$66.43	$22,320.48

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 Costs (SMAC) if NADAC unavailable.
Unit = tablet, autoinjector, or pen
Dosing based on recommended treatment doses for RA in a 75kg adult patient.
Cost for 24 weeks of therapy based on maintenance treatment dosing after initial dosing is complete.

Pemphigus Vulgaris (PV) Summary [12,13,31,32]

Pemphigus vulgaris (PV) is an autoimmune blistering disease that affects the skin and mucous membranes. The incidence of PV is estimated to be between 0.1 and 0.5 per 100,000 people per year; however, rates may vary between geographic location and ethnicity. Individuals with Jewish ancestry and inhabitants of India, Southeast Europe, and the Middle East have the greatest risk for PV. The average age of onset of PV is 40 to 60 years, and PV is considered rare in children.

The most common symptom of PV is mucosal lesions, particularly in the oral cavity. Other common sites of lesions include the mucous membranes in the conjunctiva, nose, esophagus, vulva, vagina, cervix, and anus. The pain associated with mucosal involvement of PV can be severe. PV blisters rupture and bleed easily. Oral pain is often augmented by chewing and swallowing, which may result in weight loss and malnutrition.

The diagnosis of PV is made through the assessment of clinical and laboratory findings. Clinical findings include cutaneous and mucosal blistering, hoarseness, dysphagia, dysuria, and dyspareunia. Laboratory assessment should include lesional skin or mucosal biopsy for evaluation consistent with the presentation of PV. Characteristic findings in PV include sparse inflammatory infiltrate in the dermis with eosinophils. Enzyme-linked immunosorbent assay can also be conducted to confirm a PV diagnosis.

First-line therapy for the treatment of PV is oral corticosteroids (e.g., prednisone, prednisolone, methylprednisolone). Adjuvant therapies commonly used include azathioprine and mycophenolate mofetil. The combination of Rituxan® (rituximab) with corticosteroids is an alternative first-line therapy or can be used for the treatment of resistant PV.

In June 2018, the FDA approved rituximab for the treatment of adults with moderate-to-severe PV based on a randomized, open-label, controlled, multicenter study in 90 newly diagnosed adult patients with moderate-to-severe pemphigus [74 PV and 16 pemphigus foliaceus (PF)]. Patients were stratified by baseline disease severity (moderate or severe) and randomized 1:1 to receive either a non-U.S.-approved rituximab product and short-term prednisone or long-term prednisone monotherapy. Patients randomized to the group treated with rituximab received an initial IV infusion of 1,000mg on day 1 in combination with a short-term regimen of 0.5mg/kg/day oral prednisone tapered off over 3 months if they had moderate disease or 1mg/kg/day oral prednisone tapered off over 6 months if they had severe disease. Patients received a second IV infusion of rituximab 1,000mg on day 15. Maintenance infusions of 500mg rituximab were administered at months 12 and 18. Patients randomized to the prednisone monotherapy group received an initial 1mg/kg/day oral prednisone tapered off over 12 months if they had moderate disease or 1.5mg/kg/day oral prednisone tapered off over 18 months if they had severe disease. The primary endpoint for the study was complete remission (complete epithelialization and absence of new and/or established lesions) at month 24 without the use of prednisone therapy for >2 months. Results are presented in the following table:

Table 3: Rituximab Results at Month 24

	Rituximab + Short-Term Prednisone (N=46)	Prednisone (N=44)
Number of responders [response rate (%)]	41 (89%)	15 (34%)
PV patients	34/38 (90%)	10/36 (28%)
PF patients	7/8 (88%)	5/8 (63%)

PV = pemphigus vulgaris; PF = pemphigus foliaceus; N = number

Recommendations

The College of Pharmacy recommends the addition of Ilumya™ (tildrakizumab-asmn) and Olumiant® (baricitinib) to Tier-3 of the Targeted Immunomodulator Agents Product Based Prior Authorization (PBPA) category. Current Tier-3 approval criteria for this category will apply.

Targeted Immunomodulator Tier-2 Approval Criteria:

1. An FDA approved diagnosis; and
2. A trial of at least one Tier-1 medication in the last 90 days that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or
3. For a diagnosis of Crohn's disease (CD) or ulcerative colitis (UC) authorization of a Tier-2 product requires history of failure of a mesalamine product (does not have to be within the last 90 days) and a trial of one Tier-1 in the last 90 days that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or
4. Prior stabilization on the Tier-2 medication documented within the last 100 days.

Targeted Immunomodulator Tier-3 Approval Criteria:

1. An FDA approved diagnosis; and
2. Recent trials of one Tier-1 medication and all available Tier-2 medications that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or
3. Prior stabilization on the Tier-3 medication documented within the last 100 days; or
4. A unique FDA-approved indication not covered by Tier-2 products.

Additionally, the College of Pharmacy recommends the following criteria for Rituxan® (rituximab) for the treatment of adults with moderate-to-severe pemphigus vulgaris (PV):

Rituxan® (Rituximab) Approval Criteria [Pemphigus Vulgaris (PV) Diagnosis]:

1. A diagnosis of moderate-to-severe PV; and
2. Rituxan® must be used in combination with a tapering course of glucocorticoids; and
3. Initial approvals will be for two 1,000mg intravenous (IV) infusions separated by two weeks and a 500mg infusion at month 12. Subsequent approvals may be authorized based on 6 month evaluations or upon relapse may be no sooner than 16 weeks after the previous infusion.

Targeted Immunomodulator Agents*±		
Tier-1 (DMARDs appropriate to disease state)	**Tier-2***	**Tier-3**
6-mercaptopurine	adalimumab (Humira®)+	abatacept (Orencia®)Δ
azathioprine	etanercept (Enbrel®)	adalimumab-adbm (Cyltezo™)
hydroxychloroquine		adalimumab-atto (Amjevita™)
leflunomide		alefacept (Amevive®)
mesalamine		anakinra (Kineret®)
methotrexate		apremilast (Otezla®)
minocycline		**baricitinib (Olumiant®)**
NSAIDs		brodalumab (Siliq™)
oral corticosteroids		canakinumab (Ilaris®)¥
		certolizumab pegol (Cimzia®)
		etanercept-szzs (Erelzi™)
		golimumab (Simponi® & Simponi® Aria™)
		guselkumab (Tremfya™)
		infliximab (Remicade®)
		infliximab-abda (Renflexis™)
		infliximab-dyyb (Inflectra™)
		ixekizumab (Taltz®)
		rituximab (Rituxan®)~
		sarilumab (Kevzara®)
		secukinumab (Cosentyx®)Ω
		tildrakizumab-asmn (Ilumya™)
		tocilizumab (Actemra®)π
		tofacitinib (Xeljanz® & Xeljanz® XR)Δ
		ustekinumab (Stelara®)
		vedolizumab (Entyvio™)

DMARDs = Disease modifying antirheumatic drugs, NSAIDs = Nonsteroidal anti-inflammatory drugs

*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC) or State Maximum Allowable Costs (SMAC) if NADAC unavailable. Tier-2 drugs subject to move to Tier-3. Appropriate laboratory monitoring must be verified by the prescriber prior to approval.

±Biosimilars or reference products preferred based on lowest net cost product. Authorization of higher net cost biosimilars or reference products requires a patient-specific, clinically significant reason why the member could not use the preferred formulation.

+Unique criteria applies for a diagnosis of hidradentitis suppurativa (HS) and noninfectious intermediate and posterior uveitis and panuveitis.

ΔIf the net cost of Xeljanz® XR (tofacitinib extended-release) and Orencia® ClickJect™ (abatacept autoinjector) is determined to be greater than the net cost of the immediate-release formulation of Xeljanz® or the prefilled syringe formulation of Orencia® authorization would also require a patient-specific, clinically significant reason why the member could not use the immediate-release formulation of Xeljanz® or the prefilled syringe formulation of Orencia®.

¥Unique criteria applies for a diagnosis of Cryopyrin-Associated Periodic Syndromes (CAPS), Tumor Necrosis Factor Receptor-Associated Periodic Syndrome (TRAPS), Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD), or Familial Mediterranean Fever (FMF).

~Unique criteria applies for a diagnosis of pemphigus vulgaris (PV).

ΩFor Cosentyx™ (secukinumab) only a trial of Humira® from the available Tier-2 medications will be required (based on supplemental rebate participation).

πUnique criteria applies for a diagnosis of giant cell arteritis (GCA) and chimeric antigen receptor T (CAR T) cell-induced cytokine release syndrome (CRS).

Actemra® (Tocilizumab) Approval Criteria [Giant Cell Arteritis Diagnosis]:

1. An FDA approved diagnosis of giant cell arteritis (GCA); and
2. Member must be 50 years of age or older; and
3. A history of erythrocyte sedimentation rate (ESR) of ≥30mm/hr or a history of C-reactive protein (CRP) ≥1mg/dL; and
4. Member should have a trial of glucocorticoids for a minimum of four weeks or a reason why this is not appropriate; and
5. Actemra® will be taken in combination with tapering course of a glucocorticoid upon initiation; and
6. Member must have baseline liver enzymes, absolute neutrophil count (ANC), lipid panel, and platelet count and verification that they are acceptable to prescriber; and
7. Member must not have severe hepatic impairment; and
8. Actemra® should not be initiated in patients with active or chronic infection including hepatitis B, hepatitis C, human immunodeficiency virus, or tuberculosis; and
9. Approval quantity will be based on Actemra® prescribing information and FDA approved dosing regimen.

Actemra® (Tocilizumab) Approval Criteria [Chimeric Antigen Receptor (CAR) T-Cell-Induced Cytokine Release Syndrome (CRS) Diagnosis]:

1. An FDA approved diagnosis of CAR T-cell-induced CRS.

Humira® (Adalimumab) Approval Criteria [Hidradenitis Suppurativa (HS) Diagnosis]:

1. A diagnosis of moderate-to-severe HS; and
2. Hurley Stage II or III disease; and
3. The member must have at least three abscesses or inflammatory nodules; and
4. Previous failure of at least two of the following: topical or systemic antibiotics, oral or intralesional corticosteroids, dapsone, cyclosporine, antiandrogens (spironolactone or oral contraceptives), finasteride, or surgery.

Humira® (Adalimumab) Approval Criteria [Noninfectious Intermediate and Posterior Uveitis or Panuveitis Diagnosis]:

1. A diagnosis of noninfectious intermediate uveitis, posterior uveitis, or panuveitis in adults; and
2. A failed trial with a corticosteroid injection or systemic steroid in which member has had an inadequate response; or
3. A patient-specific, clinically significant reason a trial of corticosteroid treatment is inappropriate for the member.

Ilaris® (Canakinumab) Approval Criteria [Tumor Necrosis Factor Receptor-Associated Periodic Syndrome (TRAPS), Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD), or Familial Mediterranean Fever (FMF) Diagnosis]:

1. A diagnosis of TRAPS with chronic or recurrent disease activity defined as six flares per year; or
2. A diagnosis of HIDS/MKD; or
3. A diagnosis of FMF with documented active disease despite colchicine therapy or documented intolerance to effective doses of colchicine; and

4. 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.

Ilaris® (Canakinumab) Approval Criteria [Cryopyrin-Associated Periodic Syndromes (CAPS) Diagnosis]:

1. An FDA approved indication of Cryopyrin-Associated Periodic Syndromes (CAPS) verified by genetic testing. This includes Familial Cold Auto-Inflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS) in adults and children 4 years of age and older; and
2. The member must not be using a tumor necrosis factor blocking agent (e.g., adalimumab, etanercept, infliximab) or anakinra; and
3. Ilaris® should not be initiated in patients with active or chronic infection including hepatitis B, hepatitis C, human immunodeficiency virus, or tuberculosis; and
4. The following dosing requirements must be met:
    a. Dosing should not be more often than once every 8 weeks; and
    b. Dosing (requires recent weight in kilograms):
        i. Body weight >40kg: 150mg; or
        ii. Body weight 15kg to 40kg: 2mg/kg. If inadequate response, may be increased to 3mg/kg; and
5. Approvals will be for the duration of one year.

Utilization Details of Targeted Immunomodulator Agents: Fiscal Year 2018

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS*	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
TIER-2 PRODUCTS					
ADALIMUMAB PRODUCTS					
HUMIRA PEN INJ 40MG/0.8ML	2,060	344	$11,064,937.53	5.99	$5,371.33
HUMIRA KIT 40MG/0.8ML	368	72	$1,946,913.60	5.11	$5,290.53
HUMIRA KIT 20MG/0.4ML	50	10	$202,416.36	5	$4,048.33
HUMIRA PEN INJ CD/UC/HS 40MG/0.8ML	45	43	$610,846.53	1.05	$13,574.37
HUMIRA PEN INJ PS/UV 40MG/0.8ML	31	31	$279,629.84	1	$9,020.32
HUMIRA PEN INJ 40MG/0.4ML	6	6	$39,039.54	1	$6,506.59
HUMIRA INJ 40MG/0.4ML	2	2	$9,765.16	1	$4,882.58
HUMIRA INJ 10MG/0.1ML	1	1	$4,882.58	1	$4,882.58
SUBTOTAL	**2,563**	**425**	**$14,158,431.14**	**6.03**	**$5,524.16**
ETANERCEPT PRODUCTS					
ENBREL SRCLK INJ 50MG/ML	972	174	$4,524,838.79	5.59	$4,655.18
ENBREL INJ 50MG/ML	304	60	$1,417,713.84	5.07	$4,663.53
ENBREL INJ 25MG/0.5ML	103	15	$285,631.02	6.87	$2,773.12
ENBREL INJ 25MG	60	11	$142,976.25	5.45	$2,382.94
ENBREL MINI INJ 50MG/ML	25	13	$122,222.61	1.92	$4,888.90
SUBTOTAL	**1,464**	**242**	**$6,493,382.51**	**6.05**	**$4,435.37**
TIER-2 SUBTOTAL	**4,027**	**622***	**$20,651,813.65**	**6.47**	**$5,128.34**
TIER-3 PRODUCTS					
INFLIXIMAB PRODUCTS					
REMICADE INJ 100MG	334	42	$1,991,061.52	7.95	$5,961.26

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS*	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
SUBTOTAL	**334**	**42**	**$1,991,061.52**	**7.95**	**$5,961.26**
SECUKINUMAB PRODUCTS					
COSENTYX PEN INJ 300MG DOSE	128	23	$744,466.94	5.57	$5,816.15
COSENTYX PEN INJ 150MG/ML	37	10	$282,789.07	3.7	$7,642.95
COSENTYX INJ 300MG DOSE	24	4	$132,562.07	6	$5,523.42
COSENTYX INJ 150MG/ML	2	2	$23,287.39	1	$11,643.70
SUBTOTAL	**191**	**33**	**$1,183,105.47**	**5.79**	**$6,194.27**
ABATACEPT PRODUCTS					
ORENCIA INJ 125MG/ML	108	19	$384,859.97	5.68	$3,563.52
ORENCIA CLCK INJ 125MG/ML	37	8	$136,412.70	4.63	$3,686.83
ORENCIA INJ 250MG	9	1	$36,776.43	9	$4,086.27
SUBTOTAL	**154**	**26**	**$558,049.10**	**5.92**	**$3,623.70**
TOCILIZUMAB PRODUCTS					
ACTEMRA INJ 162MG/0.9ML	72	12	$239,262.20	6	$3,323.09
ACTEMRA INJ 80MG/4ML	28	4	$18,536.84	7	$662.03
ACTEMRA INJ 400/20ML	22	2	$71,646.38	11	$3,256.65
ACTEMRA INJ 200/10ML	21	3	$26,925.72	7	$1,282.18
SUBTOTAL	**143**	**16**	**$356,371.14**	**8.94**	**$2,492.11**
CANAKINUMAB PRODUCTS					
ILARIS INJ 150MG/ML	134	23	$2,208,083.66	5.83	$16,478.24
SUBTOTAL	**134**	**23**	**$2,208,083.66**	**5.83**	**$16,478.24**
APREMILAST PRODUCTS					
OTEZLA TAB 30MG	111	24	$333,501.66	4.63	$3,004.52
OTEZLA TAB STARTER PACK 10/20/30MG	19	19	$58,817.96	1	$3,095.68
SUBTOTAL	**130**	**30**	**$392,319.62**	**4.33**	**$3,017.84**
TOFACITINIB PRODUCTS					
XELJANZ TAB 5MG	78	14	$298,915.78	5.57	$3,832.25
XELJANZ XR TAB 11MG	42	10	$161,178.92	4.2	$3,837.59
SUBTOTAL	**120**	**23**	**$460,094.70**	**5.22**	**$3,834.12**
CERTOLIZUMAB PRODUCTS					
CIMZIA PREFL KIT 200MG/ML	90	14	$330,383.38	6.43	$3,670.93
CIMZIA KIT STARTER 200MG/ML	1	1	$10,660.55	1	$10,660.55
SUBTOTAL	**91**	**14**	**$341,043.93**	**6.5**	**$3,747.74**
GOLIMUMAB PRODUCTS					
SIMPONI INJ 50/0.5ML	46	10	$191,973.42	4.6	$4,173.34
SIMPONI INJ 50/0.5ML	8	1	$32,852.64	8	$4,106.58
SUBTOTAL	**54**	**10**	**$224,826.06**	**5.4**	**$4,163.45**
USTEKINUMAB PRODUCTS					
STELARA INJ 90MG/ML	49	16	$938,078.04	3.06	$19,144.45
STELARA INJ 45MG/0.5ML	33	15	$317,561.06	2.2	$9,623.06
STELARA INJ 45MG/0.5ML	2	1	$20,605.40	2	$10,302.70
SUBTOTAL	**84**	**30**	**$1,276,244.50**	**2.8**	**$15,193.39**
IXEKIZUMAB PRODUCTS					
TALTZ INJ 80MG/ML	34	7	$233,998.15	4.86	$6,882.30
SUBTOTAL	**34**	**7**	**$233,998.15**	**4.86**	**$6,882.30**
ANAKINRA PRODUCTS					
KINERET INJ 100MG/0.67ML	17	2	$64,323.91	8.5	$3,783.76
SUBTOTAL	**17**	**2**	**$64,323.91**	**8.5**	**$3,783.76**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS*	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
GUSELKUMAB PRODUCTS					
TREMFYA INJ 100MG/ML	11	4	$131,659.29	2.75	$11,969.03
SUBTOTAL	**11**	**4**	**$131,659.29**	**2.75**	**$11,969.03**
VEDOLIZUMAB PRODUCTS					
ENTYVIO INJ 300MG	5	2	$28,747.75	2.5	$5,749.55
SUBTOTAL	**5**	**2**	**$28,747.75**	**2.5**	**$5,749.55**
SARILUMAB PRODUCTS					
KEVZARA INJ 200MG/1.14ML	5	2	$10,692.75	2.5	$2,138.55
SUBTOTAL	**5**	**2**	**$10,692.75**	**2.5**	**$2,138.55**
RITUXIMAB PRODUCTS					
RITUXAN INJ 500MG	1	1	$8,780.88	1	$8,780.88
SUBTOTAL	**1**	**1**	**$8,780.88**	**1**	**$8,780.88**
TIER-3 SUBTOTAL	**1,508**	**239***	**$9,469,402.43**	**6.31**	**$6,279.44**
TOTAL	**5,535**	**816***	**$30,121,216.08**	**6.78**	**$5,441.95**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Table includes targeted immunomodulator agents in Tier-2 and Tier-3 and does not include Tier-1 DMARDs as they are indicated for multiple diagnoses.

Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	TOTAL UNITS	COST/ CLAIM
RITUXAN INJ J9310	285	102	$2,028,920.29	2,402	$7,119.02
REMICADE INJ J1745	177	40	$586,339.07	8,357	$3,312.65
ACTEMRA INJ J3262	105	15	$263,855.01	59,466	$2,512.90
SIMPONI ARIA INJ J1602	62	21	$284,460.07	12,188	$4,588.07
ORENCIA INJ J0129	40	10	$155,959.12	3,272	$3,898.98
ENTYVIO INJ J3380	27	9	$145,783.92	7,854	$5,399.40
CIMZIA INJ J0717	18	2	$35,738.00	4,600	$1,985.44
STELARA INJ J3357	2	2	$20,181.80	350	$20,181.80
TOTAL	**715⁺**	**198***	**$3,521,237.28**	**98,489**	**$4,924.81**

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

[1] Amgen. Amgen Launches The ENBREL Mini™ Single-Dose Prefilled Cartridge With AutoTouch™ Reusable Autoinjector That Is Ergonomically Designed For Patients. *PR Newswire*. Available online at: https://www.amgen.com/media/news-releases/2017/11/amgen-launches-the-enbrel-mini-single-dose-prefilled-cartridge-with-autotouch-reusable-autoinjector-that-is-ergonomically-designed-for-patients/. Issued 11/17/2017. Last accessed 09/19/2018.

[2] Pfizer, Inc. FDA approves new Pfizer biosimilar. Available online at: https://www.pfizer.com/news/press-release/press-release-detail/fda_approves_new_pfizer_biosimilar. Issued 12/13/2017. Last accessed 09/19/2018.

[3] Sun Pharmaceutical Industries, Ltd. Sun Pharma Announces U.S. FDA Approval of Ilumya™ (tildrakizumab-asmn) for the Treatment of Moderate-to-Severe Plaque Psoriasis. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/sun-pharma-announces-us-fda-approval-of-ilumya-tildrakizumab-asmn-for-the-treatment-of-moderate-to-severe-plaque-psoriasis-300617454.html. Issued 03/21/2018. Last accessed 09/19/2018.

[4] Eli Lilly and Company. FDA Approves Olumiant® (baricitinib) 2-mg Tablets for the Treatment of Adults with Moderately-to-Severely Active Rheumatoid Arthritis. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/fda-approves-olumiant-baricitinib-2-mg-tablets-for-the-treatment-of-adults-with-moderately-to-severely-active-rheumatoid-arthritis-300658215.html. Issued 06/01/2018. Last accessed 09/19/2018.

[5] Janssen Biotech, Inc. Janssen Announces U.S. FDA Approval Of Stelara® (Ustekinumab) For The Treatment Of Adolescents With Moderate To Severe Plaque Psoriasis. Available online at: https://www.jnj.com/media-center/press-releases/janssen-announces-us-fda-approval-of-stelara-ustekinumab-for-the-treatment-of-adolescents-with-moderate-to-severe-plaque-psoriasis. Issued 10/13/2017. Last accessed 09/19/2018.

[6] Stelara® Prescribing Information. Janssen Immunology. Available online at: http://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/STELARA-pi.pdf. Last revised 06/2018. Last accessed 09/19/2018.

[7] Janssen Biotech, Inc. Simponi Aria Approved for Psoriatic Arthritis, Ankylosing Spondylitis. *Managed Care Magazine*. Available online at: https://www.managedcaremag.com/news/simponi-aria-approved-psoriatic-arthritis-ankylosing-spondylitis. Issued 10/20/2017. Last accessed 09/19/2018.

[8] Eli Lilly and Company. Taltz Receives FDA Approval to Treat Active Psoriatic Arthritis. *Managed Care Magazine*. Available online at: https://www.managedcaremag.com/news/20171204/taltz-receives-fda-approval-treat-active-psoriatic-arthritis. Issued 12/04/2017. Last accessed 09/19/2018.

[9] Pfizer, Inc. Pfizer Announces FDA Approval of Xeljanz® (tofacitinib) and Xeljanz® XR for the Treatment of Active Psoriatic Arthritis. Available online at: https://www.pfizer.com/news/press-release/press-release-detail/pfizer_announces_fda_approval_of_xeljanz_tofacitinib_and_xeljanz_xr_for_the_treatment_of_active_psoriatic_arthritis. Issued 12/14/2017. Last accessed 09/19/2018.

[10] U.S. Food and Drug Administration (FDA). FDA approves new treatment for moderately to severely active ulcerative colitis. Available online at: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm609225.htm. Issued 05/30/2018. Last accessed 09/19/2018.

[11] UCB, Inc. UCB Announces the Approval of Cimzia® (certolizumab pegol) for Moderate-to-Severe Plaque Psoriasis, Representing an Important New Option for Patients in the U.S. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/ucb-announces-the-approval-of-cimzia-certolizumab-pegol-for-moderate-to-severe-plaque-psoriasis-representing-an-important-new-option-for-patients-in-the-us-300655645.html. Issued 05/29/2018. Last accessed 09/19/2018.

[12] Rituxan® Prescribing Information. Genentech, Inc. Available online at: https://www.gene.com/download/pdf/rituxan_prescribing.pdf. Last revised 06/2018. Last accessed 09/19/2018.

[13] Ernst D. Rituxan Approved for Moderate to Severe Pemphigus Vulgaris. *Monthly Prescribing Reference* (*MPR)*. Available online at: https://www.empr.com/news/pemphigus-vulgaris-rituxan-rituximab-approved-autoimmune-blistering-disease/article/772092/. Issued 06/08/2018. Last accessed 09/19/2018.

[14] FDA. Potential Signals of Serious Risks/New Safety Information Identified from the FDA Adverse Event Reporting System (FAERS): July - September 2017. Available online at: https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/ucm592379.htm. Last revised 05/17/2018. Last accessd 09/19/2018.

[15] Brennan Z. Pfizer Not Planning US Launch of its Second Remicade Biosimilar Approved by FDA. *Regulatory Focus*. Available online at: h https://www.raps.org/regulatory-focus%E2%84%A2/news-articles/2017/12/pfizer-not-planning-us-launch-of-its-second-remicade-biosimilar-approved-by-fda . Issued 12/14/2017. Last accessed 09/19/2018.

[16] Hilton L. Pediatric Psoriasis Guidelines. *Medpage Today*. Available online at: https://www.medpagetoday.com/dermatology/psoriasis/71064. Issued 02/10/2018. Last accessed 09/21/2018.

[17] Han DH. Cimzia Label Update Provides New Information for Women of Childbearing Age. *MPR*. Available online at: https://www.empr.com/news/cimzia-certolizumab-pegol-breast-milk-placenta-transfer-infant/article/752897/. Issued 03/22/2018. Last accessed 09/21/2018.

[18] American College of Physicians. ACG updates guideline on diagnosis, management of Crohn's disease. *ACP Gastroenterology Monthly*. Available online at: https://gastroenterology.acponline.org/archives/2018/04/27/1.htm. Issued 04/27/2018. Last accessed 09/21/2018.

[19] AbbVie, Inc. AbbVie Submits Biologics License Application to U.S. FDA for Investigational Treatment Risankizumab for Moderate to Severe Plaque Psoriasis. *PR Newswire*. Available online at: https://news.abbvie.com/news/abbvie-submits-biologics-license-application-to-us-fda-for-investigational-treatment-risankizumab-for-moderate-to-severe-plaque-psoriasis.htm. Issued 04/25/2018. Last accessed 09/21/2018.

[20] Celltrion Healthcare. Truxima™. Available online at: http://www.celltrionhealthcare.com/en/products/truxima.do. Last accessed 09/26/2018.

[21] GlobalData Healthcare. Biosimilar frontrunner Celltrion to lose first-to-market advantage for Truxima in the US. *Pharmaceutical Technology*. Available online at: https://www.pharmaceutical-technology.com/comment/biosimilar-frontrunner-celltrion-lose-first-market-advantage-truxima-us/. Issued 04/13/2018. Last accessed 09/26/2018.
[22] Novartis. Sandoz receives approval in Europe for Rixathon® (biosimilar rituximab) to treat blood cancers and immunological diseases. Available online at: https://www.novartis.com/news/media-releases/sandoz-receives-approval-europe-rixathonr-biosimilar-rituximab-treat-blood. Issued 06/19/2017. Last accessed 09/26/2018.
[23] Davio K. FDA Rejects Sandoz's Proposed Rituximab Biosimilar. *The Center for Biosimilars*. Available online at: https://www.centerforbiosimilars.com/news/fda-rejects-sandozs-proposed-rituximab-biosimilar. Issued 05/02/2018. Last accessed 09/26/2018.
[24] AbbVie, Inc. Upadacitinib Meets All Primary and Ranked Secondary Endpoints Including Superiority Versus Adalimumab in Phase 3 Study in Rheumatoid Arthritis. *PR Newswire*. Available online at: https://news.abbvie.com/news/upadacitinib-meets-all-primary-and-ranked-secondary-endpoints-including-superiority-versus-adalimumab-in-phase-3-study-in-rheumatoid-arthritis.htm. Issued 04/09/2018. Last accessed 09/25/2018.
[25] Grygotis L. Baricitinib Shows Positive Results for Systemic Lupus Erythematosus in Phase 2 Study. *Rheumatology Advisor*. Available online at: https://www.rheumatologyadvisor.com/eular-2018-coverage/positive-results-with-baricitinib-in-patients-with-sle/article/773119/. Issued 06/13/2018. Last accessed 09/25/2018.
[26] Institute for Clinical and Economic Review (ICER). Targeted Immunomodulators for the Treatment of Moderate-to-Severe Plaque Psoriasis: Effectiveness and Value. New England Comparative Effectiveness Public Advisory Council. Available online at: https://icer-review.org/wp-content/uploads/2017/11/ICER_Psoriasis_Update_Final_Evidence_Report_080118.pdf. Issued 08/03/2018. Last accessed 09/26/2018.
[27] Ilumya™ Prescribing Information. Sun Pharmaceutical Industries, Ltd. Available online at: https://www.sunpharma.com/sites/default/files/pressreleases/ILUMYA%20US%20Prescribing%20Information.pdf. Last revised 03/2018. Last accessed 09/25/2018.
[28] Olumiant® Prescribing Information. Eli Lilly and Company. Available online at: http://uspl.lilly.com/olumiant/olumiant.html#pi. Last revised 05/2018. Last accessed 09/25/2018.
[29] Felson DT, Pincus T. American College of Rheumatology 20/50/70 criteria (ACR20/50/70). *ProQolid*. Available online at: https://eprovide.mapi-trust.org/instruments/american-college-of-rheumatology-20-50-70-criteria. Last revised 01/2018. Last accessed 09/25/2018.
[30] National Rheumatoid Arthritis Society. The DAS28 score. Available online at: https://www.nras.org.uk/the-das28-score. Issued 11/07/2007. Last accessed 09/25/2018.
[31] Hertl M, Sitaru C. Pathogenesis, clinical manifestations, and diagnosis of pemphigus. *UpToDate*. Available online at: https://www.uptodate.com/contents/pathogenesis-clinical-manifestations-and-diagnosis-of-pemphigus?search=pemphigus%20vulgaris&source=search_result&selectedTitle=1~42&usage_type=default&display_rank=1 . Last revised 03/13/2018. Last accessed 09/26/2018.
[32] Hertl M, Geller S. Initial management of pemphigus vulgaris and pemphigus foliaceus. *UpToDate*. Available online at: https://www.uptodate.com/contents/initial-management-of-pemphigus-vulgaris-and-pemphigus-foliaceus?search=pemphigus%20vulgaris&source=search_result&selectedTitle=2~42&usage_type=default&display_rank=2#H73755042. Last revised 08/17/2018. Last accessed 09/26/2018.

Appendix M

Fiscal Year 2018 Annual Review of Gonadotropin-Releasing Hormone (GnRH) Medications and 30-Day Notice to Prior Authorize Triptodur® (Triptorelin) and Orilissa™ (Elagolix)

Oklahoma Health Care Authority
October 2018

Current Prior Authorization Criteria

Gonadotropin-Releasing Hormone (GnRH) Medications		
Tier-1	**Tier-2**	**Tier-3**
leuprolide (Lupron Depot®)	histrelin (Supprelin® LA)	nafarelin (Synarel®)
leuprolide (Lupron Depot-Ped®)		

Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Supprelin® LA (Histrelin) and Synarel® (Nafarelin) Approval Criteria:

1. An FDA approved diagnosis of central precocious puberty confirmed by submitting the following:
    a. Documentation of onset of symptoms <8 years of age in females and 9 years of age in males; and
    b. Documentation that bone age is advanced 1 year beyond the chronological age; and
    c. Lab assessment:
        i. Documentation of abnormal basal gonadotropin levels; or
        ii. Documentation of pubertal response to a gonadotropin-releasing hormone analog stimulation test; and
2. Approvals may be granted with documentation of failed trials of lower tiered products or an FDA approved indication not covered by a lower tiered product.

Lupaneta Pack™ (Leuprolide Acetate for Depot Suspension and Norethindrone Acetate Tablets) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use the individual components.

Utilization of GnRH Medications: Fiscal Year 2018

Comparison of Fiscal Years: GnRH Medications (Pharmacy Claims)

Fiscal Year	Total Members*	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2017	155	421	$1,722,117.29	$4,090.54	$68.71	425	25,062
2018	140	369	$1,554,500.63	$4,212.74	$66.17	379	23,493
% Change	**-9.70%**	**-12.40%**	**-9.70%**	**3.00%**	**-3.70%**	**-10.80%**	**-6.30%**
Change	**-15**	**-52**	**-$167,616.66**	**$122.20**	**-$2.54**	**-46**	**-1,569**

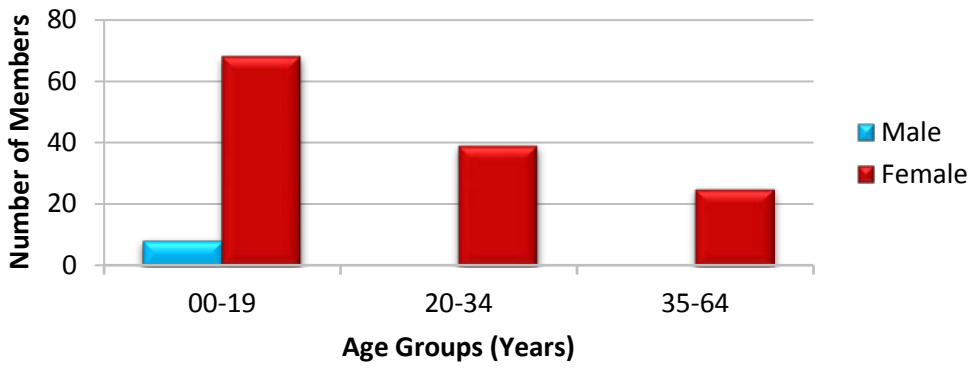
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

Fiscal Year 2018 Utilization of GnRH Medications: Medical Claims

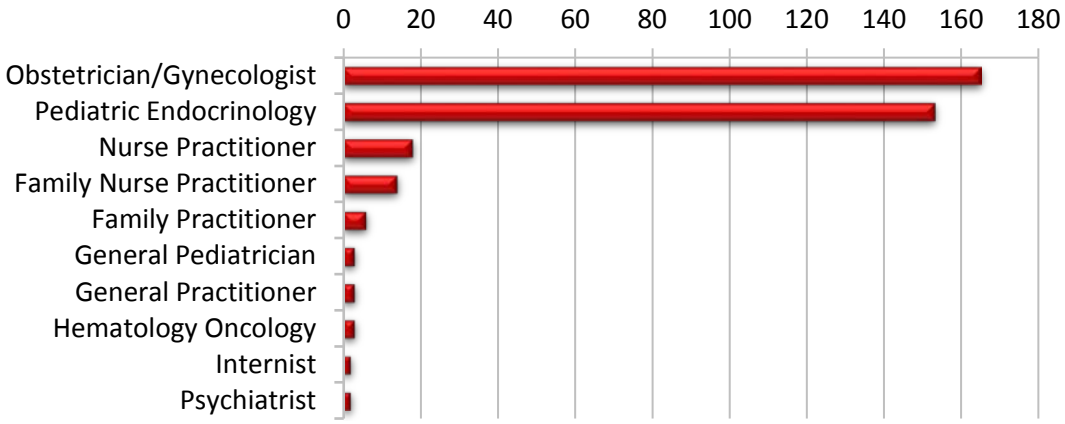
Total Members*	Total Claims+	Total Cost	Cost/Claim	Total Units
69	139	$111,393.33	$801.39	396

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

Demographics of Members Utilizing GnRH Medications: Pharmacy Claims

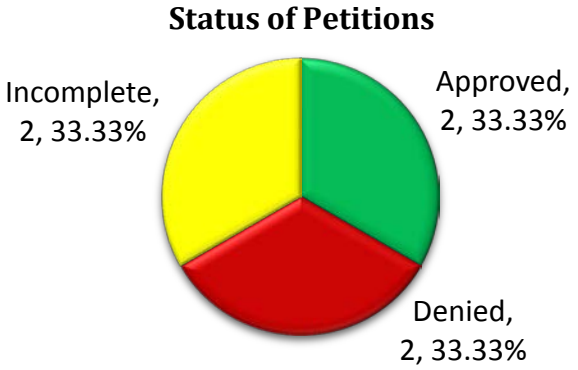


Top Prescriber Specialties of GnRH Medications By Number of Claims: Pharmacy Claims



Prior Authorization of GnRH Medications

There were 6 prior authorization requests submitted for GnRH medications during fiscal year 2018. The following chart shows the status of the submitted petitions for fiscal year 2018.



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

Anticipated Patent Expiration(s):

- Supprelin® LA (histrelin): June 2026

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

- **June 2017:** The FDA approved Triptodur® (triptorelin) for the treatment of pediatric patients 2 years of age and older with central precocious puberty (CPP). This is the first GnRH agonist approved for dosing once every 6 months for CPP.
- **July 2018:** AbbVie announced the FDA approved Orilissa™ (elagolix) for the management of moderate-to-severe pain associated with endometriosis. Elagolix is the first oral GnRH antagonist specifically developed for women with moderate-to-severe endometriosis pain.

Pipeline:

- **August 2018:** Allergan announced that United States health regulators declined to approve Esmya® (ulipristal acetate), a treatment for abnormal uterine bleeding in women with uterine fibroids, citing safety issues outside the U.S. and requesting more information. Allergan plans to meet with the FDA to determine the potential next steps for ulipristal. Ulipristal is sold in Europe. Earlier this year, regulators in Europe recommended restrictions on the use of the medication for some patients to help minimize the risk of rare but serious liver injury associated with the medication.

News:

- **August 2018:** The Institute for Clinical and Economic Review (ICER) released its Final Evidence Report and Report-at-a-Glance on elagolix for endometriosis. The report was reviewed at a July 2018 public meeting of The New England Comparative Effectiveness Public Advisory Council (CEPAC), one of ICER's three independent evidence appraisal committees. The meeting occurred prior to the FDA approval of elagolix. The Council voted that the evidence was not adequate to determine whether elagolix offers a net health benefit compared to no treatment, or compared to treatment with either a GnRH

agonist (i.e., leuprorelin acetate) or a hormonal contraceptive (i.e., depot medroxyprogesterone), due to limited and mixed evidence on potential risks and clinical effectiveness. ICER issued an Access and Affordability Alert for elagolix as part of its final report. ICER's Access and Affordability Alert is intended to provide a signal to insurers, patient groups, manufacturers, and other stakeholders when the amount of added health care costs associated with new treatments may be difficult for the health care system to absorb over the short-term without displacing other needed services or contributing to rapid growth in health care insurance costs that threaten sustainable access to high-value care of all patients. According to ICER's report, it is reasonable for insurers to develop prior authorization (PA) criteria for elagolix to ensure prudent use, based on elagolix's short-term side effects, and lack of long-term data on safety and efficacy compared to other well-established treatments.

Triptodur® (Triptorelin) Product Summary[6,7,8]

Indication(s): Triptodur® (triptorelin) is a GnRH agonist indicated for the treatment of pediatric patients 2 years and older with CPP.

Dosing:

- Triptodur® (triptorelin) is supplied as single-use kits containing one single-dose vial of triptorelin 22.5mg, one prefilled glass syringe of sterile water for injection, and two needles.
- Triptorelin must be administered under the supervision of a physician.
- It is recommended to administer triptorelin as a single intramuscular (IM) injection of 22.5mg once every 24 weeks.
- It is recommended to monitor response with luteinizing hormone (LH) levels after a GnRH or GnRH agonist stimulation test, basal LH, or serum concentration of sex steroid levels beginning 1 to 2 months following initiation of therapy, during therapy as necessary to confirm maintenance of efficacy, and with each subsequent dose.
- Height should be measured every 3 to 6 months and bone age should be monitored periodically.

Mechanism of Action: Triptorelin is a GnRH agonist. GnRH agonists, such as triptorelin, continuously stimulate pituitary gonadotrophs, which leads to receptor downregulation, desensitization of gonadotroph cells, and suppression of gonadotropins, resulting in decreased sex steroid production.

Contraindication(s):

- Hypersensitivity reactions
- Pregnancy

Warnings and Precautions:

- Initial Rise of Gonadotropins and Sex Steroid Levels: During the early phase of initial therapy or after subsequent doses, gonadotropins and sex steroids may rise above baseline because of a transient stimulatory effect of the drug. A transient increase in

clinical signs and symptoms, such as vaginal bleeding, may be observed during the first weeks of therapy or after subsequent doses.

- Psychiatric Events: Psychiatric events have been reported in patients taking GnRH agonists, including triptorelin. Postmarketing reports with this class of drugs include symptoms of emotional lability, such as impatience, anger, aggression, and crying. Patients should be monitored for development or worsening of psychiatric symptoms during treatment with triptorelin.
- Convulsions: Postmarketing reports of convulsions have been observed in patients receiving GnRH agonists, including triptorelin. This includes patients with a history of seizures, epilepsy, cerebrovascular disorders, central nervous system anomalies or tumors, and patients on concomitant medications that have been associated with convulsions such as bupropion and selective serotonin reuptake inhibitors (SSRIs). Convulsions have also been reported in patients in the absence of any of these conditions.

Use in Specific Populations:

- Pregnancy: Triptorelin is contraindicated in women who are pregnant since expected hormonal changes that occur with triptorelin treatment increase the risk for pregnancy loss. Available data with triptorelin use in pregnant women are not sufficient to determine a drug-associated risk of adverse developmental outcomes. Based on the mechanism of action in humans and findings of increased pregnancy loss in animal studies, triptorelin may cause fetal harm when administered to pregnant women.
- Lactation: There are no data on the presence of triptorelin in human milk, or the effects of the drug on the breastfed infant, or on milk production.
- Pediatric Use: The safety and effectiveness of triptorelin have been established in pediatric patients 2 years of age and older based on a single-arm study of 44 children 2 to 9 years of age with CPP.
- Renal Impairment: Triptorelin has not been studied in children with renal impairment. Adult subjects with renal impairment had higher exposure than young healthy adult males.
- Hepatic Impairment: Triptorelin has not been studied in children with hepatic impairment. Adult subjects with hepatic impairment had higher exposure than young healthy adult males.

Adverse Reactions: In clinical trials for triptorelin, the most common adverse reactions (≥4.5%) were injection site reactions, menstrual (vaginal) bleeding, hot flushes, headache, cough, and infections (bronchitis, gastroenteritis, influenza, nasopharyngitis, otitis externa, pharyngitis, sinusitis, and upper respiratory tract infection).

Efficacy: Triptorelin was studied in a single-arm, open-label study, which included 44 children 2 to 9 years of age with CPP (39 females and 5 males). All subjects were naïve to previous GnRH agonist treatment and were administered 22.5mg of triptorelin at a dosing interval of 24 weeks. Subjects were evaluated over two dosing intervals for a total of 12 months. Triptorelin 22.5mg suppressed pituitary release of LH and follicle-stimulating hormone (FSH), and consequently, gonadal secretion of estradiol in girls and testosterone in boys. At all time points evaluated,

≥93% of children achieved LH suppression to pre-pubertal levels (i.e., serum LH ≤5 IU/L 30 minutes after GnRH agonist stimulation), ≥79% of girls achieved pre-pubertal levels of estradiol (i.e., <20pg/mL), and ≥80% of boys achieved pre-pubertal levels of testosterone (i.e., <30ng/dL). Triptorelin arrested or reversed progression of clinical signs of puberty with 95% of children showing no increase in the bone age/chronological age ratio, and 89% showing stabilization of sexual maturation at month 12.

Cost Comparison:

Product	Cost Per Unit	Cost Per Year
Triptodur® 22.5mg (triptorelin)	**$16,400.00**	**$32,800.00**
Lupron Depot-Ped® 15mg (leuprolide)	$2,945.42*	$35,345.04*
Supprelin® LA (histrelin)	$30,441.90	$30,441.90

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), Specialty Pharmaceutical Allowable Cost (SPAC), or State Maximum Allowable Cost (SMAC) if NADAC unavailable.
*Lupron Depot-Ped® was first FDA approved in 1993 and has a significant federal rebate.

Orilissa™ (Elagolix) Product Summary[9,10,11]

Indication(s): Orilissa™ (elagolix) is a GnRH receptor antagonist indicated for the management of moderate-to-severe pain associated with endometriosis.

Dosing:

- Orilissa™ (elagolix) is supplied as 150mg and 200mg oral tablets.
- The recommended dose for patients with normal liver function or mild hepatic impairment is 150mg once daily for up to 24 months or 200mg twice daily for up to 6 months.
- The recommended dose for patients with moderate hepatic impairment is 150mg once daily for up to 6 months.

Mechanism of Action: Elagolix is a GnRH receptor antagonist that inhibits endogenous GnRH signaling by binding competitively to GnRH receptors in the pituitary gland. Administration of elagolix results in dose-dependent suppression of LH and FSH, leading to decreased blood concentrations of the ovarian sex hormones, estradiol and progesterone.

Contraindication(s):

- Pregnancy
- Known osteoporosis
- Severe hepatic impairment
- Strong organic anion transporting polypeptide (OATP) 1B1 inhibitors

Warnings and Precautions:

- Bone Loss: Elagolix causes dose- and duration-dependent decreases in bone mineral density (BMD) that may not be completely reversible. BMD should be assessed in women with additional risk factors for bone loss. Elagolix should not be used in women with known osteoporosis. The duration of elagolix use should be limited to reduce the

extent of bone loss. Although the effect of supplementation with calcium and vitamin D was not stated, such supplementation may be beneficial for all patients.

- Reduced Ability to Recognize Pregnancy: Elagolix may alter menstrual bleeding, which may reduce the ability to recognize pregnancy. Pregnancy testing should be performed if suspected. If pregnancy is confirmed, elagolix should be discontinued.
- Suicidal Ideation and Mood Disorders: Suicidal ideation and behavior, including one completed suicide, occurred in subjects treated with elagolix in endometriosis clinical trials. Patients should be advised to seek medical attention for suicidal ideation, suicidal behavior, new onset or worsening depression, anxiety, or other mood changes.
- Hepatic Transaminase Elevations: Dose-dependent elevations in serum alanine aminotransferase (ALT) occurred during clinical trials with elagolix. Patients should be counseled on the signs and symptoms of liver injury.
- Potential for Reduced Efficacy with Estrogen-Containing Contraceptives: Non-hormonal contraception should be used during treatment and for one week after discontinuing elagolix. Based on the mechanism of action of elagolix, estrogen-containing contraceptives are expected to reduce the efficacy of elagolix. The effect on progestin-only contraceptives on the efficacy of elagolix is unknown.

Use in Specific Populations:

- Pregnancy: Elagolix exposure early in pregnancy may increase the risk of early pregnancy loss. Elagolix use is contraindicated in pregnant women. If pregnancy occurs during treatment with elagolix, the medication should be discontinued.
- Lactation: There is no information on the presence of elagolix or its metabolites in human milk, the effects on the breastfed child, or the effects on milk production.
- Females and Males of Reproductive Potential: Based on the mechanism of action, there is a risk of early pregnancy loss if elagolix is administered to a pregnant woman. Pregnancy should be excluded prior to initiating treatment with elagolix. Women should be advised to use effective non-hormonal contraception during treatment with elagolix and for one week after discontinuing treatment.
- Pediatric Use: The safety and effectiveness of elagolix in patients younger than 18 years of age have not been established.
- Renal Impairment: No dose adjustment of elagolix is required in women with any degree of renal impairment or end-stage renal disease (including women on dialysis).
- Hepatic Impairment: No dosage adjustment of elagolix is required for women with mild hepatic impairment (Child-Pugh A). Only the 150mg once daily regimen is recommended for women with moderate hepatic impairment (Child-Pugh B) and the duration of treatment should be limited to 6 months. Elagolix is contraindicated in women with severe hepatic impairment (Child-Pugh C).

Adverse Reactions: The most common adverse reactions (>5%) in clinical trials included hot flushes and night sweats, headache, nausea, insomnia, amenorrhea, anxiety, arthralgia, depression-related adverse reactions, and mood changes.

Efficacy: The efficacy of elagolix 150mg once daily and 200mg twice daily for the management of moderate-to-severe pain associated with endometriosis was demonstrated in two

multinational, double-blind, placebo-controlled trials in 1,686 premenopausal women. The median age of women in the trials was 32 years. Each placebo-controlled trial assessed the reduction in endometriosis-associated pain over 6 months of treatment. Moderate-to-severe pain associated with endometriosis was required for entry into the studies and was assessed during screening using the composite pelvic signs and symptoms score (CPSSS) and other baseline criteria. The CPSSS is based on a modified Biberoglu and Behrman scale with five elements: three responses reported by study subjects (dysmenorrhea, dyspareunia, and non-menstrual pelvic pain) and two findings based on investigator assessment during physical examination (rating of pelvic tenderness and induration). Each element is scored from 0 (absent) to 3 (severe) for a maximum total score of 15. A total score of at least 6, with a score of at least 2 for dysmenorrhea and at least 2 for non-menstrual pelvic pain was required to qualify for randomization. Subjects were also required to have non-menstrual pelvic pain for at least four days in the preceding calendar month, defined as 35 days. Other criteria to determine eligibility for randomization included subject responses in a daily electronic diary (Endometriosis Daily Pain Impact Scale) for both dysmenorrhea and non-menstrual pelvic pain in the 35 days prior to randomization.

- Dysmenorrhea and Non-Menstrual Pelvic Pain: The co-primary efficacy endpoints were the proportion of subjects whose dysmenorrhea responded to treatment at month 3 and the proportion of subjects whose non-menstrual pelvic pain responded to treatment at month 3. Dysmenorrhea and non-menstrual pelvic pain were evaluated daily using the Endometriosis Daily Pain Impact Scale that asked subjects to rate their pain severity and its impact on daily activities during the prior 24 hours as none, mild, moderate, or severe (correlating with a score of 0 to 3, respectively, where higher scores indicated greater severity). Scores at baseline and at each month were averaged over a 35-day interval. Women were defined as responders if they experienced a reduction in dysmenorrhea and non-menstrual pelvic pain with no increase in analgesic use (NSAIDs or opioids) for endometriosis-associated pain (see Table 1). The threshold for defining responders was based on a receiver operating characteristic (ROC) analysis using the patient global impression of change as an anchor. A higher proportion of women treated with elagolix 150mg once daily or 200mg twice daily were responders for dysmenorrhea and non-menstrual pelvic pain compared to placebo in a dose-dependent manner at month 3.

Table 1. Proportion of Responders* for Dysmenorrhea and Non-Menstrual Pelvic Pain at Month 3

	Study 1			Study 2		
	Elagolix		Placebo	Elagolix		Placebo
	150mg once daily (N=248)	200mg twice daily (N=244)	N=373	150mg once daily (N=221)	200mg twice daily (N=225)	N=353
Dysmenorrhea	46%	76%	20%	43%	72%	23%
Difference from placebo	27%^	56%^		21%^	50%^	
Non-menstrual pelvic pain	50%	55%	36%	50%	58%	37%
Difference from placebo	14%^	18%^		13%[+]	21%^	

*Dysmenorrhea responder threshold: at least 0.81 (study 1) or 0.85 (study 2) decrease from baseline in dysmenorrhea score; Non-menstrual pelvic pain responder threshold: at least 0.36 point (study 1) or 0.43 point (study 2) decrease from baseline in non-menstrual pelvic pain score

[+]P≤0.01 for test of difference from placebo

^P≤0.001 for test of difference from placebo

- Dyspareunia: Dyspareunia associated with endometriosis was evaluated as a secondary endpoint using the Endometriosis Daily Pain Impact Scale. The Scale asked subjects to rate their pain during sexual intercourse in the prior 24 hours as none, mild, moderate, severe (correlating with a score of 0 to 3, respectively, where higher scores indicated greater severity), or not applicable. In Study 1 and Study 2, women treated with elagolix 200mg twice daily showed statistically significantly greater reduction in dyspareunia from baseline to month 3 than women given placebo (Study 1: 0.2; Study 2: 0.3).
- Use of Rescue Pain Medication: In Study 1 and Study 2, 59% and 60% of patients used an opioid rescue analgesic for pain at baseline. The opioid rescue analgesics used at baseline were predominantly hydrocodone/acetaminophen (APAP) and codeine/APAP at strengths of 5/300-325mg and 30/300-500mg, respectively. In Study 1, of all patients on an opioid at baseline, 98% and 2% were on hydrocodone/APAP and codeine/APAP, respectively. In Study 2, of all patients on an opioid at baseline, 50% were on hydrocodone/APAP and 16% were on codeine/APAP.

Table 2. Opioid Rescue Analgesic Use in Study 1 and 2

	Study 1			Study 2		
	Elagolix 150mg QD	Elagolix 200mg BID	Placebo	Elagolix 150mg QD	Elagolix 200mg BID	Placebo
Tablets per month at baseline (mean±SD)	15 ±24	15 ±25	13 ±21	13 ±29	12 ±26	12 ±21
# and % of patients on any dose of opioid rescue at baseline who were off opioid at Month 3*	46/150 (31%)	59/151 (39%)	36/211 (17%)	44/124 (36%)	68/134 (51%)	54/220 (25%)
# and % of patients on any dose of opioid rescue at baseline who were off opioid at Month 6*	43/149 (29%)	66/150 (44%)	36/211 (17%)	50/124 (40%)	78/134 (58%)	70/222 (32%)
# and % of patients not on opioid rescue at baseline who were on any opioid at Month 3^	9/98 (9%)	6/93 (7%)	17/162 (11%)	10/97 (10%)	10/91 (11%)	29/133 (22%)
# and % of patients not on opioid rescue at baseline who were on any opioid at Month 6^	16/98 (16%)	6/93 (7%)	32/161 (20%)	13/97 (13%)	6/91 (7%)	32/133 (24%)

QD = daily; BID = twice daily; # = number; SD = standard deviation; % = percent
*Denominator is the number of subjects on opioid rescue at baseline.
^Denominator is the number of subjects not on opioid rescue at baseline.
Please note: The clinical relevance of these data has not been demonstrated.

Cost Comparison:

Product	Cost Per Unit	Cost Per Month	Cost Per 6 Months
Orilissa™ (elagolix) 150mg	**$30.17**	**$844.76**	**$5,068.56**
Orilissa™ (elagolix) 200mg	**$15.09**	**$845.04**	**$5,070.24**
Lupron Depot® (leuprolide) 3.75mg	$1,191.39*	$1,191.39*	$7,148.34*
Synarel® (nafarelin) 2mg/mL	$354.57	$2,836.56	$17,019.36

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.
*Lupron Depot® was first FDA approved in 1989 and has a significant federal rebate.

Recommendations

The College of Pharmacy recommends the prior authorization of Orilissa™ (elagolix) with the following criteria:

Orilissa™ (Elagolix) Approval Criteria:

1. An FDA approved diagnosis of moderate-to-severe pain associated with endometriosis; and
2. Member must be 18 years of age or older; and
3. Member must not have known osteoporosis; and
4. Female members must not be pregnant and must have a negative pregnancy test prior to initiation of therapy; and
5. Female members of reproductive potential must be willing to use effective non-hormonal contraception during treatment with Orilissa™ and for at least one week after discontinuing treatment; and
6. Member must not have severe hepatic impairment (Child-Pugh C); and
7. Member must not be taking strong organic anion transporting polypeptide (OATP) 1B1 inhibitors (e.g., cyclosporine, gemfibrozil); and
8. Orilissa™ must be prescribed by, or in consultation with, an obstetrician/gynecologist a or specialist with expertise in the treatment of endometriosis; and
9. A failed trial at least one month in duration with nonsteroidal anti-inflammatory drugs (NSAIDs) or a patient-specific, clinically significant reason why the member cannot use NSAIDs; and
10. A failed trial at least three months in duration of hormonal contraceptives or a patient-specific, clinically significant reason why the member cannot use hormonal contraceptives; and
11. A patient-specific, clinically significant reason why the member cannot use leuprolide depot formulations which are available without prior authorization; and
12. Dosing and lifetime approval duration will be limited based on the following:
    a. Coexisting condition of moderate hepatic impairment (Child-Pugh B):
        i. 150mg once daily for a maximum of 6 months; and
    b. Normal liver function or mild hepatic impairment (Child-Pugh A):
        i. 150mg once daily for a maximum of 24 months; or
        ii. 200mg twice daily for a maximum of 6 months.

Additionally, the College of Pharmacy recommends the placement of Triptodur® (triptorelin) into Tier-3 of the Gonadotropin-Releasing Hormone (GnRH) Medications Product Based Prior Authorization (PBPA) category as shown in red:

Supprelin® LA (Histrelin), Synarel® (Nafarelin), and Triptodur® (Triptorelin) Approval Criteria:

1. An FDA approved diagnosis of central precocious puberty confirmed by submitting the following:
   a. Documentation of onset of symptoms <8 years of age in females and 9 years of age in males; and
   b. Documentation that bone age is advanced 1 year beyond the chronological age; and
   c. Lab assessment:
      i. Documentation of abnormal basal gonadotropin levels; or
      ii. Documentation of pubertal response to a gonadotropin-releasing hormone analog stimulation test; and
2. Approvals may be granted with documentation of failed trials of lower tiered products or an FDA approved indication not covered by a lower tiered product.

Gonadotropin-Releasing Hormone (GnRH) Medications		
Tier-1	**Tier-2**	**Tier-3**
leuprolide (Lupron® Depot)	histrelin (Supprelin® LA)	nafarelin (Synarel®)
leuprolide (Lupron Depot-Ped®)		**triptorelin (Triptodur®)**

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 GnRH Medications: Fiscal Year 2018

Pharmacy Claims: Fiscal Year 2018

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS*	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
LUPR DEP-PED INJ 3M 30MG	88	31	$674,779.15	$91.58	$7,667.94	43.41%
LUPRON DEPOT INJ 11.25MG	75	49	$258,564.69	$40.19	$3,447.53	16.63%
LUPR DEP-PED INJ 11.25MG	57	21	$406,390.53	$88.71	$7,129.66	26.14%
LUPRON DEPOT INJ 3.75MG	100	33	$122,160.71	$38.07	$1,221.61	7.86%
LUPR DEP-PED INJ 7.5MG	28	3	$38,437.90	$60.44	$1,372.78	2.47%
LUPRON DEPOT INJ 22.5MG	9	5	$36,869.65	$46.55	$4,096.63	2.37%
LUPRON DEPOT INJ 7.5MG	7	2	$9,708.87	$46.68	$1,386.98	0.62%
LUPR DEP-PED INJ 11.25MG	2	2	$5,369.62	$29.83	$2,684.81	0.35%
LUPR DEP-PED INJ 15MG	2	1	$1,496.16	$26.72	$748.08	0.10%
LEUPROLIDE INJ 1MG/0.2ML	1	1	$723.35	$24.11	$723.35	0.05%
TOTAL	**369**	**140**	**$1,554,500.63**	**$66.17**	**$4,212.74**	**100%**

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

Medical Claims: Fiscal Year 2018

PRODUCT UTILIZED	TOTAL CLAIMS[+]	TOTAL MEMBERS*	TOTAL COST	COST/ CLAIM
J1950 LUPRON DEPOT-PED	39	9	$63,265.69	$1,622.20
J9217 ELIGARD/LUPRON DEPOT	78	39	$45,425.28	$582.38
J9218 LEUPROLIDE ACETATE	22	21	$2,702.36	$122.83
TOTAL	**139**	**69**	**$111,393.33**	**$801.39**

[+]Total number of unduplicated claims.
*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 08/2018. Last accessed 09/18/2018.
[2] Han DH. FDA Approved Triptodur for Central Precocious Puberty. *MPR*. Available online at: https://www.empr.com/news/triptodur-triptorelin-pediatric-precocious-puberty/article/672526/. Issued 06/30/2017. Last accessed 08/23/2018.
[3] AbbVie, Inc. AbbVie Receives U.S. FDA Approval of Orilissa™ (elagolix) for the Management of Moderate to Severe Pain Associated with Endometriosis. *PR Newswire*. Available online at: https://news.abbvie.com/news/abbvie-receives-us-fda-approval-orilissa-elagolix-for-management-moderate-to-severe-pain-associated-with-endometriosis.htm. Issued 07/24/2018. Last accessed 08/23/2018.
[4] Reuters Staff. UPDATE 1-FDA rejects Allergan's Esmya fibroid treatment. *Reuters*. Available online at: https://www.reuters.com/article/allergan-fda/update-1-fda-rejects-allergans-esmya-fibroid-treatment-idUSL3N1VC5I9. Issued 08/21/2018. Last accessed 08/23/2018.
[5] Institute for Clinical and Economic Review (ICER). A Look At Elagolix For Endometriosis. Available online at: https://icer-review.org/wp-content/uploads/2018/08/ICER_Endometriosis_RAAG_080318.pdf. Issued 07/2018. Last accessed 09/10/2018.
[6] Triptodur™ (triptorelin) Prescribing Information. Arbor Pharmaceuticals, LLC. Available online at: http://triptodur.com/hcp/Triptodur%20PI%20Rev.%2009.2017.pdf. Last revised 09/2017. Last accessed 08/23/2018.
[7] Triptorelin (Triptodur) for Central Precocious Puberty. *The Medical Letter*. 2018; 60:7-8.
[8] Lupron Depot-Ped® Prescribing Information. AbbVie, Inc. Available online at: https://www.rxabbvie.com/pdf/lupronpediatric.pdf. Last revised 05/2017. Last accessed 08/23/2018.
[9] Orilissa™ (elagolix) Prescribing Information. AbbVie, Inc. Available online at: https://www.rxabbvie.com/pdf/orilissa_pi.pdf. Last revised 07/2018. Last accessed 08/23/2018.
[10] Elagolix (Orilissa) – An Oral GnRH Antagonist for Endometriosis Pain. *The Medical Letter*. 2018; 60: 158-160.
[11] Lupron Depot® Prescribing Information. AbbVie, Inc. Available online at: https://www.rxabbvie.com/pdf/lupronuro_pi.pdf. Last revised 06/2016. Last accessed 08/23/2018.

Appendix N

Fiscal Year 2018 Annual Review of Bladder Control Medications and 30-Day Notice to Prior Authorize Nocdurna® (Desmopressin Acetate Sublingual Tablet)

Oklahoma Health Care Authority
October 2018

Current Prior Authorization Criteria

Bladder Control Medications			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
fesoterodine (Toviaz®)	tolterodine (Detrol®)	darifenacin (Enablex®)	desmopressin acetate nasal spray (Noctiva™)+
oxybutynin (Ditropan®)	trospium (Sanctura®)	mirabegron (Myrbetriq®)	oxybutynin patch (Oxytrol®)+
oxybutynin ER (Ditropan XL®)		oxybutynin gel (Gelnique®)	
		solifenacin (VESIcare®)	
		tolterodine ER (Detrol LA®)	
		trospium ER (Sanctura XR®)	

Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
ER = extended release; PA = prior authorization
+Unique criteria specific to Oxytrol® (oxybutynin patch) and Noctiva™ (desmopressin acetate nasal spray) applies.

Bladder Control Medications Tier-2 Approval Criteria:

1. A trial of all Tier-1 medications that yielded an inadequate clinical response or adverse effects; or
2. A unique indication which the Tier-1 medications lack.

Bladder Control Medications Tier-3 Approval Criteria:

1. A trial of all Tier-1 and Tier-2 medications that yielded inadequate clinical response or adverse effects; or
2. A unique indication which the Tier-1 and Tier-2 medications lack.

Oxytrol® (Oxybutynin Patch) Approval Criteria:

1. An FDA approved diagnosis of overactive bladder; and
2. A patient-specific, clinically significant reason why all lower tiered medications are not appropriate for the member; and
3. A quantity limit of 8 patches every 30 days will apply.

Noctiva™ (Desmopressin Acetate Nasal Spray) Approval Criteria:

1. An FDA approved diagnosis of nocturia due to nocturnal polyuria in adults 50 years of age and older; and
2. All other causes of nocturia have been ruled out or adequately treated [e.g., benign prostatic hyperplasia (BPH), overactive bladder (OAB), obstructive sleep apnea (OSA)]; and
3. The prescriber must confirm the member has a 6-month history of at least two nocturic episodes per night; and
4. Member has failed behavior modifications including reducing caffeine intake, alcohol intake, and nighttime fluid intake; and
5. Member must have failed a trial of DDAVP® (desmopressin acetate tablets) or have a patient-specific, clinically significant reason why the tablet formulation cannot be used; and
6. The prescriber must be willing to measure serum sodium levels within seven days of anticipated start of treatment and document levels are acceptable; and
7. The prescriber must agree to monitor serum sodium levels within one month of starting treatment or increasing the dose; and
8. The prescriber must confirm the member is not taking any of the following:
    a. Other medications via the nasal route; or
    b. Loop diuretics; and
9. The prescriber must confirm the member does not have renal impairment with an estimated glomerular filtration rate (eGFR) <50mL/min/1.73m^2; and
10. Initial approvals will be for the duration of 3 months, for continued authorization the prescriber must provide the following:
    a. Documentation that serum sodium levels are acceptable to the prescriber; and
    b. Documentation that the member is responding to treatment.

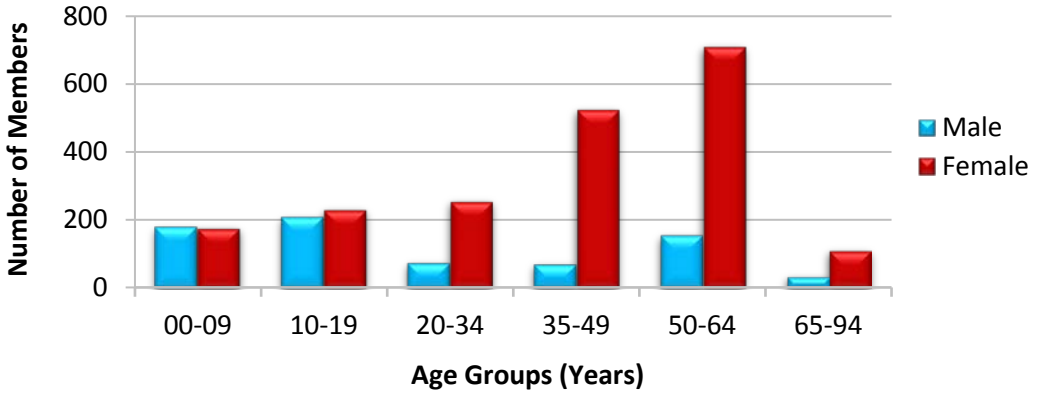
Utilization of Bladder Control Medications: Fiscal Year 2018

Comparison of Fiscal Years

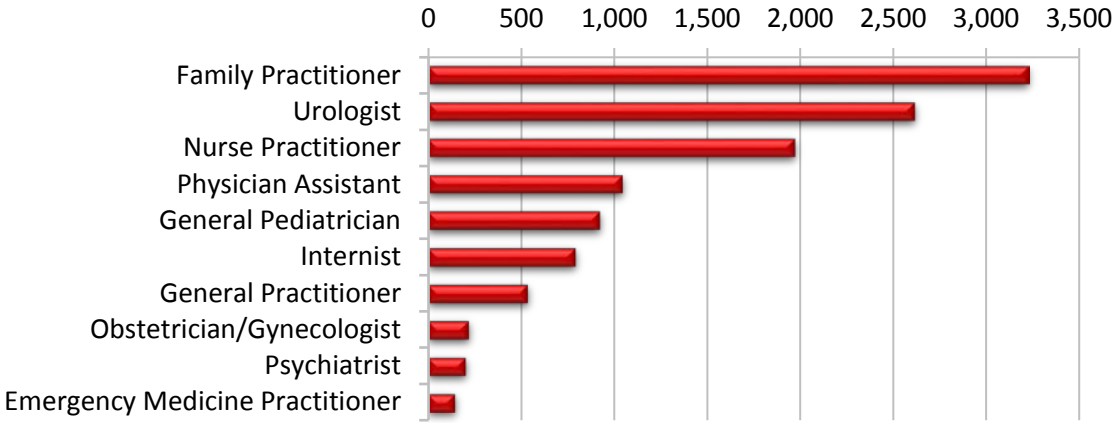
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2017	2,778	12,324	$657,297.96	$53.33	$1.65	878,592	397,267
2018	2,717	12,187	$700,767.90	$57.50	$1.75	844,968	400,153
% Change	**-2.20%**	**-1.10%**	**6.60%**	**7.80%**	**6.10%**	**-3.80%**	**0.70%**
Change	**-61**	**-137**	**$43,469.94**	**$4.17**	**$0.10**	**-33,624**	**2,886**

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

Demographics of Members Utilizing Bladder Control Medications



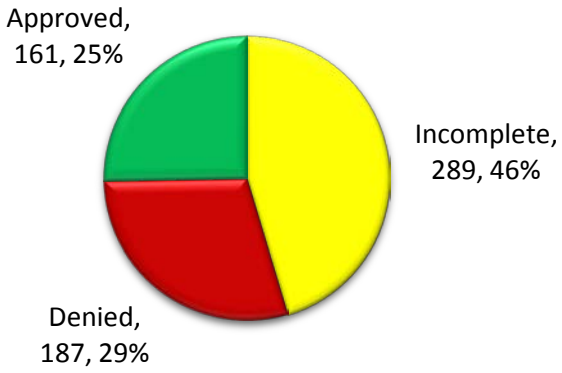
Top Prescriber Specialties of Bladder Control Medications by Number of Claims



Prior Authorization of Bladder Control Medications

There were 637 prior authorization requests submitted for bladder control medications during fiscal year 2018. Computer edits are in place to detect lower tiered medications in a member's recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions for fiscal year 2018.

Status of Petitions



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

Anticipated Patent Expiration(s):

- VESIcare® (solifenacin): May 2019
- Oxytrol® (oxybutynin patch): April 2020
- Toviaz® (fesoterodine): June 2027
- Myrbetriq® (mirabegron): October 2028
- Noctiva™ (desmopressin acetate nasal spray): June 2030
- Gelnique® (oxybutynin gel): March 2031

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

- **May 2018:** Astellas Pharma, Inc. announced the FDA approved a supplemental New Drug Application (sNDA) for the use of Myrbetriq® (mirabegron) in combination with VESIcare® (solifenacin) for the treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence (UUI), urgency, and urinary frequency. Both medications are products of Astellas Pharma and are FDA approved as monotherapy for OAB. The approval follows consideration of data from three large, global Phase 3 trials. These trials (SYNERGY I, SYNERGY II and BESIDE) evaluated combination therapy with mirabegron and solifenacin compared with each drug as monotherapy or placebo. The SYNERGY I trial enrolled 6,991 patients across 435 study locations in 42 countries. It evaluated the safety profile of combinations of mirabegron and solifenacin compared with each drug as monotherapy and placebo in patients who had experienced symptoms of OAB for at least 3 months. The 52-week SYNERGY II trial enrolled 2,084 patients across 251 sites in 32 countries. It evaluated the long-term safety profile of combination of mirabegron 50mg and solifenacin 5mg compared with each drug as monotherapy and placebo in patients who had experienced symptoms of OAB for at least 3 months. The BESIDE trial enrolled 2,174 patients across 281 sites in 31 countries. This trial evaluated the efficacy, safety, and tolerability of mirabegron 50mg as an add-on therapy with solifenacin 5mg versus solifenacin 5mg and 10mg alone in OAB patients who had an inadequate response to a 4-week treatment with solifenacin 5mg monotherapy. The primary end point was a change from baseline to end of treatment (EOT) in the mean number of incontinence episodes per 24 hours. At EOT, 12 weeks, the combination was found to be superior to solifenacin 5mg alone, with significant improvements in daily incontinence ($P=0.001$). Significant improvements were also noted in daily micturitions ($P<0.001$), meeting a key secondary endpoint.
- **June 2018:** The FDA approved Ferring Pharmaceuticals' New Drug Application (NDA) for Nocdurna® (desmopressin sublingual tablet), a nocturia treatment, rejecting petitions from Serenity Pharmaceuticals and Avadel requesting that it deny the application. Avadel petitioned the agency to deny the NDA unless the company conducted clinical trials that include Phase 3 data and at least two clinical studies for both genders for gender-specific dosage regimens. Serenity petitioned the FDA to deny the NDA because Ferring had not demonstrated the drug's safety or clinical benefit for use in patients with nocturia, and the company's study design was insufficient to accurately assess the safety risks.

News:

- **September 2017:** Avadel Pharmaceuticals entered into a license agreement with Serenity Pharmaceuticals, LLC. The agreement granted Avadel the sole right to commercialize and further develop Noctiva™ (desmopressin acetate nasal spray) in the United States and Canada. Noctiva™ is a proprietary, low-dose formulation of desmopressin acetate administered through a patent-protected intranasal delivery system. It was the first product approved by the FDA for the treatment of nocturia due to nocturnal polyuria. The deal included a $50 million upfront payment. Based on market growth potential, the current patient pool for treating nocturia is estimated to be worth over $2 billion.

Pipeline:

- **Solabegron:** Velicept Therapeutics announced in March 2018 the initiation of Phase 2B clinical studies testing solabegron, a selective beta-3 agonist, in patients with OAB. The studies will primarily evaluate the mean change in number of micturitions per day, as logged regularly by patients. One of the Phase 2B trials will be a multicenter, randomized, double-blind, vehicle-controlled trial that will enroll 375 women 18 to 80 years of age with symptoms of OAB. Patients will receive 125mg or 175mg solabegron twice daily, or placebo, over 12 weeks. Velicept's plan is to present topline data at the end of 2018 or beginning of 2019, and select doses for a Phase 3 trial.
- **Vibegron:** Urovant Sciences, a global biopharmaceutical company, announced in March 2018, that it had initiated an international Phase 3 trial, EMPOWUR, to evaluate the safety and efficacy of vibegron, an investigational oral beta-3 adrenergic agonist, in adults with symptoms of OAB. The EMPOWUR study is a randomized, double-blind, placebo- and active comparator-controlled international Phase 3 clinical trial in men and women with symptoms of OAB. Patients will be randomized to one of three groups for a 12-week treatment period: vibegron 75mg orally once daily, placebo orally once daily, or tolterodine extended-release (ER) 4mg orally once daily. The co-primary efficacy endpoints of the study are change from baseline in the average number of micturitions per 24 hours and change from baseline in the average number of UUI episodes per 24 hours in patients with an average of ≥1 UUI episode(s) per day prior to treatment. Vibegron is also being developed the treatment of OAB in men with benign prostatic hyperplasia (BPH) and the treatment of pain associated with irritable bowel syndrome (IBS).

Nocdurna® (Desmopressin Acetate Sublingual Tablet) Product Summary[10,11,12]

FDA Approval: June 2018

Indication(s): Nocdurna® (desmopressin acetate sublingual tablet) is a vasopressin analog indicated for the treatment of nocturia due to nocturnal polyuria in adults who awaken at least two times per night to void.

Dosing:

- Nocdurna® is supplied as sublingual (SL) tablets in two strengths, 27.7mcg and 55.3mcg, in a carton containing 30 SL tablets (3 blister packs with 10 tablets each).
- The recommended dosing is 27.7mcg once daily for women and 55.3mcg once daily for men.
- The dose should be taken one hour before bedtime and administered without water.
- The tablet should be kept under the tongue until it has fully dissolved.
- Patients should be instructed to empty their bladder immediately before bedtime, and to limit fluid intake to a minimum from 1 hour before until 8 hours after administration.

Mechanism of Action: The antidiuretic effects of desmopressin are mediated by stimulation of vasopressin 2 (V2) receptors, thereby increasing water re-absorption in the kidneys and reducing urine production.

Boxed Warning: Hyponatremia

- Nocdurna® can cause hyponatremia, which may be life-threatening if severe.
- Nocdurna® is contraindicated in patients at increased risk of severe hyponatremia, such as patients with excessive fluid intake, illnesses that can cause fluid or electrolyte imbalances, and in those using loop diuretics or systemic or inhaled glucocorticoids.
- Prescribers should ensure serum sodium concentrations are normal before patients start or resume Nocdurna®. Serum sodium should be measured within one week and approximately one month after initiating therapy and periodically during treatment. Serum sodium should be monitored more frequently in patients 65 years of age and older and in patients at increased risk of hyponatremia.
- If hyponatremia occurs, Nocdurna® may need to be temporarily or permanently discontinued.

Warnings and Precautions:

- Hyponatremia: Nocdurna® can cause hyponatremia (see boxed warning). Fluid intake should be limited to a minimum from 1 hour before administration until 8 hours after administration. Women are more sensitive to the effects of Nocdurna® compared to men. The recommended dose for women is lower than for men because women had a higher risk of hyponatremia with the 55.3mcg dose in clinical trials.
- Fluid Retention: Nocdurna® can cause fluid retention, which can worsen underlying conditions that are susceptible to volume status. Nocdurna® is contraindicated in patients with heart failure or uncontrolled hypertension (HTN). Nocdurna® is not recommended in patients at risk for increased intracranial pressure or those with a history of urinary retention.

Contraindication(s):

- Hyponatremia or a history of hyponatremia
- Polydipsia
- Concomitant use with loop diuretics
- Concomitant use with systemic or inhaled glucocorticoids

- Renal impairment with an estimated glomerular filtration rate (eGFR) <50mL/min/1.73m^2
- Known or suspected syndrome of inappropriate antidiuretic hormone (SIADH) secretion
- During illnesses that can cause fluid or electrolyte imbalance, such as gastroenteritis, salt-wasting nephropathies, or systemic infection
- Heart failure
- Uncontrolled HTN

Adverse Reactions: The most common adverse reactions reported by more than 2% of patients with nocturia due to nocturnal polyuria who were treated with Nocdurna® included dry mouth, hyponatremia or blood sodium decrease, headache, or dizziness. These reactions occurred at a higher incidence with Nocdurna® dosed at 27.7mcg or 55.3mcg than with placebo.

Use in Specific Populations:

- Pregnancy: Nocdurna® is not recommended for the treatment of nocturia in pregnant women. Nocturia is usually related to normal, physiologic changes during pregnancy that do not require treatment with Nocdurna®. There are no data with Nocdurna® use in pregnant women to inform any drug-associated risks.
- Lactation: Desmopressin (the active ingredient in Nocdurna®) is present in small amounts in human milk. There is no information on the effects of Nocdurna® on the breastfed infant or on milk production.
- Pediatric Use: The safety and effectiveness of Nocdurna® have not been established in pediatric patients.
- Geriatric Use: Clinical studies of desmopressin (the active ingredient in Nocdurna®) have shown an increased risk of hyponatremia in patients 65 years of age or older compared to those younger than 65 years of age.
- Renal Impairment: No dose adjustment of Nocdurna® is required for patients with an eGFR ≥50mL/min/1.73m^2. Nocdurna® is contraindicated in patients with an eGFR <50mL/min/1.73m^2.

Efficacy: The efficacy of Nocdurna® in the treatment of adults with nocturia due to nocturnal polyuria was established in two 3-month randomized, double-blind, placebo-controlled, multicenter trials in adults 18 years of age and older. Nocturnal polyuria was defined as nighttime urine production exceeding one-third of the 24-hour urine production confirmed with a 24-hour urine frequency/volume chart. Study 1 enrolled only women and Study 2 enrolled only men. At baseline, patients were required to document at least two nocturnal voids per night in a consecutive 3-day diary collected during screening. Randomization for Studies 1 and 2 was stratified by age group (<65 vs. ≥65 years). Subjects with severe daytime voiding dysfunction and other possible causes of nocturia (e.g., uncontrolled diabetes mellitus, obstructive sleep apnea) were excluded. The co-primary efficacy endpoints in each trial were the change in number of nocturia episodes per night from baseline during the 3-month treatment period, and 33% responder status during 3 months of treatment. A 33% responder was defined as a subject with a decrease of at least 33% in the mean number of nocturnal voids compared to baseline. The co-primary endpoints were assessed by longitudinal analysis.

- Study 1: A total of 237 women with nocturia due to nocturnal polyuria were randomized to receive either Nocdurna® 27.7mcg (N=121) or placebo (N=116) every night, approximately 1 hour prior to bedtime, for 3 months. A gender difference in sensitivity to desmopressin was found with a relative male-to-female dose ratio of 2.7, and 25mcg of desmopressin (27.7mcg desmopressin acetate) was effective with no associated reports of serum sodium ≤125mmol/L in females. This study in women was designed to confirm safety and efficacy of 25mcg desmopressin, and establish dose recommendations for nocturia. For the Nocdurna® treated group, there was a statistically significant change in baseline in mean number of nocturnal voids during 3 months of treatment (-0.22 voids, P=0.028). The 33% responder rate also reached statistical significance during 3 months of treatment (odds ratio 1.85, P=0.006).
- Study 2: A total of 230 men with nocturia due to nocturnal polyuria were randomized to receive Nocdurna® 55.3mcg (N=102) or placebo (N=128) every night, approximately 1 hour prior to bedtime, for 3 months. There was a statistically significant change in baseline in mean number of nocturnal voids during 3 months of treatment (-0.37 voids, P<0.0001), for the Nocdurna® treated group. During 3 months of treatment, the 33% responder rate also reached statistical significance (odds ratio 1.98, P=0.0009).

Cost Comparison:

Medication	Cost Per Unit	Cost Per 30 Days
Nocdurna® (desmopressin 27.7mcg & 55.3mcg SL tablet)	**Unknown**	**Unknown**
Noctiva™ (desmopressin 0.83mcg & 1.66mcg nasal spray)	$111.84	$424.99
desmopressin 0.1mg tablet	$0.77	$23.10*

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.
Unit= tablet or gram; SL = sublingual
*Cost per 30 days based on off-label dosing for nocturia of 100mcg at bedtime.

Recommendations

The College of Pharmacy recommends placement of Nocdurna® (desmopressin acetate sublingual tablets) into the Special Prior Authorization (PA) Tier of the Bladder Control Medications Product Based Prior Authorization (PBPA) category with criteria similar to Noctiva™ (desmopressin acetate nasal spray):

Nocdurna® (Desmopressin Acetate Sublingual Tablets) Approval Criteria:

1. An FDA approved diagnosis of nocturia due to nocturnal polyuria in adults who awaken at least 2 times per night to void; and
2. All other causes of nocturia have been ruled out or adequately treated [e.g., benign prostatic hyperplasia (BPH), overactive bladder (OAB), obstructive sleep apnea (OSA)]; and
3. The prescriber must confirm the member has a 6-month history of at least two nocturic episodes per night; and
4. Member has failed behavior modifications including reducing caffeine intake, alcohol intake, and nighttime fluid intake; and

5. Member must have failed a trial of DDAVP® (desmopressin acetate tablets) or have a patient-specific, clinically significant reason why the standard tablet formulation cannot be used; and
6. The prescriber must be willing to measure serum sodium levels prior to starting treatment and document levels are acceptable; and
7. The prescriber must agree to monitor serum sodium levels within the first week and approximately one month after starting treatment, and periodically during treatment; and
8. The prescriber must confirm the member is not taking loop diuretics; and
9. The prescriber must confirm the member does not have renal impairment with an estimated glomerular filtration rate (eGFR) <50mL/min/1.73m^2; and
10. Initial approvals will be for the duration of 3 months, for continued authorization the prescriber must provide the following:
    a. Documentation that serum sodium levels are acceptable to the prescriber; and
    b. Documentation that the member is responding to treatment; and
11. Approvals will be limited to the 27.7mcg dose for female members; and
12. A quantity limit of 30 tablets per 30 days will apply.

The College of Pharmacy also recommends updating the Noctiva™ (desmopressin acetate nasal spray) criteria as shown in red to be consistent with Nocdurna® (desmopressin acetate sublingual tablets) criteria and clarify the quantity limit to ensure appropriate use:

Noctiva™ (Desmopressin Acetate Nasal Spray) Approval Criteria:

1. An FDA approved diagnosis of nocturia due to nocturnal polyuria in adults ~~50 years of age and older~~; and
2. All other causes of nocturia have been ruled out or adequately treated [e.g., benign prostatic hyperplasia (BPH), overactive bladder (OAB), obstructive sleep apnea (OSA)]; and
3. The prescriber must confirm the member has a 6-month history of at least two nocturic episodes per night; and
4. Member has failed behavior modifications including reducing caffeine intake, alcohol intake, and nighttime fluid intake; and
5. Member must have failed a trial of DDAVP® (desmopressin tablets) or have a patient-specific, clinically significant reason why the tablet formulation cannot be used; and
6. The prescriber must be willing to measure serum sodium levels within seven days of anticipated start of treatment and document levels are acceptable; and
7. The prescriber must agree to monitor serum sodium levels within one month of starting treatment or increasing the dose; and
8. The prescriber must confirm the member is not taking any of the following:
    a. Other medications via the nasal route; or
    b. Loop diuretics; and
9. The prescriber must confirm the member does not have renal impairment with an estimated glomerular filtration rate (eGFR) below 50mL/min/1.73m^2; and

10. Initial approvals will be for the duration of 3 months, for continued authorization the prescriber must provide the following:
    a. Documentation that serum sodium levels are acceptable to the prescriber; and
    b. Documentation that the member is responding to treatment; and
11. A quantity limit of one bottle (3.8g) per 30 days will apply.

Additionally, the College of Pharmacy recommends updating the Bladder Control Medications PBPA Tier-3 criteria to include the use of Myrbetriq® in combination with VESIcare®.

Bladder Control Medications Tier-3 Approval Criteria:

1. A trial of all Tier-1 and Tier-2 medications that yielded inadequate clinical response or adverse effects; or
2. A unique indication which the Tier-1 and Tier-2 medications lack.
3. For use of Myrbetriq® (mirabegeron) in combination with VESIcare® (solifenacin) the member must have failed monotherapy with either mirabegeron or solifenacin (minimum 4-week trial) defined by continued symptoms of urge urinary incontinence, urgency, and urinary frequency. Current tier structure rules will also apply.

Finally, the College of Pharmacy recommends the following:

1. Move trospium (Sanctura®) from Tier-2 to Tier-1 based on national average drug acquisition cost (NADAC).
2. Move tolterodine ER (Detrol LA®) from Tier-3 to Tier-2 based on NADAC. Current Tier-2 criteria will apply.

Bladder Control Medications			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
fesoterodine (Toviaz®)	tolterodine (Detrol®)	darifenacin (Enablex®)	desmopressin acetate nasal spray (Noctiva™)+
oxybutynin (Ditropan®)	**tolterodine ER (Detrol LA®)**	mirabegron (Myrbetriq®)Δ	**desmopressin acetate sublingual tablets (Nocdurna®)+**
oxybutynin ER (Ditropan XL®)		oxybutynin gel (Gelnique®)	oxybutynin patch (Oxytrol®)+
trospium (Sanctura®)		solifenacin (VESIcare®)Δ	
		trospium ER (Sanctura XR®)	

Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
ER = extended release; PA = prior authorization
+Unique criteria specific to Oxytrol® (oxybutynin patch), Noctiva™ (desmopressin acetate nasal spray), and Nocdurna® (desmopressin acetate sublingual tablet) applies.
ΔUnique criteria specific to use of Myrbetriq (mirabegron) in combination with VESIcare (solifenacin) applies.

Utilization Details of Bladder Control Medications: Fiscal Year 2018

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
TIER-1 PRODUCTS					
OXYBUTYNIN PRODUCTS					
OXYBUTYNIN TAB 5MG	5,313	1,315	$140,597.27	$0.86	$26.46
OXYBUTYNIN TAB 10MG ER	1,944	508	$56,076.32	$0.76	$28.85
OXYBUTYNIN TAB 5MG ER	1,276	402	$37,545.67	$0.86	$29.42
OXYBUTYNIN SYP 5MG/5ML	889	265	$13,747.46	$0.56	$15.46
OXYBUTYNIN TAB 15MG ER	830	180	$28,132.07	$0.87	$33.89
SUBTOTAL	**10,252**	**2,670**	**$276,098.79**	**$0.82**	**$26.93**
FESOTERODINE PRODUCTS$^{\Delta}$					
TOVIAZ TAB 4MG	332	109	$98,573.16	$10.04	$296.91
TOVIAZ TAB 8MG	329	79	$100,633.19	$10.28	$305.88
SUBTOTAL	**661**	**188**	**$199,206.35**	**$10.16**	**$301.37**
TIER-1 SUBTOTAL	**10,913**	**2,858**	**$475,305.14**	**$1.33**	**$43.55**
TIER-2 PRODUCTS					
TOLTERODINE PRODUCTS					
TOLTERODINE TAB 2MG	288	45	$18,376.08	$2.02	$63.81
TOLTERODINE TAB 1MG	34	6	$2,389.92	$2.35	$70.29
SUBTOTAL	**322**	**51**	**$20,766.00**	**$2.06**	**$64.49**
TROSPIUM PRODUCTS					
TROSPIUM CL TAB 20MG	62	19	$2,823.72	$1.55	$45.54
SUBTOTAL	**62**	**19**	**$2,823.72**	**$1.55**	**$45.54**
TIER-2 SUBTOTAL	**384**	**70**	**$23,589.72**	**$1.98**	**$61.43**
TIER-3 PRODUCTS					
TROSPIUM PRODUCTS					
TROSPIUM CHL CAP 60MG ER	385	65	$68,710.26	$4.91	$178.47
SUBTOTAL	**385**	**65**	**$68,710.26**	**$4.91**	**$178.47**
TOLTERODINE PRODUCTS					
TOLTERODINE CAP 4MG ER	155	20	$12,733.43	$2.78	$82.15
TOLTERODINE CAP 2MG ER	6	1	$574.90	$3.19	$95.82
SUBTOTAL	**161**	**21**	**$13,308.33**	**$2.80**	**$82.66**
SOLIFENACIN PRODUCTS					
VESICARE TAB 5MG	101	16	$39,959.76	$10.50	$395.64
VESICARE TAB 10MG	81	13	$31,480.55	$11.49	$388.65
SUBTOTAL	**182**	**29**	**$71,440.31**	**$10.92**	**$392.53**
MIRABEGRON PRODUCTS					
MYRBETRIQ TAB 50MG	66	10	$21,984.29	$11.10	$333.10
MYRBETRIQ TAB 25MG	46	8	$15,385.45	$11.15	$334.47
SUBTOTAL	**112**	**18**	**$37,369.74**	**$11.12**	**$333.66**
DARIFENACIN PRODUCTS					
DARIFENACIN TAB 15MG ER	46	5	$9,759.18	$6.85	$212.16
DARIFENACIN TAB 7.5MG ER	1	1	$183.21	$6.11	$183.21

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
SUBTOTAL	**47**	**6**	**$9,942.39**	**$6.83**	**$211.54**
OXYBUTYNIN PRODUCTS					
GELNIQUE GEL 10%	2	1	$747.12	$12.45	$373.56
GELNIQUE GEL 10% PUMP	1	1	$354.89	$11.83	$354.89
SUBTOTAL	**3**	**2**	**$1,102.01**	**$12.24**	**$367.34**
TIER-3 SUBTOTAL	**890**	**141**	**$201,873.04**	**$6.68**	**$226.82**
TOTAL	**12,187**	**2,717***	**$700,767.90**	**$1.75**	**$57.50**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Δ Fesoterodine products moved from Tier-3 to Tier-1 on January 1, 2017 due to net cost after rebates.

---

[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 06/2018. Last accessed 08/08/2018.
[2] Astellas Pharma, Inc. FDA Approves Supplemental New Drug Application for Myrbetriq® (mirabegron) for Use in Combination with solifenacin succinate for the Treatment of Overactive Bladder Symptoms. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/fda-approves-supplemental-new-drug-application-for-myrbetriq-mirabegron-for-use-in-combination-with-solifenacin-succinate-for-the-treatment-of-overactive-bladder-symptoms-300644079.html. Issued 05/07/2018. Last accessed 09/14/2018.
[3] Brown, T. FDA Approves Mirabegron, Solifenacin Combo for OAB. *Medscape*. Available online at: https://www.medscape.com/viewarticle/896394. Issued 05/09/2018. Last accessed 09/14/2018.
[4] Drake MY, Chapple C, Esen AA, et al. Efficacy and Safety of Mirabegron Add-on Therapy to Solifenacin in Incontinent Overactive Bladder Patients with an Inadequate Response to Initial 4-Week Solifenacin Monotherapy: A Randomised Double-blind Multicentre Phase 3B Study (BESIDE). *Eur Urol* 2016; 70(1):136-145.
[5] FDA Approves Ferring's Nocdurna NDA, Nixing Two Petitions. *FDA NEWS*. Available online at: https://www.fdanews.com/articles/187355-fda-approves-ferrings-nocdurna-nda-nixing-two-petitions?utm_source=TrendMD&utm_medium=cpc&utm_campaign=Drug_Daily_Bulletin_TrendMD_0. Issued 06/26/2018. Last accessed 09/18/2018.
[6] Avadel Pharmaceuticals Enters into Exclusive License Agreement for Noctiva™. *Globe Newswire*. Available online at: https://globenewswire.com/news-release/2017/09/05/1107931/0/en/Avadel-Pharmaceuticals-Enters-into-Exclusive-License-Agreement-for-Noctiva.html. Issued 09/05/2017. Last accessed 09/18/2018.
[7] Solabegron Advances To Phase 2B Trials for Overactive Bladder. *MD Magazine*. Available online at: https://www.mdmag.com/medical-news/solabegron-advances-to-phase-2b-trials-for-overactive-bladder. Issued 03/25/2018. Last accessed 09/18/2018.
[8] Urovant Sciences. Urovant Sciences Initiates Phase 3 Clinical Program for Vibegron in Patients with Overactive Bladder. Available online at: https://urovant.com/2018/03/28/urovant-sciences-initiates-phase-3-clinical-program-for-vibegron-in-patients-with-overactive-bladder/. Issued 03/28/2018. Last accessed 09/14/2018.
[9] Urovant Sciences. Pipeline. Vibegron. Available online at: https://urovant.com/pipeline/. Last accessed 09/14/2018.
[10] Nocdurna® Prescribing Information. Ferring Pharmaceuticals, Inc. Available online at: http://www.ferringusa.com/wp-content/uploads/2018/06/NOCDURNA-Prescribing-Information.pdf. Last revised 06/2018. Last accessed 09/14/2018.
[11] Sand PK, Dmochoswki RR, Reddy J, et al. Efficacy and Safety of Low Dose Desmopressin Orally Disintegrating Tablet in Women with Nocturia: Results of a Multicenter, Randomized, Double-Blind, Placebo Controlled, Parallel Group Study. *J Urol* 2013; 190:958-964.
[12] Weiss JP, Herschorn S, Albei CD, et al. Efficacy and Safety of Low Dose Desmopressin Orally Disintegrating Tablet in Men with Nocturia: Results of a Multicenter, Randomized, Double-Blind, Placebo Controlled, Parallel Group Study. *J Urol* 2013; 190:965-972.

Appendix O

Fiscal Year 2018 Annual Review of Constipation and Diarrhea Medications

Oklahoma Health Care Authority
October 2018

Current Prior Authorization Criteria

Amitiza® (Lubiprostone) Approval Criteria [Chronic Idiopathic Constipation (CIC) or Irritable Bowel Syndrome with Constipation (IBS-C) Diagnosis]:

1. An FDA approved diagnosis of CIC in members 18 years of age or older, or IBS-C in female members 18 years of age or older; and
2. Documentation that constipation-causing therapies for other disease states have been discontinued (excluding opioid pain medications for cancer patients); and
3. Documented and updated colon screening for members older than 50 years of age; and
4. Documentation of hydration attempts and trials of at least three different types of products that failed to relieve constipation. Trials must be within the past 90 days. Products may be over-the-counter (OTC) or prescription (does not include fiber or stool softeners); and
    a. One of the three trials must be polyethylene glycol 3350 (PEG-3350); and
    b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
5. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment.
6. A quantity limit of 60 capsules for a 30-day supply will apply.

Amitiza® (Lubiprostone) Approval Criteria [Opioid-Induced Constipation (OIC) Diagnosis]:

1. An FDA approved diagnosis of OIC in members 18 years of age or older with chronic, non-cancer pain who are currently on chronic opioid therapy, except methadone, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation; and
2. Documentation of the underlying cause of chronic pain, or reason why member is on chronic opioid therapy; and
3. Documented and updated colon screening for members older than 50 years of age; and
4. Documentation of hydration attempts and trials of at least three different types of products that failed to relieve constipation. Trials must be within the past 90 days. Products may be over-the-counter (OTC) or prescription (does not include fiber or stool softeners); and
    a. One of the three trials must be polyethylene glycol 3350 (PEG-3350); and
    b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
5. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment.

6. Amitiza® must be discontinued if treatment with the opioid pain medication is also discontinued.
7. A quantity limit of 60 capsules for a 30-day supply will apply.

Linzess® (Linaclotide) Approval Criteria:

1. An FDA approved diagnosis of chronic idiopathic constipation (CIC) or irritable bowel syndrome with constipation (IBS-C) in members 18 years of age or older; and
2. Documentation that constipation-causing therapies for other disease states have been discontinued (excluding opioid pain medications for cancer patients); and
3. Documented and updated colon screening for members older than 50 years of age; and
4. Documentation of hydration attempts and trials of at least three different types of products that failed to relieve constipation. Trials must be within the past 90 days. Products may be over-the-counter (OTC) or prescription (does not include fiber or stool softeners); and
    a. One of the three trials must be polyethylene glycol 3350 (PEG-3350); and
    b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
5. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment.
6. A quantity limit of 30 capsules for a 30-day supply will apply.

Motofen® (Difenoxin/Atropine) Approval Criteria:

1. An FDA approved diagnosis of acute nonspecific diarrhea or acute exacerbations of chronic functional diarrhea; and
2. Member must not be 2 years of age or younger; and
3. Member must not have diarrhea associated with organisms that penetrate the intestinal mucosa (e.g., toxigenic *Escherichia coli, Salmonella species, Shigella*) or pseudomembranous colitis associated with broad spectrum antibiotics; and
4. A patient-specific, clinically significant reason why the member cannot use Lomotil® (diphenoxylate/atropine) and loperamide must be provided; and
5. A quantity limit of 16 tablets per 2 days will apply.

Movantik® (Naloxegol) Approval Criteria:

1. An FDA approved diagnosis of opioid-induced constipation (OIC) in members 18 years of age or older with chronic, non-cancer pain who are currently on chronic opioid therapy, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation; and
2. Member must not have known or suspected gastrointestinal obstruction; and
3. Documentation of the underlying cause of chronic pain, or reason why member is on chronic opioid therapy; and
4. Documented and updated colon screening for members older than 50 years of age; and
5. Documentation of hydration attempts and trials of at least three different types of products that failed to relieve constipation. Trials must be within the past 90 days. Products may be over-the-counter (OTC) or prescription (does not include fiber or stool softeners); and

    a. One of the three trials must be polyethylene glycol 3350 (PEG-3350); and
    b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
6. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment.
7. Movantik® must be discontinued if treatment with the opioid pain medication is also discontinued.
8. A quantity limit of 30 tablets for a 30-day supply will apply.

Relistor® (Methylnaltrexone) Tablets Approval Criteria:

1. An FDA approved diagnosis of opioid-induced constipation (OIC) in members 18 years of age or older with chronic, non-cancer pain who are currently on chronic opioid therapy, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation; and
2. Member must not have known or suspected gastrointestinal obstruction; and
3. Documentation of the underlying cause of chronic pain, or reason why member is on chronic opioid therapy; and
4. Documented and updated colon screening for members older than 50 years of age; and
5. Documentation of hydration attempts and trials of at least three different types of products that failed to relieve constipation. Trials must be within the past 90 days. Products may be over-the-counter (OTC) or prescription (does not include fiber or stool softeners); and
    a. One of the three trials must be polyethylene glycol 3350 (PEG-3350); and
    b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
6. A patient-specific, clinically significant reason why member cannot use Amitiza® (lubiprostone) or Movantik® (naloxegol) must be provided; and
7. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment.
8. Relistor® must be discontinued if treatment with the opioid pain medication is also discontinued.
9. A quantity limit of 90 tablets for a 30-day supply will apply.

Relistor® (Methylnaltrexone) Injection Approval Criteria [Opioid-Induced Constipation (OIC) in Chronic Non-Cancer Pain Diagnosis]:

1. An FDA approved diagnosis of OIC in members 18 years of age or older with chronic, non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation; and
2. Documentation of the underlying cause of chronic pain, or reason why member is on chronic opioid therapy; and
3. Member must have current use of opioid medications; and
4. Documented and updated colon screening for members older than 50 years of age; and
5. Documentation of hydration attempts and trials of at least three different types of products that failed to relieve constipation. Trials must be within the past 90

days. Products may be over-the-counter (OTC) or prescription (does not include fiber or stool softeners); and
    a. One of the three trials must be polyethylene glycol 3350 (PEG-3350); and
    b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
6. Member must not have known or suspected gastrointestinal obstruction; and
7. A patient-specific, clinically significant reason why member cannot use Amitiza® (lubiprostone) or Movantik® (naloxegol) must be provided; and
8. A patient-specific, clinically significant reason why member cannot use the tablet formulation of Relistor® must be provided; and
9. The 12mg single-use vials, syringes, or kits will be the preferred products. Criteria for consideration of 8mg single-use syringes:
    a. Weight range of 38kg to 62kg; and/or
    b. Caregiver unable to draw up dose from vial.
10. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment.
11. Relistor® must be discontinued if treatment with the opioid pain medication is also discontinued.
12. A quantity limit of 30 units per month will apply.

Relistor® (Methylnaltrexone) Injection Approval Criteria [Opioid-Induced Constipation (OIC) in Terminal Disease Diagnosis Receiving Palliative Care]:

1. An FDA approved diagnosis of OIC in patients with severe terminal disease who are receiving only palliative care (life expectancy less than six months); and
2. Current use of opioid medications; and
3. Documentation of hydration attempts and trials of at least three different types of products that failed to relieve constipation. Trials must be within the past 90 days. Products may be over-the-counter (OTC) or prescription (does not include fiber or stool softeners); and
    a. One of the three trials must be polyethylene glycol 3350 (PEG-3350); and
    b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
4. Member must not have known or suspected gastrointestinal obstruction; and
5. The 12mg single-use vials, syringes, or kits will be the preferred products. Criteria for consideration of 8mg single-use syringes:
    a. Weight range of 38kg to 62kg; and/or
    b. Caregiver unable to draw up dose from vial.
6. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment.
7. Relistor® must be discontinued if treatment with the opioid pain medication is also discontinued.
8. A quantity limit of 30 units per month will apply.

Symproic® (Naldemedine) Approval Criteria:

1. An FDA approved diagnosis of opioid-induced constipation (OIC) in members 18 years of age or older with chronic, non-cancer pain who are currently on chronic opioid therapy, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation; and
2. Member must not have known or suspected gastrointestinal obstruction; and
3. Documentation of the underlying cause of chronic pain, or reason why member is on chronic opioid therapy; and
4. Documented and updated colon screening for members older than 50 years of age; and
5. Documentation of hydration attempts and trials of at least three different types of products that failed to relieve constipation. Trials must be within the past 90 days. Products may be over-the-counter (OTC) or prescription (does not include fiber or stool softeners); and
    a. One of the three trials must be polyethylene glycol 3350 (PEG-3350); and
    b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
6. A patient-specific, clinically significant reason why member cannot use Amitiza® (lubiprostone) or Movantik® (naloxegol) must be provided; and
7. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment.
8. Symproic® must be discontinued if treatment with the opioid pain medication is also discontinued.
9. A quantity limit of 30 tablets for a 30-day supply will apply.

Trulance® (Plecanatide) Approval Criteria:

1. An FDA approved diagnosis of chronic idiopathic constipation (CIC) in members 18 years of age or older; and
2. Documentation that constipation-causing therapies for other disease states have been discontinued (excluding opioid pain medications for cancer patients); and
3. Documented and updated colon screening for members older than 50 years of age; and
4. Documentation of hydration attempts and trials of at least three different types of products that failed to relieve constipation. Trials must be within the past 90 days. Products may be over-the-counter (OTC) or prescription (does not include fiber or stool softeners); and
    a. One of the three trials must be polyethylene glycol 3350 (PEG-3350); and
    b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
5. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment.
6. A quantity limit of 30 tablets for a 30-day supply will apply.

Viberzi® (Eluxadoline) Approval Criteria:

1. An FDA approved diagnosis of irritable bowel syndrome with diarrhea (IBS-D); and
2. Member must be 18 years of age or older; and

3. Member must not have any of the contraindications for use of Viberzi® (e.g., removed gallbladder; biliary duct obstruction or sphincter of Oddi disease or dysfunction; alcoholism, alcohol abuse, or alcohol addiction; history of pancreatitis or structural diseases of the pancreas; severe hepatic impairment; history of chronic or severe constipation; mechanical gastrointestinal obstruction); and
4. Documentation of trials of two of the following three medications that failed to relieve diarrhea: loperamide, dicyclomine, or diphenoxylate/atropine (each trial should be for at least 10 to 14 consecutive days at the recommended dosing). Trials must be within the past 90 days. Documentation should be provided including dates, dosing, and reason for trial failure.
5. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment.
6. A quantity limit of 60 tablets for a 30-day supply will apply.

Xermelo® (Telotristat Ethyl) Approval Criteria:

1. An FDA approved diagnosis of carcinoid syndrome diarrhea in combination with somatostatin analog (SSA) therapy in adults inadequately controlled by SSA therapy; and
2. Member must be 18 years of age or older; and
3. Member must have been taking a stable dose of SSA therapy for the last three months and be inadequately controlled (four or more bowel movements per day); and
4. Prescriber must verify member will continue taking SSA therapy in combination with Xermelo®; and
5. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment.
6. A quantity limit of 90 tablets for a 30-day supply will apply.

Xifaxan® (Rifaximin) 200mg Approval Criteria:

1. An FDA approved diagnosis of traveler's diarrhea (TD); and
2. Member must be 12 years of age or older; and
3. TD must be due to noninvasive strains of *Escherichia coli*; and
4. A quantity limit of 9 tablets for a 3-day supply will apply.

Xifaxan® (Rifaximin) 550mg Approval Criteria:

1. An FDA approved indication for the reduction in risk of overt hepatic encephalopathy (HE) recurrence; and
    a. Xifaxan® 550mg will not require a prior authorization and claims will pay at the point of sale if the member has a reported diagnosis of hepatic encephalopathy or hepatic failure within the past 12 months of claims history; or
    b. If the member does not have a reported diagnosis, a manual prior authorization will be required for coverage consideration; or
2. An FDA approved diagnosis of irritable bowel syndrome with diarrhea (IBS-D); and
    a. For the diagnosis of IBS-D: Documentation of trials of two of the following three medications that failed to relieve diarrhea: loperamide, dicyclomine, or diphenoxylate/atropine (each trial should be for at least 10 to 14 consecutive days at the recommended dosing). Trials must be within the past 90 days.

Documentation should be provided including dates, dosing, and reason for trial failure; and

b. For the diagnosis of IBS-D: Member must be 18 years of age or older.

3. A quantity limit of 60 tablets for a 30-day supply will apply. Members with the diagnosis of IBS-D needing 42 tablets for a 14-day treatment regimen (550mg three times daily for 14 days) will be approved for a quantity limit override upon meeting Xifaxan® approval criteria. Members with IBS-D who experience a recurrence of symptoms can be retreated up to two times with the same dosage regimen (550mg three times daily for 14 days).

Utilization of Constipation and Diarrhea Medications: Fiscal Year 2018

Comparison of Fiscal Years: Constipation and Diarrhea Medications

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2017	177	822	$300,790.27	$365.92	$12.13	31,758	24,792
2018	165	889	$348,875.40	$392.44	$13.11	34,531	26,621
% Change	**-6.80%**	**8.20%**	**16.00%**	**7.20%**	**8.10%**	**8.70%**	**7.40%**
Change	**-12**	**67**	**$48,085.13**	**$26.52**	**$0.98**	**2,773**	**1,829**

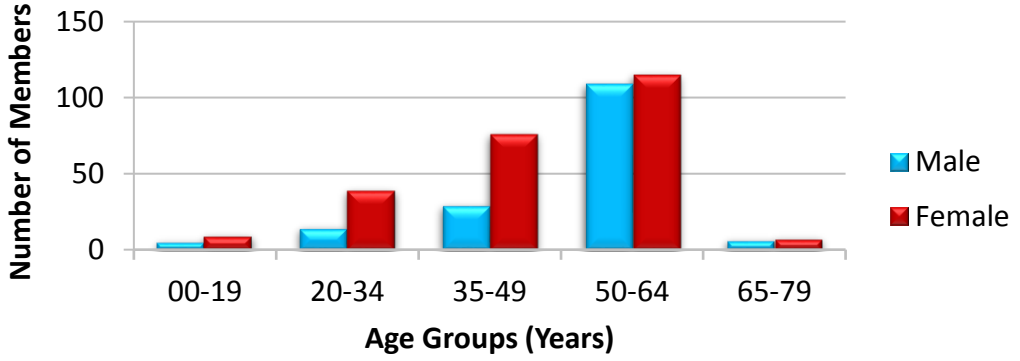
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs. Please note, the above data does not include Xifaxan® (rifaximin).

Comparison of Fiscal Years: Xifaxan® (Rifaximin)

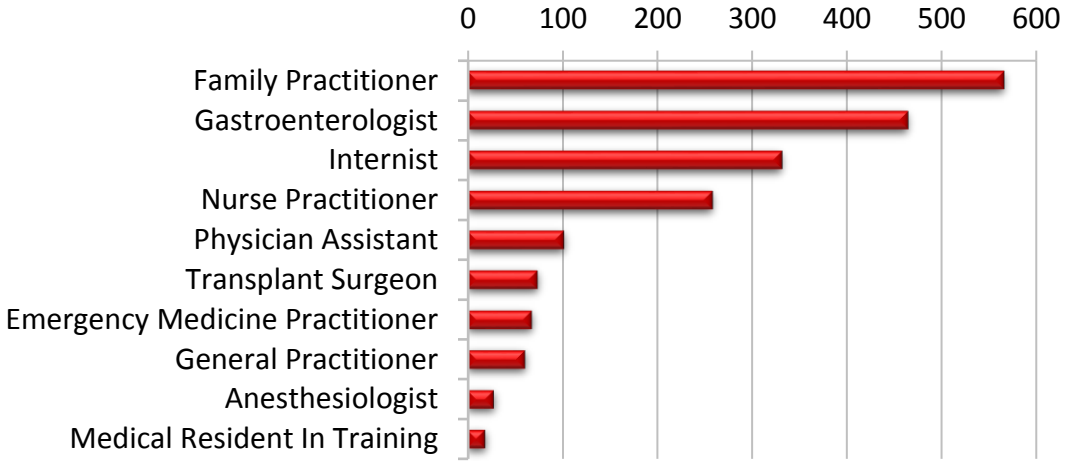
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2017	266	1,116	$1,979,145.98	$1,773.43	$62.80	62,547	31,516
2018	246	1,175	$2,150,664.84	$1,830.35	$66.04	64,941	32,565
% Change	**-7.50%**	**5.30%**	**8.70%**	**3.20%**	**5.20%**	**3.80%**	**3.30%**
Change	**-20**	**59**	**$171,518.86**	**$56.92**	**$3.24**	**2,394**	**1,049**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs. Xifaxan® was first FDA approved in 2004 and has a significant federal rebate. Please note, the majority of utilization of rifaximin was for the 550mg strength for the reduction in risk of overt hepatic encephalopathy (HE) recurrence.

Demographics of Members Utilizing Constipation and Diarrhea Medications



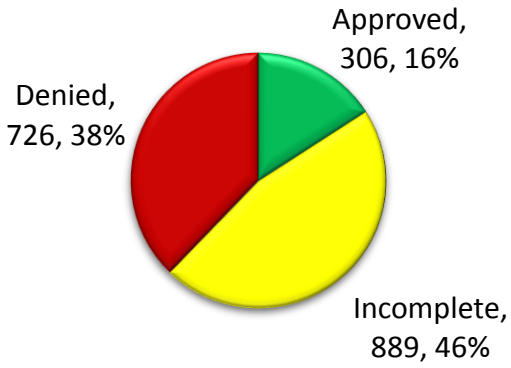
Top Prescriber Specialties of Constipation and Diarrhea Medications by Number of Claims



Prior Authorization of Constipation and Diarrhea Medications

There were 1,921 prior authorization requests submitted for constipation and diarrhea medications during fiscal year 2018. The following chart shows the status of the submitted petitions for fiscal year 2018.

Status of Petitions



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

Anticipated Patent Expiration(s):

- Amitiza® (lubiprostone capsules): October 2027
- Xifaxan® (rifaximin tablets): March 2030
- Xermelo® (telotristat tablets): April 2030
- Relistor® (methylnaltrexone subcutaneous injection): December 2030
- Relistor® (methylnaltrexone tablets): March 2031
- Symproic® (naldemedine tablets): November 2031
- Movantik® (naloxegol tablets): April 2032
- Viberzi® (eluxadoline tablets): March 2033
- Linzess® (linaclotide capsules): August 2033
- Trulance® (plecanatide tablets): June 2034

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

- **January 2018:** The FDA approved Trulance® (plecanatide) for the treatment of irritable bowel syndrome with constipation (IBS-C) in adults. Trulance® was first FDA approved in January 2017 for the treatment of chronic idiopathic constipation (CIC) in adults. The recommended dosage of plecanatide for either diagnosis is 3mg taken orally once daily; tablets should be swallowed whole and may be taken with or without food. For adult patients with swallowing difficulties, plecanatide tablets can be crushed and administered orally either in applesauce or with water, or administered with water via a nasogastric or gastric feeding tube. Plecanatide is structurally related to human uroguanylin and functions as a guanylate cyclase-C (GC-C) agonist; activation of GC-C results in increased intestinal fluid and accelerated transit. Plecanatide has a boxed warning for the risk of serious dehydration in pediatric patients and is contraindicated in patients younger than 6 years of age. The safety and effectiveness of plecanatide have not been established in patients younger than 18 years of age; use of plecanatide should be avoided in patients younger than 18 years of age.

News:

- **May 2018:** Clinicians should consider naloxone or naldemedine for opioid-induced constipation (OIC) when laxatives fail, according to a systemic review and network meta-analysis published online in the journal *Gut.* Several different types of drugs are available for treating OIC, including peripherally acting mu-opioid receptor antagonists (PAMORAs), prokinetics, and secretagogues, but their competitive effectiveness is not clear. For the meta-analysis, researchers included 27 randomized, controlled trials of pharmacological therapies in OIC with a total of 9,149 patients. The primary analysis defined no response as failure to achieve three or more bowel movements (BMs) per week with an increase of one or more BMs per week over baseline, or an average of three or more BMs per week. The meta-analysis found naloxone to be the safest (least likely to cause adverse effects) and most effective treatment for OIC and was significantly better than subcutaneous methylnaltrexone and lubiprostone. Naldemedine was the next best drug and was superior to naloxegol and methylnaltrexone. However, when failure to achieve an average of three or more BMs per week with an increase of one or more BMs per week over baseline was used to define non-response to therapy, which is a more rigorous endpoint, naldemedine was considered the most effective drug. The meta-analysis noted up to 50% of opioid users report constipation and that fewer than half of all patients with OIC benefit from laxatives. It is concluded that based on the findings of the systemic review and meta-analysis, together with evidence from the pharmacoeconomic literature demonstrating that naloxone is highly likely to be cost-effective, naloxone or naldemedine should be the clinician's first choice of pharmacological therapy for OIC when laxatives fail.

Pipeline:

- **Prucalopride (SHP555):** Shire announced the submission of a New Drug Application (NDA) to the FDA for prucalopride in March 2018 as a potential, once-daily, oral treatment option for CIC in adults. Prucalopride, a high affinity, selective serotonin type

4 (5-HT_4) receptor agonist, is a gastrointestinal (GI) prokinetic agent that stimulates colonic peristalsis, increasing bowel motility. Prucalopride has been studied in more than 90 clinical trials worldwide over the last 20 years, including five main Phase 3 and one Phase 4 double-blind, placebo-controlled clinical trials that informed the NDA submission. An integrated analysis of the six main randomized, controlled clinical trials evaluated the global efficacy and safety of prucalopride 2mg daily in men and women with chronic constipation. Overall, there were 2,484 adult patients included in the integrated efficacy analysis and 2,552 adult patients included in the integrated safety analysis; all patients included received prucalopride ≤2mg/day or placebo. Significantly more patients treated with prucalopride versus placebo (27.8% vs. 13.2%; P<0.001) achieved an average of three or more spontaneous complete BMs (SCBMs) per week over the 12-week treatment period. The most common treatment-emergent adverse effects (TEAEs) in the prucalopride group were GI disorders (nausea, diarrhea, and abdominal pain) and headache. The proportion of patients who experienced any adverse cardiovascular (CV) events were comparable between groups (1.8% for placebo vs. 2.0% for prucalopride). Given that drugs similar to prucalopride have been associated with adverse CV events in the past, Shire conducted an observational, pharmacoepidemiology safety study to estimate, in real-world settings, the risk of major adverse CV events (MACE) in patients treated with prucalopride compared to patients treated with polyethylene glycol (PEG). Study results were included in the NDA to provide the FDA additional understanding of the CV safety profile of prucalopride and were later presented at the 2018 Digestive Disease Week (DDW) annual meeting in June 2018. Findings were consistent with no evidence of an overall increase in the risk of MACE in patients using prucalopride compared with PEG. Prucalopride is highly selective and has greater than 150-fold higher affinity for 5-HT_4 receptors than for other receptors. This differs from other 5-HT_4 agonists such as tegaserod and cisapride, which at therapeutic concentrations also interact with other receptors and this may account for the adverse CV events that have resulted in the restricted availability of these medications (tegaserod was withdrawn from the market; cisapride is only available through an investigational limited access program). Prucalopride is currently approved for the treatment of chronic constipation in Europe, Canada, and Israel. The NDA for prucalopride has a designated Prescription Drug User Fee Act (PDUFA) action date of December 21, 2018.

- **Dolcanatide (SP-333):** Synergy Pharmaceuticals, the manufacturer of Trulance® (plecanatide), is currently developing dolcanatide, which is designed to replicate the activity of uroguanylin, a naturally occurring human GI peptide that plays an important role in supporting normal bowel function, with enhanced resistance to standard digestive breakdown by proteases in the intestines. Uroguanylin physiologically regulates bowel function, fluid balance, and stool consistency through GC-C receptor activation. In addition, GC-C receptor activation may lead to decreased inflammation and pain sensation in the GI tract. Dolcanatide is currently in Phase 2 clinical trials for OIC and Phase 1 clinical trials for ulcerative colitis. Synergy Pharmaceuticals are also considering OIC as a potential life cycle growth opportunity for Trulance® (plecanatide).

- **ORP-101:** OrphoMed is currently developing ORP-101, a metabolically stable, peripherally active partial agonist of the mu-opioid receptor and antagonist of the kappa-opioid receptor, designed to mitigate colonic hypersensitivity due to intestinal hyperalgesia and associated motility dysfunction in IBS with diarrhea (IBS-D). In multiple clinically relevant animal models, ORP-101 has repeatedly been shown to suppress general and colon-specific hyperalgesic signals without central nervous system (CNS) penetration and without constriction of the sphincter of Oddi, which could cause acute pancreatitis. ORP-101 was granted Fast Track designation from the FDA in April 2018 for the treatment of IBS-D and is currently in Phase 1 clinical trials for IBS-D. OrphoMed is also currently in early development of ORP-102, a metabolically stable, non-systemic full antagonist of the mu-opioid receptor, designed to mitigate abdominal distress following chronic exposure to systemic opioids, and ORP-103, a metabolically stable modulator of intestinal serotonin and norepinephrine, designed to address intestinal motility disorders.

Cost Comparison: Constipation Medications

Medication	Recommended Dose	Cost/Month*
Chronic Idiopathic Constipation (CIC) Indication		
Amitiza® (lubiprostone) 24mcg cap	24mcg PO BID	$356.40
Linzess® (linaclotide) 145mcg cap	72mcg or 145mcg PO QDay	$371.40
Trulance® (plecanatide) 3mg tab	3mg PO QDay	$371.40
Irritable Bowel Syndrome with Constipation (IBS-C) Indication		
Amitiza® (lubiprostone) 8mcg cap	8mcg PO BID	$356.40
Linzess® (linaclotide) 290mcg cap	290mcg PO QDay	$372.00
Trulance® (plecanatide) 3mg tab	3mg PO QDay	$371.40
Opioid-Induced Constipation (OIC) Indication⁺		
Amitiza® (lubiprostone) 24mcg cap	24mcg PO BID	$356.40
Movantik® (naloxegol) 25mg tab	12.5mg or 25mg PO QDay	$331.20
Relistor® (methylnaltrexone) 150mg tab	450mg PO QDay	$1,568.70
Relistor® (methylnaltrexone) 12mg/0.6mL inj¥	12mg subQ QDay	$3,135.60α
Symproic® (naldemedine) 0.2mg tab	0.2mg PO QDay	$301.50

cap = capsule; tab = tablet; inj = injection; PO = by mouth; BID = twice daily; QDay = once daily; subQ = subcutaneous
*Costs are based on National Average Drug Acquisition Costs (NADAC) and do not reflect rebated prices or net costs.
⁺Medications included in the table are indicated for the treatment of OIC in adult patients with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation.
¥Relistor® injection is also indicated for the treatment of OIC in patients with severe terminal disease who are receiving only palliative care, with recommended weight-based dosing with subQ injections every other day as needed.
αCost/month for Relistor® injection is based on once daily use of 12mg/0.6mL syringes.

Recommendations

The College of Pharmacy recommends the following updates to the current prior authorization criteria for the constipation and diarrhea medications (changes noted in red):

1. Updating the approval criteria for Trulance® (plecanatide), based on the new FDA approved indication for the treatment of IBS-C.

2. Removing the requirement of a reason why the member cannot use Amitiza® or Movantik® from the approval criteria for Symproic® (naldemedine), based on similar net costs for the treatment of OIC.
3. Adding a reason why the member cannot use Symproic® (naldemedine) to the approval criteria for Relistor® (methylnaltrexone) tablets and injection for the diagnosis of OIC in members with chronic, non-cancer pain, based on net costs.

Trulance® (Plecanatide) Approval Criteria:

1. An FDA approved diagnosis of chronic idiopathic constipation (CIC) or irritable bowel syndrome with constipation (IBS-C) in members 18 years of age or older; and
2. Documentation that constipation-causing therapies for other disease states have been discontinued (excluding opioid pain medications for cancer patients); and
3. Documented and updated colon screening for members older than 50 years of age; and
4. Documentation of hydration attempts and trials of at least three different types of products that failed to relieve constipation. Trials must be within the past 90 days. Products may be over-the-counter (OTC) or prescription (does not include fiber or stool softeners); and
    a. One of the three trials must be polyethylene glycol 3350 (PEG-3350); and
    b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
5. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment.
6. A quantity limit of 30 tablets for a 30 day supply will apply.

Symproic® (Naldemedine) Approval Criteria:

1. An FDA approved diagnosis of opioid-induced constipation (OIC) in members 18 years of age or older with chronic, non-cancer pain who are currently on chronic opioid therapy, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation; and
2. Member must not have known or suspected gastrointestinal obstruction; and
3. Documentation of the underlying cause of chronic pain, or reason why member is on chronic opioid therapy; and
4. Documented and updated colon screening for members older than 50 years of age; and
5. Documentation of hydration attempts and trials of at least three different types of products that failed to relieve constipation. Trials must be within the past 90 days. Products may be over-the-counter (OTC) or prescription (does not include fiber or stool softeners); and
    a. One of the three trials must be polyethylene glycol 3350 (PEG-3350); and
    b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
~~6. A patient-specific, clinically significant reason why member cannot use Amitiza® (lubiprostone) or Movantik® (naloxegol) must be provided; and~~
7. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment.

8. Symproic® must be discontinued if treatment with the opioid pain medication is also discontinued.
9. A quantity limit of 30 tablets for a 30-day supply will apply.

Relistor® (Methylnaltrexone) Tablets Approval Criteria:

1. An FDA approved diagnosis of opioid-induced constipation (OIC) in members 18 years of age or older with chronic, non-cancer pain who are currently on chronic opioid therapy, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation; and
2. Member must not have known or suspected gastrointestinal obstruction; and
3. Documentation of the underlying cause of chronic pain, or reason why member is on chronic opioid therapy; and
4. Documented and updated colon screening for members older than 50 years of age; and
5. Documentation of hydration attempts and trials of at least three different types of products that failed to relieve constipation. Trials must be within the past 90 days. Products may be over-the-counter (OTC) or prescription (does not include fiber or stool softeners); and
    a. One of the three trials must be polyethylene glycol 3350 (PEG-3350); and
    b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
6. A patient-specific, clinically significant reason why member cannot use Amitiza® (lubiprostone), Movantik® (naloxegol), or Symproic® (naldemedine) must be provided; and
7. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment.
8. Relistor® must be discontinued if treatment with the opioid pain medication is also discontinued.
9. A quantity limit of 90 tablets for a 30-day supply will apply.

Relistor® (Methylnaltrexone) Injection Approval Criteria [Opioid-Induced Constipation (OIC) in Chronic Non-Cancer Pain Diagnosis]:

1. An FDA approved diagnosis of OIC in members 18 years of age or older with chronic, non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation; and
2. Documentation of the underlying cause of chronic pain, or reason why member is on chronic opioid therapy; and
3. Member must have current use of opioid medications; and
4. Documented and updated colon screening for members older than 50 years of age; and
5. Documentation of hydration attempts and trials of at least three different types of products that failed to relieve constipation. Trials must be within the past 90 days. Products may be over-the-counter (OTC) or prescription (does not include fiber or stool softeners); and
    a. One of the three trials must be polyethylene glycol 3350 (PEG-3350); and

   b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
6. Member must not have known or suspected gastrointestinal obstruction; and
7. A patient-specific, clinically significant reason why member cannot use Amitiza® (lubiprostone), Movantik® (naloxegol), or Symproic® (naldemedine) must be provided; and
8. A patient-specific, clinically significant reason why member cannot use the tablet formulation of Relistor® must be provided; and
9. The 12mg single-use vials, syringes, or kits will be the preferred products. Criteria for consideration of 8mg single-use syringes:
   a. Weight range of 38kg to 62kg; and/or
   b. Caregiver unable to draw up dose from vial.
10. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment.
11. Relistor® must be discontinued if treatment with the opioid pain medication is also discontinued.
12. A quantity limit of 30 units per month will apply.

Utilization Details of Constipation and Diarrhea Medications: Fiscal Year 2018

Constipation and Diarrhea Medications

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
LINACLOTIDE PRODUCTS						
LINZESS CAP 145MCG	265	51	$93,984.63	$354.66	5.2	26.94%
LINZESS CAP 290MCG	221	33	$76,191.34	$344.76	6.7	21.84%
LINZESS CAP 72MCG	16	4	$5,848.99	$365.56	4.0	1.68%
SUBTOTAL	**502**	**88**	**$176,024.96**	**$350.65**	**5.7**	**50.45%**
LUBIPROSTONE PRODUCTS						
AMITIZA CAP 24MCG	198	38	$65,176.60	$329.17	5.2	18.68%
AMITIZA CAP 8MCG	44	14	$15,076.13	$342.64	3.1	4.32%
SUBTOTAL	**242**	**52**	**$80,252.73**	**$331.62**	**4.7**	**23.00%**
NALOXEGOL PRODUCTS						
MOVANTIK TAB 25MG	73	21	$23,162.51	$317.29	3.5	6.64%
MOVANTIK TAB 12.5MG	9	4	$2,791.17	$310.13	2.3	0.80%
SUBTOTAL	**82**	**25**	**$25,953.68**	**$316.51**	**3.3**	**7.44%**
ELUXADOLINE PRODUCTS						
VIBERZI TAB 100MG	20	3	$20,467.22	$1,023.36	6.7	5.87%
VIBERZI TAB 75MG	9	4	$9,544.07	$1,060.45	2.3	2.74%
SUBTOTAL	**29**	**7**	**$30,011.29**	**$1,034.87**	**4.1**	**8.60%**
METHYLNALTREXONE PRODUCTS						
RELISTOR TAB 150MG	15	5	$22,994.35	$1,532.96	3.0	6.59%
RELISTOR INJ 12/0.6ML	9	2	$10,332.87	$1,148.10	4.5	2.96%
SUBTOTAL	**24**	**7**	**$33,327.22**	**$1,388.63**	**3.4**	**9.55%**
PLECANATIDE PRODUCTS						

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
TRULANCE TAB 3MG	7	4	$2,348.66	$335.52	1.8	0.67%
SUBTOTAL	**7**	**4**	**$2,348.66**	**$335.52**	**1.8**	**0.67%**
NALDEMEDINE PRODUCTS						
SYMPROIC TAB 0.2MG	3	2	$956.86	$318.95	1.5	0.27%
SUBTOTAL	**3**	**2**	**$956.86**	**$318.95**	**1.5**	**0.27%**
TOTAL	**889**	**165***	**$348,875.40**	**$392.44**	**5.4**	**100%**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs. Please note, the above data does not include Xifaxan® (rifaximin).

Xifaxan® (Rifaximin)

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
RIFAXIMIN PRODUCTS						
XIFAXAN TAB 550MG	1,164	244	$2,145,794.51	$1,843.47	4.8	99.77%
XIFAXAN TAB 200MG	11	3	$4,870.33	$442.76	3.7	0.23%
TOTAL	**1,175**	**246***	**$2,150,664.84**	**$1,830.35**	**4.8**	**100%**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs. Xifaxan® was first FDA approved in 2004 and has a significant federal rebate. Please note, the majority of utilization of rifaximin 550mg was for the reduction in risk of overt hepatic encephalopathy (HE) recurrence.

---

[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 08/2018. Last accessed 09/18/2018.
[2] Synergy Pharmaceuticals News Release: Synergy Pharmaceuticals Announces FDA Approval of Trulance® (Plecanatide) for the Treatment of Irritable Bowel Syndrome with Constipation (IBS-C) in Adults. Available online at: https://ir.synergypharma.com/press-releases/detail/1861/synergy-pharmaceuticals-announces-fda-approval-of. Issued 01/25/2018. Last accessed 09/18/2018.
[3] Trulance® (Plecanatide) Prescribing Information. Synergy Pharmaceuticals. Available online at: https://www.trulance.com/prescribing-information.pdf. Last revised 02/2018. Last accessed 09/18/2018.
[4] Trulance® (Plecanatide) Package Insert. MedLibrary.org. Available online at: https://medlibrary.org/lib/rx/meds/trulance-immediate-release-1/. Last revised 02/07/2018. Last accessed 09/18/2018.
[5] Luthra P, Burr NE, Brenner DM, et al. Efficacy of Pharmacological Therapies for the Treatment of Opioid-Induced Constipation: Systematic Review and Network Meta-Analysis. *Gut* 2018; doi: 10.1136/gutjnl-2018-316001.
[6] Shire News Release: U.S. FDA Accepts New Drug Application for Prucalopride (SHP555) for Chronic Idiopathic Constipation. Available online at: https://www.shire.com/en/newsroom/2018/march/jo7p3e. Issued 03/05/2018. Last accessed 09/19/2018.
[7] Shire News Release: New Data on the Cardiovascular Safety of Prucalopride Presented at 2018 Digestive Disease Week Annual Meeting. Available online at: https://www.shire.com/en/newsroom/2018/june/bptr3q. Issued 06/03/2018. Last accessed 09/19/2018.
[8] Synergy Pharmaceuticals Research and Development: Dolcanatide. Available online at: https://www.synergypharma.com/research-and-development/dolcanatide. Last accessed 09/19/2018.
[9] OrphoMed Pipeline: ORP-101. Available online at: https://www.orphomed.com/pipeline/orp-101/. Last accessed 09/19/2018.
[10] OrphoMed News Release: FDA Grants Fast Track Designation for OrphoMed's ORP-101 for Treatment of IBS-D. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/fda-grants-fast-track-designation-for-orphomeds-orp-101-for-treatment-of-ibs-d-300634550.html. Issued 04/25/2018. Last accessed 09/19/2018.

- **ORP-101:** OrphoMed is currently developing ORP-101, a metabolically stable, peripherally active partial agonist of the mu-opioid receptor and antagonist of the kappa-opioid receptor, designed to mitigate colonic hypersensitivity due to intestinal hyperalgesia and associated motility dysfunction in IBS with diarrhea (IBS-D). In multiple clinically relevant animal models, ORP-101 has repeatedly been shown to suppress general and colon-specific hyperalgesic signals without central nervous system (CNS) penetration and without constriction of the sphincter of Oddi, which could cause acute pancreatitis. ORP-101 was granted Fast Track designation from the FDA in April 2018 for the treatment of IBS-D and is currently in Phase 1 clinical trials for IBS-D. OrphoMed is also currently in early development of ORP-102, a metabolically stable, non-systemic full antagonist of the mu-opioid receptor, designed to mitigate abdominal distress following chronic exposure to systemic opioids, and ORP-103, a metabolically stable modulator of intestinal serotonin and norepinephrine, designed to address intestinal motility disorders.

Cost Comparison: Constipation Medications

Medication	Recommended Dose	Cost/Month*
Chronic Idiopathic Constipation (CIC) Indication		
Amitiza® (lubiprostone) 24mcg cap	24mcg PO BID	$356.40
Linzess® (linaclotide) 145mcg cap	72mcg or 145mcg PO QDay	$371.40
Trulance® (plecanatide) 3mg tab	3mg PO QDay	$371.40
Irritable Bowel Syndrome with Constipation (IBS-C) Indication		
Amitiza® (lubiprostone) 8mcg cap	8mcg PO BID	$356.40
Linzess® (linaclotide) 290mcg cap	290mcg PO QDay	$372.00
Trulance® (plecanatide) 3mg tab	3mg PO QDay	$371.40
Opioid-Induced Constipation (OIC) Indication⁺		
Amitiza® (lubiprostone) 24mcg cap	24mcg PO BID	$356.40
Movantik® (naloxegol) 25mg tab	12.5mg or 25mg PO QDay	$331.20
Relistor® (methylnaltrexone) 150mg tab	450mg PO QDay	$1,568.70
Relistor® (methylnaltrexone) 12mg/0.6mL inj¥	12mg subQ QDay	$3,135.60α
Symproic® (naldemedine) 0.2mg tab	0.2mg PO QDay	$301.50

cap = capsule; tab = tablet; inj = injection; PO = by mouth; BID = twice daily; QDay = once daily; subQ = subcutaneous
*Costs are based on National Average Drug Acquisition Costs (NADAC) and do not reflect rebated prices or net costs.
⁺Medications included in the table are indicated for the treatment of OIC in adult patients with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation.
¥Relistor® injection is also indicated for the treatment of OIC in patients with severe terminal disease who are receiving only palliative care, with recommended weight-based dosing with subQ injections every other day as needed.
αCost/month for Relistor® injection is based on once daily use of 12mg/0.6mL syringes.

Recommendations

The College of Pharmacy recommends the following updates to the current prior authorization criteria for the constipation and diarrhea medications (changes noted in red):

1. Updating the approval criteria for Trulance® (plecanatide), based on the new FDA approved indication for the treatment of IBS-C.

Appendix P

Fiscal Year 2018 Annual Review of Topical Corticosteroids and 30-Day Notice to Prior Authorize Impoyz™ (Clobetasol Propionate 0.025% Cream)

Oklahoma Health Care Authority
October 2018

Current Prior Authorization Criteria

Tier-1 products are covered with no prior authorization necessary.

Tier-2 Topical Corticosteroid Approval Criteria:

1. Documented trials of all Tier-1 topical corticosteroids of similar potency in the past 30 days that did not yield adequate relief; and
2. If Tier-1 trials are completed and do not yield adequate relief, a patient-specific, clinically significant reason for requesting a Tier-2 in the same potency instead of trying a higher potency medication must be provided; and
3. When the same medication is available in Tier-1, a patient-specific, clinically significant reason must be provided for using a special dosage formulation of that medication in Tier-2 (e.g., foams, shampoos, sprays, kits); and
4. Topical corticosteroid kits require tier trials and a patient-specific, clinically significant reason for use of the kit over other standard formulations.

Tier-3 Topical Corticosteroid Approval Criteria:

1. Documented trials of all Tier-1 and Tier-2 topical corticosteroids of similar potency in the past 90 days that did not yield adequate relief; and
2. If Tier-1 and Tier-2 trials are completed and do not yield adequate relief, a patient-specific, clinically significant reason for requesting a Tier-3 in the same potency instead of trying a higher potency medication must be provided; and
3. When the same medication is available in Tier-1 or Tier-2, a patient-specific, clinically significant reason must be provided for using a special dosage form of that medication in Tier-3 (e.g., foams, shampoos, sprays, kits); and
4. Topical corticosteroid kits require tier trials and a patient-specific, clinically significant reason for use of the kit over other standard formulations.

Topical Corticosteroids					
Tier-1		**Tier-2**		**Tier-3**	
Ultra-High to High Potency					
augmented betamethasone dipropionate 0.05% (**Diprolene AF®**)	**C**	amcinonide 0.1%	**C,O,L**	clobetasol propionate 0.05% (**Clobex®**)	**Sh,Spr**
augmented betamethasone dipropionate 0.05% (**Diprolene®**)	**G**	augmented betamethasone dipropionate 0.05% (**Diprolene®**)	**O,L**	clobetasol propionate 0.05% (**Olux®, Olux-E®**)	**F**

Topical Corticosteroids					
Tier-1		**Tier-2**		**Tier-3**	
betamethasone dipropionate 0.05% (**Diprosone®**)	**O**	betamethasone dipropionate 0.05% (**Diprosone®**)	**C**	clobetasol propionate 0.05% (**Temovate®**)	**O**
clobetasol propionate 0.05% (**Temovate®**)	**C,So**	clobetasol propionate 0.05% (**Clobex®**)	**L**	desoximetasone 0.25% (**Topicort®**)	**C,O,Spr**
fluocinonide 0.05%	**C,O,So**	clobetasol propionate 0.05% (**Temovate®**)	**G**		
halobetasol propionate 0.05% (**Ultravate®**)	**C**	desoximetasone 0.05% (**Topicort®**)	**G**		
		diflorasone diacetate 0.05% (**Apexicon®**)	**C**		
		diflorasone diacetate 0.05% (**Apexicon E®**)	**C,O**		
		fluocinonide 0.05%	**G**		
		fluocinonide 0.1% (**Vanos®**)	**C**		
		flurandrenolide tape 0.05% (**Cordran®**)	**Tape**		
		halcinonide 0.1% (**Halog®**)	**C,O**		
		halobetasol propionate 0.05% (**Ultravate®**)	**L,O**		
		halobetasol propionate/lactic acid 0.05%/10% (**Ultravate X®**)	**C**		
Medium/High to Medium Potency					
betamethasone dipropionate 0.05%	**L**	betamethasone dipropionate/calcipotriene 0.064%/0.005% (**Taclonex®**)	**O,Sus, Spr**	betamethasone dipropionate 0.05% (**Sernivo®**)	**Spr**
betamethasone valerate 0.1% (**Beta-Val®**)	**C,O,L**	betamethasone valerate 0.12% (**Luxiq®**)	**F**	hydrocortisone valerate 0.2% (**Westcort®**)	**C,O**
fluticasone propionate 0.05% (**Cutivate®**)	**C,O**	calcipotriene/betamethasone dipropionate 0.064%/0.005% (**Enstilar®**)	**F**		
mometasone furoate 0.1% (**Elocon®**)	**C,L**	desoximetasone 0.05% (**Topicort LP®**)	**C,O**		
triamcinolone acetonide 0.025%	**C,O,L**	fluocinolone acetonide 0.025% (**Synalar®**)	**C,O**		
		fluocinonide emollient 0.05% (**Lidex E®**)	**C**		
		flurandrenolide 0.05%	**C,L,O**		
		fluticasone propionate 0.05% (**Cutivate®**)	**L**		
		hydrocortisone butyrate 0.1%	**C,O,So**		
		hydrocortisone probutate 0.1% (**Pandel®**)	**C**		
		mometasone furoate 0.1%	**O**		
		prednicarbate 0.1% (**Dermatop®**)	**O,C**		

Topical Corticosteroids					
Tier-1		**Tier-2**		**Tier-3**	
		triamcinolone acetonide 0.147mg/g (**Kenalog®**)	**Spr**		
Low Potency					
desonide 0.05% (**Desonate®**)	**G**	alclometasone dipropionate 0.05% (**Aclovate®**)	**C,O**	fluocinolone acetonide 0.01% (**Derma-Smoothe®; Derma-Smoothe FS®**)	**Oil**
fluocinolone acetonide 0.01% (**Capex®**)	**Sh**	clocortolone pivalate 0.1% (**Cloderm®**)	**C**		
fluocinolone acetonide 0.01% (**Synalar®**)	**C**	desonide 0.05% (**Verdeso®**)	**F**		
hydrocortisone acetate 2.5%	**C,O,L**	desonide 0.05%	**L**		
hydrocortisone/urea1 %/10% (**U-Cort®**)		desonide emollient 0.05%	**C,O**		
	C	fluocinolone acetonide 0.01% (**Synalar®**)	**So**		
		hydrocortisone 2.5% (**Texacort®**)	**So**		
		hydrocortisone/pramoxine 1%/1% (**Pramosone®**)	**C,L**		

C= Cream; O = Ointment; L = Lotion; G = Gel, Sh = Shampoo; So = Solution; Spr = Spray; Sus = Suspension; F = Foam
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 Topical Corticosteroids: Fiscal Year 2018

Comparison of Fiscal Years

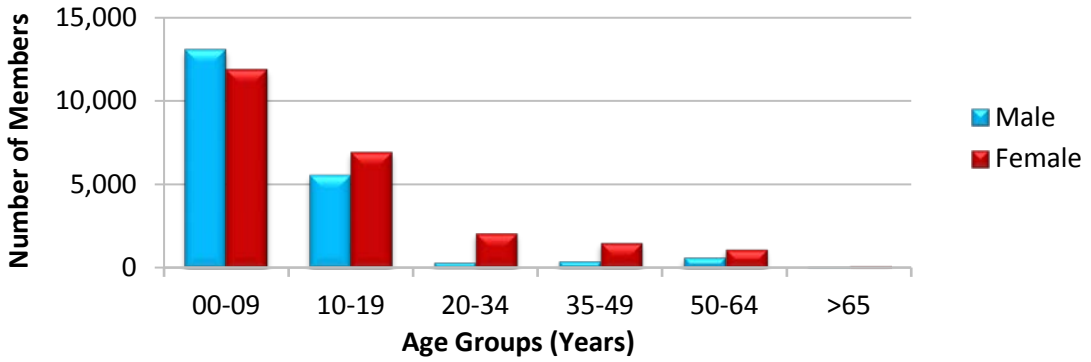
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2017	45,842	69,157	$1,230,285.68	$17.79	$1.13	4,232,500	1,093,299
2018	43,980	66,875	$1,287,921.29	$19.26	$1.21	4,204,005	1,063,231
% Change	**-4.10%**	**-3.30%**	**4.70%**	**8.30%**	**7.10%**	**-0.70%**	**-2.80%**
Change	**-1,862**	**-2,282**	**$57,635.61**	**$1.47**	**$0.08**	**-28,495**	**-30,068**

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

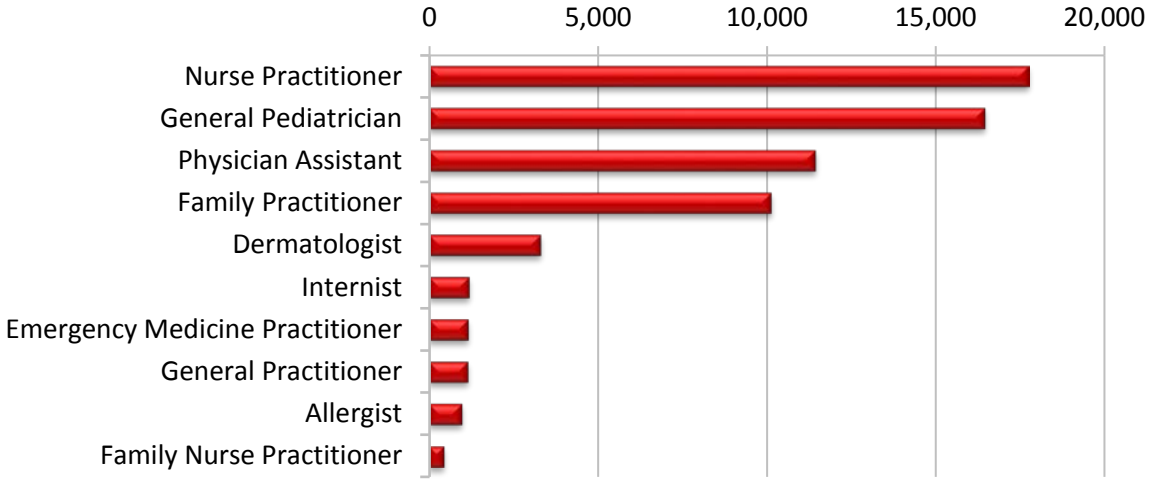
- The prior authorization criteria changes for the Topical Corticosteroids Product Based Prior Authorization (PBPA) Tier Chart was voted on by the Drug Utilization Review (DUR) Board in October of 2017 and went into effect January 24, 2018. Members who were using the products at the time the prior authorization went into effect were not "grandfathered".
- Please note this category is heavily influenced by rebates and costs do not reflect rebated prices or net costs.
- Eucrisa® (crisaborole ointment) is a steroid-free, phosphodiesterase 4 inhibitor topical ointment indicated for the treatment of mild-to-moderate atopic dermatitis in patients

two years of age and older. The manufacturer of Eucrisa® has currently provided a supplemental rebate to provide access to Eucrisa® without prior authorization for members 2 years of age and older. The prior authorization for ages 2 years and older was removed from Eucrisa® on January 1, 2018 and may account for decreased topical corticosteroid utilization.[1]

Demographics of Members Utilizing Topical Corticosteroids



Top Prescriber Specialties of Topical Corticosteroids by Number of Claims



Prior Authorization of Topical Corticosteroids

There were 1,171 prior authorization requests submitted for topical corticosteroids during fiscal year 2018. The following chart shows the status of the submitted petitions for fiscal year 2018.

Status of Petitions

Market News and Updates[2,3,4,5,6,7,8]

Anticipated Patent Expiration(s):

- Capex® (fluocinolone 0.01% shampoo), Texacort® (hydrocortisone 2.5% topical solution), Halog® (halcinonide 0.1% cream and ointment), Cordran® (flurandrenolide 4mcg/cm^2 tape), Pandel® (hydrocortisone 0.1% cream), MiCort™ HC (hydrocortisone 2.5% cream) and U-Cort® (hydrocortisone/urea 1%/10% cream) are not available generically, but have no unexpired patents or exclusivities.
- Desonate® (desonide 0.05% gel): August 2020
- Topicort® (desoximetasone 0.25% spray): September 2028
- Verdeso® (desonide 0.05% foam): November 2028
- Sernivo® (betamethasone dipropionate topical spray 0.05%): August 2030
- Ultravate® (halobetasol lotion 0.05%): June 2033
- Impoyz™ (clobetasol propionate cream 0.025%): March 2035

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

- **Impoyz™ (clobetasol propionate 0.025% cream):** In November 2017, the FDA approved Impoyz™ (clobetasol propionate 0.025% cream), a new lower strength topical formulation of clobetasol. Impoyz™ cream is a topical corticosteroid indicated for the treatment of moderate-to-severe plaque psoriasis in patients 18 years of age and older. Impoyz™ 0.025% cream is available in 60g and 112g size tubes, and the recommended administration is a thin layer applied to the affected skin areas twice daily. Impoyz™ cream can be used for up to two consecutive weeks of treatment. The total dosage of Impoyz™ cream should not exceed 50g per week and use should be discontinued when control is achieved. The active ingredient, clobetasol propionate, is currently available in the 0.05% strength in several formulations including cream, foam, gel, lotion, ointment, liquid spray, topical solution, and shampoo. Impoyz™ cream recently became available on the market as of May 2018 and the Wholesale Acquisition Cost (WAC) of Impoyz™ cream is $7.50 per gram, resulting in a cost of $450.00 per 60g tube. Impoyz™ cream currently does have not a drug rebate agreement and is therefore not a covered SoonerCare product at this time.

Pipeline:

- **August 2018:** Ortho Dermatologics announced it has resubmitted a New Drug Application (NDA) to the FDA for DUOBRII™ (halobetasol propionate/tazarotene) lotion

for the treatment of plaque psoriasis. The FDA issued a Complete Response Letter (CRL) in June 2018 for the NDA for DUOBRII™ regarding pharmacokinetic data. Ortho Dermatoloigics stated that after meeting with the FDA and understanding the additional pharmacokinetic data required for DUOBRII™, they have resubmitted the NDA ahead of schedule. Halobetasol propionate and tazarotene, when used separately to treat plaque psoriasis, are limited to a four-week (or less) duration of use and have a high rate of adverse events, respectively. Based on existing data from DUOBRII™ and other clinical studies, the combination of these ingredients in DUOBRII™ with a dual mechanism of action, potentially allows for expanded duration of use with a proven safety profile, according to a company press release.

Recommendations

The College of Pharmacy recommends the placement of Impoyz™ (clobetasol propionate cream 0.025%) into Tier-3 of the Ultra-High to High Potency category of the Topical Corticosteroids PBPA Tier Chart. Current Tier-3 criteria would apply.

Additionally ,the College of Pharmacy recommends the following changes to the Topical Corticosteroids PBPA category:

1. Move Synalar® (fluocinolone acetonide 0.01% cream) from Tier-1 to Tier-2 under Low Potency category of the Topical Corticosteroid PBPA Tier Chart based on net cost.
2. Move desonide 0.05% lotion and desonide emollient 0.05% cream and ointment from Tier-2 to Tier-3 under Low Potency category of the Topical Corticosteroid PBPA Tier Chart based on net cost.
3. Move mometasone furoate 0.1% ointment from Tier-2 to Tier-1 under Medium/High to Medium Potency category of the Topical Corticosteroid PBPA Tier Chart based on net cost.

Tier-1 products are covered with no prior authorization necessary.

Tier-2 Topical Corticosteroid Approval Criteria:

1. Documented trials of all Tier-1 topical corticosteroids of similar potency in the past 30 days that did not yield adequate relief; and
2. If Tier-1 trials are completed and do not yield adequate relief, a patient-specific, clinically significant reason for requesting a Tier-2 in the same potency instead of trying a higher potency medication must be provided; and
3. When the same medication is available in Tier-1, a patient-specific, clinically significant reason must be provided for using a special dosage formulation of that medication in Tier-2 (e.g., foams, shampoos, sprays, kits); and
4. Topical corticosteroid kits require tier trials and a patient-specific, clinically significant reason for use of the kit over other standard formulations.

Tier-3 Topical Corticosteroid Approval Criteria:

1. Documented trials of all Tier-1 and Tier-2 topical corticosteroids of similar potency in the past 90 days that did not yield adequate relief; and

2. If Tier-1 and Tier-2 trials are completed and do not yield adequate relief, a patient-specific, clinically significant reason for requesting a Tier-3 in the same potency instead of trying a higher potency medication must be provided; and
3. When the same medication is available in Tier-1 or Tier-2, a patient-specific, clinically significant reason must be provided for using a special dosage form of that medication in Tier-3 (e.g., foams, shampoos, sprays, kits); and
4. Topical corticosteroid kits require tier trials and a patient-specific, clinically significant reason for use of the kit over other standard formulations.

Topical Corticosteroids					
Tier-1		**Tier-2**		**Tier-3**	
Ultra-High to High Potency					
augmented betamethasone dipropionate 0.05% (**Diprolene AF®**)	**C**	amcinonide 0.1%	**C,O,L**	**clobetasol propionate 0.025% (Impoyz™)**	**C**
augmented betamethasone dipropionate 0.05% (**Diprolene®**)	**G**	augmented betamethasone dipropionate 0.05% (**Diprolene®**)	**O,L**	clobetasol propionate 0.05% (**Clobex®**)	**Sh,Spr**
betamethasone dipropionate 0.05% (**Diprosone®**)	**O**	betamethasone dipropionate 0.05% (**Diprosone®**)	**C**	clobetasol propionate 0.05% (**Olux®, Olux-E®**)	**F**
clobetasol propionate 0.05% (**Temovate®**)	**C,So**	clobetasol propionate 0.05% (**Clobex®**)	**L**	clobetasol propionate 0.05% (**Temovate®**)	**O**
fluocinonide 0.05%	**C,O,So**	clobetasol propionate 0.05% (**Temovate®**)	**G**	desoximetasone 0.25% (**Topicort®**)	**C,O,Spr**
halobetasol propionate 0.05% (**Ultravate®**)	**C**	desoximetasone 0.05% (**Topicort®**)	**G**		
		diflorasone diacetate 0.05% (**Apexicon®**)	**C**		
		diflorasone diacetate 0.05% (**Apexicon E®**)	**C,O**		
		fluocinonide 0.05%	**G**		
		fluocinonide 0.1% (**Vanos®**)	**C**		
		flurandrenolide tape 0.05% (**Cordran®**)	**Tape**		
		halcinonide 0.1% (**Halog®**)	**C,O**		
		halobetasol propionate 0.05% (**Ultravate®**)	**L,O**		
		halobetasol propionate/lactic acid 0.05%/10% (**Ultravate X®**)	**C**		
Medium/High to Medium Potency					
betamethasone dipropionate 0.05%	**L**	betamethasone dipropionate/calcipotriene 0.064%/0.005% (**Taclonex®**)	**O,Sus, Spr**	betamethasone dipropionate 0.05% (**Sernivo®**)	**Spr**
betamethasone valerate 0.1% (**Beta-Val®**)	**C,O,L**	betamethasone valerate 0.12% (**Luxiq®**)	**F**	hydrocortisone valerate 0.2% (**Westcort®**)	**C,O**

Topical Corticosteroids					
Tier-1		**Tier-2**		**Tier-3**	
fluticasone propionate 0.05% (**Cutivate®**)	**C,O**	calcipotriene/betamethasone dipropionate 0.064%/0.005% (**Enstilar®**)	**F**		
mometasone furoate 0.1% (**Elocon®**)	**C,L,O**	desoximetasone 0.05% (**Topicort LP®**)	**C,O**		
triamcinolone acetonide 0.025%	**C,O,L**	fluocinolone acetonide 0.025% (**Synalar®**)	**C,O**		
		fluocinonide emollient 0.05% (**Lidex E®**)	**C**		
		flurandrenolide 0.05%	**C,L,O**		
		fluticasone propionate 0.05% (**Cutivate®**)	**L**		
		hydrocortisone butyrate 0.1%	**C,O,So**		
		hydrocortisone probutate 0.1% (**Pandel®**)	**C**		
		prednicarbate 0.1% (**Dermatop®**)	**O,C**		
		triamcinolone acetonide 0.147mg/g (**Kenalog®**)	**Spr**		
Low Potency					
desonide 0.05% (**Desonate®**)	**G**	alclometasone dipropionate 0.05% (**Aclovate®**)	**C,O**	fluocinolone acetonide 0.01% (**Derma-Smoothe®; Derma-Smoothe FS®**)	**Oil**
fluocinolone acetonide 0.01% (**Capex®**)	**Sh**	clocortolone pivalate 0.1% (**Cloderm®**)	**C**	**desonide 0.05%**	**L**
hydrocortisone acetate 2.5%	**C,O,L**	desonide 0.05% (**Verdeso®**)	**F**	**desonide emollient 0.05%**	**C,O**
hydrocortisone/urea 1%/10% (**U-Cort®**)	**C**	fluocinolone acetonide 0.01% (**Synalar®**)	**So,C**		
		hydrocortisone 2.5% (**Texacort®**)	**So**		
		hydrocortisone/pramoxine 1%/1% (**Pramosone®**)	**C,L**		

C= Cream; O = Ointment; L = Lotion; G = Gel, Sh = Shampoo; So = Solution; Spr = Spray; Sus = Suspension; F = Foam
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 Topical Corticosteroids: Fiscal Year 2018

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
TIER-1 MEDICATIONS						
LOW-POTENCY PRODUCTS						
HYDROCORT CRE 2.5%	4,362	3,426	$51,453.52	$0.84	$11.80	4.00%
HYDROCORT OIN 2.5%	2,658	1,720	$40,100.51	$1.25	$15.09	3.11%
HYDROCORT CRE 1%	1,905	1,634	$21,062.51	$1.13	$11.06	1.64%
HYDROCORT LOT 2.5%	445	361	$11,622.30	$1.46	$26.12	0.90%
HYDROCORT OIN 1%	325	285	$4,094.74	$1.27	$12.60	0.32%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
DESONATE GEL 0.05%	119	93	$65,157.23	$23.00	$547.54	5.06%
FLUOCIN ACET CRE 0.01%	62	35	$4,671.91	$5.26	$75.35	0.36%
CAPEX SHA 0.01%	49	43	$19,217.40	$19.65	$392.19	1.49%
SUBTOTAL	**9,925**	**7,597**	**$217,380.12**	**$1.70**	**$21.90**	**16.88%**
MEDIUM-HIGH TO MEDIUM POTENCY PRODUCTS						
TRIAMCINOLON CRE 0.1%	24,680	18,884	$331,690.38	$0.83	$13.44	25.75%
TRIAMCINOLON OIN 0.1%	11,403	8,372	$166,388.05	$0.84	$14.59	12.92%
TRIAMCINOLON CRE 0.025%	5,442	4,321	$71,278.77	$0.91	$13.10	5.53%
TRIAMCINOLON CRE 0.5%	2,797	2,083	$52,551.94	$1.42	$18.79	4.08%
TRIAMCINOLON OIN 0.025%	2,639	2,109	$42,950.84	$1.10	$16.28	3.33%
MOMETASONE CRE 0.1%	1,606	1,152	$33,495.67	$1.21	$20.86	2.60%
FLUTICASONE CRE 0.05%	1,105	785	$26,289.25	$1.45	$23.79	2.04%
TRIAMCINOLON OIN 0.5%	999	758	$20,891.11	$1.59	$20.91	1.62%
BETAMETH VAL CRE 0.1%	452	314	$18,231.64	$2.40	$40.34	1.42%
TRIAMCINOLON LOT 0.1%	440	361	$16,150.33	$1.95	$36.71	1.25%
FLUTICASONE OIN 0.005%	365	196	$11,488.56	$1.56	$31.48	0.89%
TRIAMCINOLON LOT 0.025%	222	185	$8,215.23	$2.05	$37.01	0.64%
BETAMETH VAL OIN 0.1%	149	125	$5,000.83	$1.97	$33.56	0.39%
BETAMETH DIP LOT 0.05%	134	82	$6,194.12	$1.97	$46.22	0.48%
MOMETASONE SOL 0.1%	121	90	$2,471.42	$0.92	$20.42	0.19%
BETAMETH VAL LOT 0.1%	42	33	$2,358.05	$3.02	$56.14	0.18%
TRIANEX OIN 0.05%	37	29	$1,579.22	$1.63	$42.68	0.12%
SUBTOTAL	**52,633**	**39,879**	**$817,225.41**	**$0.96**	**$15.53**	**63.43%**
ULTRA-HIGH TO HIGH POTENCY PRODUCTS						
AUG BETAMET CRE 0.05%	1,083	748	$21,943.89	$1.08	$20.26	1.70%
BETAMETH DIP OIN 0.05%	715	469	$61,786.19	$4.75	$86.41	4.80%
FLUOCINONIDE SOL 0.05%	598	401	$40,869.72	$2.97	$68.34	3.17%
FLUOCINONIDE CRE 0.05%	428	275	$23,714.21	$2.62	$55.41	1.84%
CLOBETASOL CRE 0.05%	389	304	$24,637.33	$3.72	$63.34	1.91%
FLUOCINONIDE OIN 0.05%	356	228	$25,707.82	$3.68	$72.21	2.00%
CLOBETASOL SOL 0.05%	291	209	$15,120.26	$1.72	$51.96	1.17%
HALOBETASOL CRE 0.05%	127	81	$11,393.34	$4.72	$89.71	0.88%
AUG BETAMET GEL 0.05%	22	17	$1,882.92	$3.97	$85.59	0.15%
CLOBETASOL E CRE 0.05%	16	16	$1,468.16	$4.91	$91.76	0.11%
SUBTOTAL	**4,025**	**2,748**	**$228,523.84**	**$2.79**	**$56.78**	**17.73%**
TIER-2 MEDICATIONS						
LOW-POTENCY PRODUCTS						
ALCLOMETAS OIN 0.05%	186	122	$14,485.35	$3.97	$77.88	1.12%
ALCLOMETAS CRE 0.05%	70	57	$4,102.12	$3.52	$58.60	0.32%
DESONIDE LOT 0.05%	6	2	$1,390.03	$23.17	$231.67	0.11%
FLUOCIN ACET SOL 0.01%	4	4	$380.20	$4.27	$95.05	0.03%
DESONIDE CRE 0.05%	2	1	$237.08	$3.95	$118.54	0.02%
SUBTOTAL	**268**	**186**	**$20,594.78**	**$4.10**	**$76.85**	**1.60%**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
MEDIUM-HIGH TO MEDIUM POTENCY PRODUCTS						
MOMETASONE OIN 0.1%	3	2	$64.21	$0.80	$21.40	0.00%
SUBTOTAL	**3**	**2**	**$64.21**	**$0.80**	**$21.40**	**0.00%**
TIER-3 MEDICATIONS						
LOW-POTENCY PRODUCTS						
FLUOCIN ACET OIL SCALP 0.01%	6	2	$884.13	$6.55	$147.36	0.07%
FLUOCIN ACET OIL 0.01%	2	2	$273.64	$4.56	$136.82	0.02%
SUBTOTAL	**8**	**4**	**$1,157.77**	**$5.94**	**$144.72**	**0.09%**
ULTRA-HIGH TO HIGH POTENCY PRODUCTS						
CLOBETASOL SHA 0.05%	8	2	$1,620.88	$6.75	$202.61	0.13%
CLOBETASOL OIN 0.05%	3	3	$337.49	$4.96	$112.50	0.03%
TOPICORT SPR 0.25%	2	1	$1,016.79	$16.95	$508.40	0.08%
SUBTOTAL	**13**	**6**	**$2,975.16**	**$8.08**	**$228.86**	**0.24%**
TOTAL	**66,875**	**43,980***	**$1,287,921.29**	**$1.21**	**$19.26**	**100%**

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

[1] Eucrisa™ (Crisaborole 2% Ointment) Prescribing Information. Pfizer Laboratories, Inc. Available online at: http://labeling.pfizer.com/ShowLabeling.aspx?id=5331. Last revised 10/2017. Last accessed 09/24/2018.
[2] Valeant Pharmaceuticals International, Inc. FDA Issues Complete Response Letter for DUOBRII™ (Halobetasol Propionate and Tazarotene) Lotion. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/fda-issues-complete-response-letter-for-duobrii-halobetasol-propionate-and-tazarotene-lotion-300667565.html. Issued 06/18/2018. Last accessed 09/24/2018.
[3] Bausch Health Companies Inc. Ortho Dermatologics Resubmits U.S. New Drug Application for DUOBRII™ (Halobetasol Propionate and Tazarotene) Lotion. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/ortho-dermatologics-resubmits-us-new-drug-application-for-duobrii-halobetasol-propionate-and-tazarotene-lotion-300697693.html. Issued 08/15/2018. Last accessed 09/24/2018.
[4] Baush Health Companies Inc. Ortho Dermatologics Announces Publication of Pivotal Efficacy and Safety Data for Psoriasis Treatment DUOBRII™ in the Journal of the American Academy of Dermatology. Press Release. Available online at: https://ir.bauschhealth.com/news-releases/2018/04-09-2018-121351083. Issued 04/09/2018. Last accessed 09/24/2018.
[5] 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 08/2018. Last accessed 09/19/2018.
[6] FDA Drug Approvals. Impoyz™ (clobetasol propionate) cream. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2017/209483Orig1s000TOC.cfm. Issued 03/14/2017. Last accessed 09/19/2018.
[7] Encore Dermatology, Inc. Encore Dermatology Inc. Announces the Launch of Impoyz™ (Clobetasol Propionate) Cream 0.025%, a newly formulated high-potency topical corticosteroid. Available online at: http://www.encorederm.com/news/item/news-article-1-copy-3. Issued 05/01/2018. Last accessed 09/19/2018.
[8] Impoyz™ (Clobetasol Propionate) Cream 0.025% Prescribing Information. Encore Dermatology, Inc. Available online at: http://www.encorederm.com/images/documents/Impoyz-Package-Insert--Patient-Information.pdf. Last revised 11/2017. Last accessed 09/18/2018.

Appendix Q

Fiscal Year 2018 Annual Review of Gout Medications and 30-Day Notice to Prior Authorize Krystexxa® (Pegloticase)

Oklahoma Health Care Authority
October 2018

Current Prior Authorization Criteria

Colcrys® (Colchicine Tablets) and Mitigare® (Colchicine Capsules) Approval Criteria:

1. A quantity of six tablets for a three day supply is available without prior authorization for treatment of acute gouty attacks; and
2. Failure of allopurinol after six months of treatment defined by persistent gouty attacks with serum urate levels >6.0mg/dL; and
3. A patient-specific, clinically significant reason why colchicine/probenecid would not be a viable option for the member; and
4. A quantity limit of 60 tablets per 30 days will apply for gout.
5. Members with a diagnosis of Familial Mediterranean Fever verified by genetic testing may be approved for up to 2.4mg per day.

Uloric® (Febuxostat) Approval Criteria:

1. Failure of allopurinol defined by persistent gouty attacks with serum urate levels >6.0mg/dL; and
2. A patient-specific, clinically significant reason why allopurinol would not be a viable option for the member; and
3. A quantity limit of 30 tablets per 30 days will apply.

Zurampic® (Lesinurad) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of gout in patients who have not achieved target serum uric acid (sUA) levels with a xanthine oxidase inhibitor (XOI) alone; and
3. Failure of allopurinol and febuxostat alone defined by serum urate levels >6.0mg/dL; and
4. Prescriber must verify that the member has a creatinine clearance >45mL/min prior to initiating treatment and for continued approval; and
5. Prescriber must verify that the member will take Zurampic® concomitantly with a XOI; and
6. Prescriber must document that the member is not taking >325mg of aspirin per day and that the member is not taking any epoxide hydrolase inhibitors; and
7. Prescriber must document that the member has no contraindications for use of Zurampic® including any of the following: Tumor lysis syndrome or Lesch-Nyhan syndrome, severe renal impairment (CrCl <30mL/min), end-stage renal disease, kidney transplant recipients, or patients on dialysis; and
8. A quantity limit of one tablet daily will apply.

Duzallo® (Lesinurad/Allopurinol) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved indication for the treatment of symptomatic hyperuricemia associated with gout in patients who have not achieved target serum uric acid (sUA) levels with a medically appropriate daily dose of allopurinol alone; and
3. Failure of allopurinol or febuxostat alone defined by serum urate levels >6.0mg/dL; and
4. Prior to starting treatment with Duzallo®, the member must be taking at least 300mg of allopurinol daily, unless creatinine clearance (CrCl) <60mL/min, then 200mg daily is required. Duzallo® 200mg/200mg will only be approved for members with a CrCl <60mL/min; and
5. Prescriber must verify that the member has a CrCl >45mL/min prior to initiating treatment. For continued approval, the prescriber must verify CrCl is >45mL/min and serum creatinine is not greater than two times baseline when Duzallo® was initiated; and
6. Prescriber must document that the member has no contraindications for use of Duzallo® including any of the following: Tumor lysis syndrome or Lesch-Nyhan syndrome, severe renal impairment (CrCl <30mL/min), end-stage renal disease, kidney transplant recipients, or patients on dialysis; and
7. A quantity limit of one tablet daily will apply.

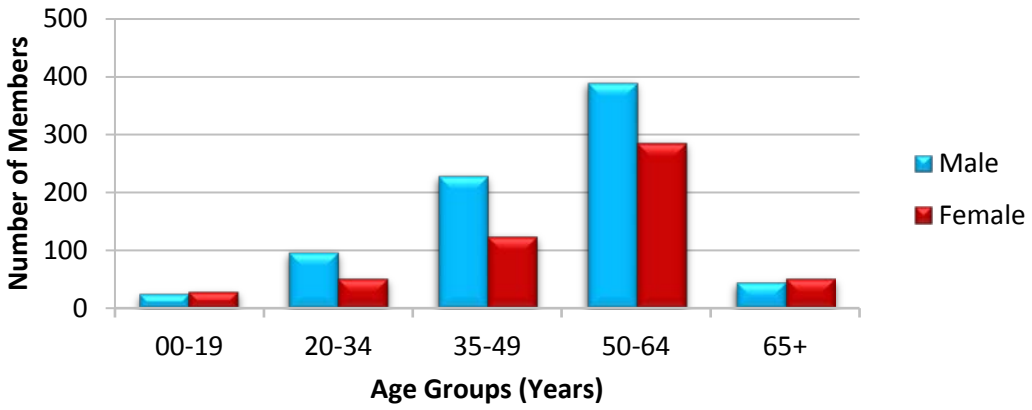
Utilization of Gout Medications: Fiscal Year 2018

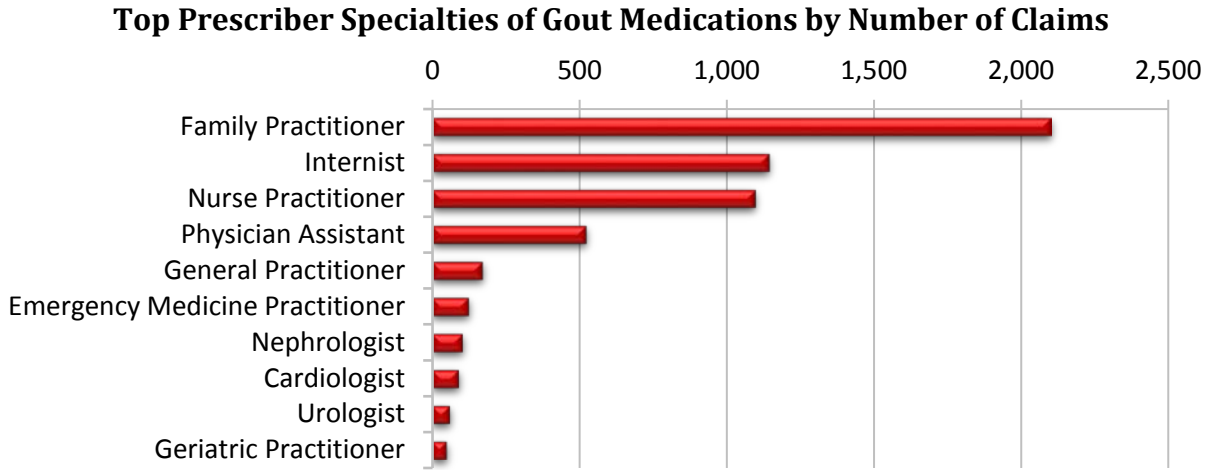
Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2017	1,309	5,943	$169,459.42	$28.51	$0.76	299,847	221,892
2018	1,330	5,769	$183,900.06	$31.88	$0.85	280,353	216,020
% Change	**1.60%**	**-2.90%**	**8.50%**	**11.80%**	**11.80%**	**-6.50%**	**-2.60%**
Change	**21**	**-174**	**$14,440.64**	**$3.37**	**$0.09**	**-19,494**	**-5,872**

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

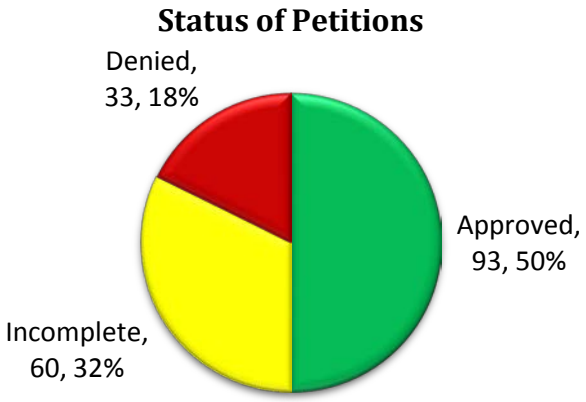
Demographics of Members Utilizing Gout Medications





Prior Authorization of Gout Medications

There were 186 prior authorization requests submitted for gout medications during fiscal year 2018. The following chart shows the status of the submitted petitions for fiscal year 2018.



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

Anticipated Patent Expiration(s):

- Colcrys® (colchicine tablets): February 2029
- Uloric® (febuxostat tablets): September 2031
- Duzallo® (lesinurad/allopurinol tablets): February 2032
- Zurampic® (lesinurad tablets): February 2032
- Mitigare® (colchicine capsules): August 2033

Both Colcrys® and Mitigare® have unexpired patents, but unconventional actions led to generic product availability. In 2009, the U.S. Food and Drug Administration (FDA) approved the first branded version of colchicine, Colcrys® (colchicine 0.6mg tablets). All other formulations, which had not gone through the FDA's review process, were removed from the market at that time under the FDA's regulatory authorities. In September 2014, another branded formulation, Mitigare® (colchicine 0.6mg capsules), was approved by the FDA. Soon after, in January 2015, West-Ward

Pharmaceuticals Corp. launched the authorized generic, colchicine 0.6mg capsules. Prasco Laboratories and Takeda Pharmaceuticals U.S.A., Inc. followed suit in January 2015 by entering into a distribution and supply agreement for the rights to distribute colchicine tablets, the authorized generic of Colcrys® (colchicine 0.6mg tablets). In July 2018, Par Pharmaceutical also started shipping an authorized generic of Colcrys® (colchicine 0.6mg tablets) after several court battles over the production of a generic colchicine 0.6mg tablets. The College of Pharmacy will continue to monitor costs of colchicine products as more generic formulations become available.

News:

- **June 2018:** Public Citizen, a consumer advocacy group, petitioned the FDA to remove Uloric® (febuxostat) from the market. This petition was the result of new study data that was released showing that patients with gout and coexisting cardiovascular (CV) conditions had a higher incidence of CV death and all-cause mortality. The FDA released a public safety announcement regarding the risk of heart related deaths in November 2017 based on preliminary data from the CARES trial. The CARES trial released the full study data in March 2018. This study was a multi-center, double-blind, randomized controlled trial that enrolled patients with gout and CV disease. The primary composite endpoint was the first occurrence of CV death, nonfatal myocardial infarction (MI), nonfatal stroke, or need for urgent revascularization for unstable angina. The study found that febuxostat was noninferior to allopurinol in relation to the primary composite endpoint, but there were higher rates of CV death and all-cause mortality in the febuxostat group.

Pipeline:

- **Arhalofenate:** Arhalofenate is a novel anti-inflammatory uricosuric agent. Five Phase 2 trials were completed in January 2015, and the therapy is prepared to start discussions with the FDA to begin Phase 3 trials. Arhalofenate lowers serum uric acid (sUA) by blocking the reabsorption of uric acid in the proximal tubules of the kidney by inhibiting a renal uric acid transporter called URAT1.

Krystexxa® (Pegloticase) Product Summary[7]

Indication(s): Krystexxa® (pegloticase) is a PEGylated uric acid specific enzyme indicated for the treatment of chronic gout in adult patients refractory to conventional therapy.

Dosing:

- Krystexxa® (pegloticase) is supplied as a 1mL sterile concentrate for dilution containing 8mg of pegloticase protein expressed in uricase protein amounts.
- The recommended dose for adult patients is 8mg given as an intravenous (IV) infusion every 2 weeks.
- The IV infusion of pegloticase should be administered over no less than 120 minutes. Patients should be pre-medicated with antihistamines and corticosteroids prior to infusion.
- Patients should discontinue oral urate-lowering agents prior to starting pegloticase, and sUA levels should be monitored prior to each infusion.

Boxed Warning: Anaphylaxis and Infusion Reactions; Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency Associated Hemolysis and Methemoglobinemia

- Anaphylaxis and infusion reactions have been reported to occur during and after administration of pegloticase and may occur at any time during treatment.
- Pegloticase should be administered in a health care setting by a health care provider prepared to manage anaphylaxis. Patients should be pre-medicated with antihistamines and corticosteroids. They should also be monitored after administration of pegloticase.
- sUA levels should be monitored prior to infusions and consideration given to discontinuing treatment if two consecutive levels are >6mg/dL.
- Patients should be screened for G6PD deficiency prior to starting pegloticase. Hemolysis and methemoglobinemia have been reported in patients with G6PD deficiency. Pegloticase should not be administered to patients with G6PD deficiency.

Mechanism of Action: Pegloticase is a uric acid specific enzyme which is a recombinant uricase and achieves its therapeutic effect by catalyzing the oxidation of uric acid to allantoin, thereby lowering sUA. Allantoin is an inert and water soluble purine metabolite that is readily eliminated by renal excretion.

Contraindication(s):

- G6PD deficiency

Warnings and Precautions:

- Anaphylaxis: Anaphylaxis generally occurred within 2 hours after treatment administration of pegloticase. The frequency of anaphylaxis in clinical trials was about 6%, despite all patients being treated with at least one dose of oral antihistamine(s), plus a corticosteroid and/or acetaminophen. Patients receiving pegloticase should be pre-medicated with antihistamines and corticosteroids, and pegloticase should be administered in a health care setting by a health care professional that is prepared to manage anaphylaxis. Anaphylaxis risk is higher when uric acid levels are >6mg/dL. Oral urate lowering medications can blunt the rise of urate, so they should be discontinued prior to starting therapy with pegloticase. Less severe nonanaphylactic infusion related reactions also occurred in patients including: chest pain, erythema, pruritus, and dyspnea. If infusion related reactions occur, the infusion may be stopped and restarted or the rate may be adjusted.
- G6PD Deficiency Associated Hemolysis and Methemoglobinemia: Patients at risk for G6PD deficiency should be screened prior to starting pegloticase.
- Gout Flares: Patients starting on urate lowering therapies are at an increased risk for gout flares when starting treatment. Patients should be started on gout flare prophylaxis at least 1 week prior to starting pegloticase, and continued on gout flare prophylaxis for at least 6 months.
- Congestive Heart Failure (CHF): Cases of CHF exacerbations were noted in the clinical trials. Caution and close monitoring should be exercised for patients who have CHF and are starting pegloticase.

- Re-treatment with Krystexxa® (pegloticase)/Immunogenicity: Re-treatment of patients that have been off pegloticase for >4 weeks has not been studied. Antibodies developed in >90% of patients treated with pegloticase during the clinical trial and post-market studies. Because of an increased risk of anaphylaxis, it is not recommended to re-start patients on pegloticase after they have been off therapy for >4 weeks.

Use in Specific Populations:

- Pregnancy: There have been no human studies in patients taking pegloticase that are pregnant. Animal data showed no evidence of structural abnormalities in rats and rabbits.
- Lactation: It is not known whether pegloticase is excreted in human milk.
- Pediatric Use: Safety and efficacy in patients younger than 18 years of age have not been established.
- Geriatric Use: More than 30% of patients included in the clinical trials were older than 65 years of age. There was no noted differences in safety or efficacy between the older and younger patients. No dose adjustments are needed for patients 65 years of age or older.
- Renal Impairment: There are no dose adjustments required for renal impairment. Patients with a creatinine clearance (CrCl) of <60mL/min were included in the clinical trials with no dose adjustments.

Adverse Reactions: Adverse reactions that occurred in >5% of the patients during clinical trials include: gout flare, infusion reactions, nausea, contusion or ecchymosis, nasopharyngistis, constipation, chest pain, anaphylaxis, and vomiting.

Efficacy: Two replicate, multicenter, randomized, double-blind, placebo-controlled studies evaluated the efficacy of pegloticase in adult patients with chronic gout refractory to conventional therapies. Studies were stratified for the presence of tophi and patients were randomized to pegloticase 8mg every 2 weeks, every 4 weeks, or placebo in a 2:2:1 ratio. All patients received prophylaxis with oral antihistamine(s), IV corticosteroid(s), and IV acetaminophen. Patients were also given gout flare prophylaxis starting at least 1 week before pegloticase treatment began. The mean age for the study was 55 years, 82% of patients were male, mean body mass index (BMI) was 33kg/m^2, mean duration of gout was 15 years, and mean baseline sUA was 10mg/dL. The primary endpoint for both trials was the proportion of patients achieving plasma uric acid <6mg/dL for >80% for the time during study months 3 and 6.

Treatment Group	N	# (%) of Subjects Who Met Response Criteria	95% CI	P-Value
Trial 1				
8mg every 2 weeks	43	20 (47%)	[32%, 61%]	<0.001
8mg every 4 weeks	41	8 (20%)	[7%, 32%]	0.044
Placebo	20	0 (0%)		
Trial 2				
8mg every 2 weeks	42	16 (38%)	[23%, 53%]	<0.001

Treatment Group	N	# (%) of Subjects Who Met Response Criteria	95% CI	P-Value
8mg every 4 weeks	43	21 (49%)	[34%, 64%]	<0.001
Placebo	23	0 (0%)		

N = number; # = number; % = percent; CI = confidence interval

The treatment of tophi was assesse as secondary efficacy endpoint of the treatment of tophi was assessed. At month 6, the percentage of patients with tophi at the beginning of the study who achieved a complete response (defined as 100% resolution of at least one target tophus, no new tophi appearing, and no single tophus showing progression) was 45%, 26%, and 8% in the 2 week, 4 week, and placebo groups, respectively.

Recommendations

The College of Pharmacy recommends the prior authorization of Krystexxa® (pegloticase) with the following criteria:

Krystexxa® (Pegloticase) Approval Criteria:

1. An FDA approved diagnosis of gout; and
2. Member must have symptomatic gout with:
    a. ≥3 gout flares in the previous 18 months; or
    b. ≥1 gout tophus; or
    c. Gouty arthritis; and
3. Failure of all urate lowering therapies (i.e., allopurinol, febuxostat, lesinurad) titrated to the maximum tolerable dose for at least 3 months; and
4. Baseline serum uric acid (sUA) >6mg/dL; and
5. Pegloticase must be administered in a health care setting by a health care provider prepared to manage anaphylaxis; and
6. Prescriber must attest that the member will be pre-medicated with antihistamines and corticosteroids to reduce the risk of anaphylaxis; and
7. Prescriber must document that member does not have or is not high-risk for glucose-6-phosphate dehydrogenase (G6PD) deficiency prior to starting pegloticase; and
8. Member must discontinue oral urate-lowering agents prior to starting pegloticase; and
9. Member must receive gout flare prophylaxis with non-steroidal anti-inflammatory drug(s) (NSAIDs) or colchicine at least 1 week before initiation of pegloticase therapy and continue for at least 6 months unless medically contraindicated or member is unable to tolerate therapy; and
10. Approvals will be for the duration of 6 months.
11. Reauthorizations may be granted if the prescriber documents the member is responding well to treatment, and member has not exceeded >4 consecutive weeks without therapy.

Utilization Details of Gout Medications: Fiscal Year 2018

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS*	TOTAL COST	COST/ DAY	COST/ CLAIM
ALLOPURINOL PRODUCTS					
ALLOPURINOL TAB 300MG	2,495	592	$40,207.52	$0.37	$16.12
ALLOPURINOL TAB 100MG	2,266	599	$28,393.72	$0.30	$12.53
SUBTOTAL	**4,761**	**1,191**	**$68,601.24**	**$0.34**	**$14.41**
COLCHICINE PRODUCTS					
COLCHICINE TAB 0.6MG	538	189	$26,337.35	$7.71	$48.95
COLCHICINE CAP 0.6MG	77	27	$7,330.13	$7.73	$95.20
COLCRYS TAB 0.6MG	53	37	$2,848.83	$8.19	$53.75
MITIGARE CAP 0.6MG	3	2	$121.11	$10.09	$40.37
PROBEN/COLCH TAB 500-0.5MG	72	23	$3,031.81	$1.29	$42.11
SUBTOTAL	**743**	**278**	**$39,669.23**	**$5.61**	**$53.39**
FEBUXOSTAT PRODUCTS					
ULORIC TAB 40MG	174	31	$47,774.73	$9.64	$274.57
ULORIC TAB 80MG	91	12	$27,854.86	$10.20	$306.10
SUBTOTAL	**265**	**43**	**$75,629.59**	**$9.84**	**$285.39**
TOTAL	**5,769**	**1,330***	**$183,900.06**	**$0.85**	**$31.88**

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

[1] Endo International Plc. Endo Begins Shipment of Authorized Generic Version of Colcrys® (colchicine, USP) in the United States. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/endo-begins-shipment-of-authorized-generic-version-of-colcrys-colchicine-usp-in-the-united-states-300675173.html. Issued 07/02/2018. Last accessed 09/17/2018.
[2] 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. Issued 11/15/2018. Last accessed 09/10/2018.
[3] FDA. FDA Drug Safety Communication: FDA to evaluate increased risk of heart-related death and death from all causes with the gout medicine febuxostat (Uloric). Available online at: https://www.fda.gov/Drugs/DrugSafety/ucm584702.htm. Last revised 08/22/2018. Last accessed 09/10/2018.
[4] White WB, Sagg KG, Becker MA, et al. Cardiovascular Safety of Febuxostat or Allopurinol in Patients with Gout. *N Engl J Med* 2018; 378:1200-1210.
[5] Terry M. Consumer Group Pressures FDA to Pull Takeda's Gout Drug Off the Market. *BioSpace*. Available online at: https://www.biospace.com/article/consumer-group-pressures-fda-to-pull-takeda-s-gout-drug-off-the-market. Issued 06/22/2018. Last accessed 09/10/2018.
[6] Poiley J, Steinberg AS, Choi YJ, et al. A Randomized, Double-Blind, Active- and Placebo-Controlled Efficacy and Safety Study of Arhalofenate for Reducing Flare in Patients With Gout. *Arthritis Rheumatol* 2016; 68(8):2027-2034.
[7] Krystexxa® Prescribing Information. Horizon Pharma PLC. Available online at: https://hznp.azureedge.net/public/KRYSTEXXA_Prescribing_Information.pdf. Last revised 07/2018. Last accessed 09/20/2018.

Appendix R

Industry News and Updates

Oklahoma Health Care Authority
October 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]

News:

- **Sexually Transmitted Diseases (STDs):** According to the Centers for Disease Control and Prevention (CDC), preliminary data indicate that rates of three STDs (*Chlamydia* infection, gonorrhea, and syphilis) hit an all-time high in 2017. The CDC stated that the United States is on track to have 555,608 cases of gonorrhea, 30,644 cases of primary and secondary syphilis, and 1.7 million cases of *Chlamydia* infection in 2017. This represents 200,000 more cases of the three reportable STDs than in 2016, and it is the fourth year in a row that the United States has had a significant increase in those conditions. Several reasons were cited for the steady increase in sexually transmitted infections, including: a lack of education about and awareness of sexual health and STDs; a lack of screening by physicians; patients not asking for screening or treatment; and decades of underfunding of public health efforts to prevent, diagnose, and treat the conditions.
- **Hospital Groups:** In an effort to combat chronic drug shortages and high prescription prices, several major hospital groups launched their own generic drug company. The new company, Civica Rx, plans to begin with 14 commonly used hospital drugs that have long been in short supply. Due to competitive reasons, the company is not releasing the drugs' names, but they will include a mix of generic pills, patches, and injectable drugs for treating infections, pain, and heart conditions. For more than a decade, drug shortages have been widespread, particularly for inexpensive medications, due to manufacturers consolidating, stopping production of low-profit medicines, and needing to fix manufacturing problems. Hospitals frequently must try to find scarce medicines, often at large price markups or they must come up with workarounds that may not be as effective or safe. Civica Rx aims to reduce drug prices by approximately 20%, as well as create a reliable supply of medicines for its 500 hospitals. The drugs will also be sold to nonmember hospitals, at a slightly higher price. The company plans to make some of the generics itself and hire companies to produce others. Civica Rx plans to get its first medicines on the market by mid- to late 2019.
- **Single-Dose Flu Drug:** According to results of a recent study published in *The New England Journal of Medicine*, the investigational drug baloxavir marboxil successfully and safely reduced influenza symptoms and viral load after only one dose. Baloxavir is a

selective inhibitor of influenza cap-dependent endonuclease and has shown therapeutic activity in preclinical models of influenza A and B. Researchers conducted two randomized, double-blind, controlled trials involving patients with acute uncomplicated influenza to further examine this drug. After a placebo-controlled trial in which patients were given doses ranging from 10 to 40mg, the researchers conducted a placebo- and oseltamivir-controlled trial of single, weight-based doses of baloxavir (40 or 80mg) in patients 12 to 64 years of age. The median time to symptom alleviation was 23.4 to 28.2 hours shorter in the baloxavir group compared to the placebo group in the Phase 2 trial. In the Phase 3 trial, the time to alleviation was 53.7 hours for baloxavir, compared to 80.2 hours with placebo, and was similar with baloxavir and oseltamivir. Reductions in viral load after 1 day were greater with baloxavir compared to placebo or oseltamivir. Adverse events were reported in 20.7% of baloxavir recipients, 24.6% of placebo recipients, and 24.8% of oseltamivir recipients.

---

[1] Ault A. Three STDs Hit All-Time High in 2017, New CDC Data Show. *Medscape*. Available online at: https://www.medscape.com/viewarticle/901298?nlid=124753_3901&src=wnl_newsalrt_180828_MSCPEDIT&uac=163910MN&impID=1724480&faf=1#vp_1. Issued 08/28/2018. Last accessed 08/31/2018.

[2] Johnson LA. Hospital groups launch own company to make generic drugs. *Associated Press*. Available online at: https://apnews.com/b7c79634241c4df6a73b9d075991b0ca/Hospital-groups-launch-own-company-to-make-generic-drugs. Issued 09/06/2018. Last accessed 09/07/2018.

[3] Potts M. Single-Dose Flu Drug Could Be Promising. *Managed Health Care*. Available online at: https://www.managedhealthcareconnect.com/content/single-dose-flu-drug-could-be-promising. Issued 09/10/2018. Last accessed 09/18/2018.

Appendix S

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

FDA NEWS RELEASE

For Immediate Release: September 13th, 2018

FDA approves new kind of treatment for hairy cell leukemia

The FDA approved Lumoxiti (moxetumomab pasudotox-tdfk) injection for intravenous use for the treatment of adult patients with relapsed or refractory hairy cell leukemia (HCL) who have received at least two prior systemic therapies, including treatment with a purine nucleoside analog. Lumoxiti is a CD22-directed cytotoxin and is the first of this type of treatment for patients with HCL.

HCL is a rare, slow-growing cancer of the blood in which the bone marrow makes too many B cells (lymphocytes), a type of white blood cell that fights infection. HCL is named after these extra B cells which look "hairy" when viewed under a microscope. As the number of leukemia cells increases, fewer healthy white blood cells, red blood cells and platelets are produced.

The efficacy of Lumoxiti was studied in a single-arm, open-label clinical trial of 80 patients who had received prior treatment for HCL with at least two systemic therapies, including a purine nucleoside analog. The trial measured durable complete response (CR), defined as maintenance of hematologic remission for more than 180 days after achievement of CR. Thirty percent of patients in the trial achieved durable CR, and the overall response rate (number of patients with partial or complete response to therapy) was 75 percent.

Common side effects of Lumoxiti include infusion-related reactions, swelling caused by excess fluid in body tissue (edema), nausea, fatigue, headache, fever (pyrexia), constipation, anemia and diarrhea.

The prescribing information for Lumoxiti includes a Boxed Warning to advise health care professionals and patients about the risk of developing capillary leak syndrome, a condition in which fluid and proteins leak out of tiny blood vessels into surrounding tissues. Symptoms of capillary leak syndrome include difficulty breathing, weight gain, hypotension, or swelling of arms, legs and/or face. The Boxed Warning also notes the risk of hemolytic uremic syndrome, a condition caused by the abnormal destruction of red blood cells. Patients should be made aware of the importance of maintaining adequate fluid intake, and blood chemistry values should be monitored frequently. Other serious warnings include: decreased renal function, infusion-related reactions and electrolyte abnormalities. Women who are breastfeeding should not be given Lumoxiti.

The FDA granted this application Fast Track and Priority Review designations. Lumoxiti also received Orphan Drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases.

The FDA granted the approval of Lumoxiti to AstraZeneca Pharmaceuticals.

FDA NEWS RELEASE

For Immediate Release: September 28th, 2018

FDA approves first treatment for advanced form of the second most common skin cancer

New drug targets PD-1 pathway

The FDA approved Libtayo (cemiplimab-rwlc) injection for intravenous use for the treatment of patients with metastatic cutaneous squamous cell carcinoma (CSCC) or locally advanced CSCC who are not candidates for curative surgery or curative radiation. This is the first FDA approval of a drug specifically for advanced CSCC. Libtayo works by targeting the cellular pathway known as PD-1 (protein found on the body's immune cells and some cancer cells). By blocking this pathway, the drug may help the body's immune system fight the cancer cells.

CSCC is the second most common human cancer in the United States with an estimated annual incidence of approximately 700,000 cases. The most common form of skin cancer is basal cell cancer. Squamous cells are thin, flat cells that look like fish scales and are found in the tissue that forms the surface of the skin. CSCC usually develops in skin areas that have been regularly exposed to the sun or other forms of ultraviolet radiation. While the majority of patients with CSCC are cured with surgical resection, a small percentage of patients will develop advanced disease that no longer responds to local treatments including surgery and radiation. Advanced CSCC may cause disfigurement at the site of the tumor and local complications such as bleeding or infection, or it may spread (metastasize) to local lymph nodes, distant tissues and organs and become life-threatening.

The safety and efficacy of Libtayo was studied in two open label clinical trials. A total of 108 patients (75 with metastatic disease and 33 with locally-advanced disease) were included in the efficacy evaluation. The study's primary endpoint was objective response rate, or the percentage of patients who experienced partial shrinkage or complete disappearance of their tumor(s) after treatment. Results showed that 47.2 percent of all patients treated with Libtayo had their tumors shrink or disappear. The majority of these patients had ongoing responses at the time of data analysis.
Common side effects of Libtayo include fatigue, rash and diarrhea. Libtayo must be dispensed with a patient Medication Guide that describes uses of the drug and its serious warnings. Libtayo can cause the immune system to attack normal organs and tissues in any area of the body and can affect the way they work. These reactions can sometimes become severe or life-threatening and can lead to death. These reactions include the risk of immune-mediated adverse reactions including lung problems (pneumonitis), intestinal problems (colitis), liver problems (hepatitis), hormone gland problems (endocrinopathies), skin (dermatologic) problems and kidney problems. Patients should also be monitored for infusion-related reactions.
Libtayo can cause harm to a developing fetus; women should be advised of the potential risk to the fetus and to use effective contraception.
The FDA granted this application Breakthrough Therapy and Priority Review designations.
The FDA granted the approval of Libtayo to Regeneron Pharmaceuticals, Inc.

FDA NEWS RELEASE

For Immediate Release: September 28th, 2018

FDA approves a new antibacterial drug to treat a serious lung disease using a novel pathway to spur innovation

First drug granted approval under FDA's Limited Population Pathway for Antibacterial and Antifungal Drugs, instituted to spur development of antibiotics for unmet medical needs

The FDA approved a new drug, Arikayce (amikacin liposome inhalation suspension), for the treatment of lung disease caused by a group of bacteria, Mycobacterium avium complex (MAC) in a limited population of patients with the disease who do not respond to conventional treatment (refractory disease).
MAC is a type of nontuberculous mycobacteria (NTM) commonly found in water and soil. Symptoms of disease in patients with MAC include persistent cough, fatigue, weight loss, night sweats, and occasionally shortness of breath and coughing up of blood.
Arikayce is the first drug to be approved under the Limited Population Pathway for Antibacterial and Antifungal Drugs, or LPAD pathway, established by Congress under the 21st Century Cures Act to advance development and approval of antibacterial and antifungal drugs to treat serious or life-threatening infections in a limited population of patients with unmet need. Approval under the LPAD pathway may be supported by a streamlined clinical development program. These programs may involve smaller, shorter or fewer clinical trials. As required for drugs approved under the LPAD pathway, labeling for Arikayce includes certain statements to convey that the drug has been shown to be safe and effective only for use in a limited population.
Arikayce also was approved under the Accelerated Approval pathway. Under this approach, the FDA may approve drugs for serious or life-threatening diseases or conditions where the drug is shown to have an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit to patients. The approval of Arikayce was based on achieving three consecutive negative monthly sputum cultures by month six of treatment. The sponsor of Arikayce will be required by the FDA to conduct an additional, post-market study to describe the clinical benefits of Arikayce.
The safety and efficacy of Arikayce, an inhaled treatment taken through a nebulizer, was demonstrated in a randomized, controlled clinical trial where patients were assigned to one of two treatment groups. One group of patients received Arikayce plus a background multi-drug antibacterial regimen, while the other treatment group received a background multi-drug antibacterial regimen alone. By the sixth month of treatment, 29 percent of patients treated with Arikayce had no growth of mycobacteria in their sputum cultures for three consecutive months compared to 9 percent of patients who were not treated with Arikayce.
The Arikayce prescribing information includes a Boxed Warning regarding the increased risk of respiratory conditions including hypersensitivity pneumonitis (inflamed lungs), bronchospasm (tightening of the airway), exacerbation of underlying lung disease and hemoptysis (spitting up blood) that have led to hospitalizations in some cases. Other common side effects in patients taking Arikayce were dysphonia (difficulty speaking), cough, ototoxicity (damaged hearing), upper airway irritation, musculoskeletal pain, fatigue, diarrhea and nausea.

The FDA granted this application Fast Track, Breakthrough Therapy, Priority Review, and Qualified Infectious Disease Product (QIDP) designations. QIDP designation is given to antibacterial products that treat serious or life-threatening infections under the Generating Antibiotic Incentives Now (GAIN) title of the FDA Safety and Innovation Act. Arikayce also received Orphan Drug designation, which provides additional incentives to assist and encourage the development of drugs for rare diseases.
The FDA granted approval of Arikayce to Insmed, Inc. of Bridgewater, NJ.

Safety Announcements

FDA Drug Safety Communication: FDA to evaluate potential risk of neural tube birth defects with HIV medicine dolutegravir (Juluca, Tivicay, Triumeq)

[09/20/2018] The FDA is alerting the public that serious cases of neural tube birth defects involving the brain, spine, and spinal cord have been reported in babies born to women treated with dolutegravir used to treat human immunodeficiency virus (HIV). Preliminary results from an ongoing observational study in Botswana found that women who received dolutegravir at the time of becoming pregnant or early in the first trimester appear to be at higher risk for these defects.
Neural tube defects are birth defects that can occur early in pregnancy when the spinal cord, brain, and related structures do not form properly. To date, in this observational study there are no reported cases of babies born with neural tube defects to women starting dolutegravir later in pregnancy. The FDA is investigating this new safety issue and will update the public when they have more information.
Dolutegravir is an FDA-approved antiretroviral medicine used in combination with other antiretroviral medicines to treat HIV, the virus that can cause acquired immunodeficiency syndrome (AIDS). Dolutegravir works by blocking integrase, an HIV enzyme, to prevent the virus from multiplying and can reduce the amount of HIV in the body. Stopping dolutegravir without first talking to a prescriber can cause the HIV infection to become worse. Approved in 2013, dolutegravir has been on the market for 5 years, and is available as a single ingredient product under the brand name Tivicay and as a fixed dose combination tablet with other HIV medicines under the brand names Juluca and Triumeq.
Patients should not stop taking dolutegravir without first talking to their health care professional because stopping their medicine can cause the HIV infection to worsen. In addition:

- If patients are already pregnant, stopping a dolutegravir-containing regimen without switching to alternative HIV medicines could cause the amount of virus to increase and spread HIV to the baby.
- If patients are taking a dolutegravir-containing regimen at the time of becoming pregnant and during the first trimester of pregnancy, there is a risk that the baby may develop neural tube defects. Neural tube defects happen early in pregnancy, before many women even know they are pregnant. For this reason, women of childbearing age should talk to their health care professional about other non-dolutegravir-containing antiretroviral medicines.
- Patients should tell their health care professional if they are pregnant or are planning to become pregnant before they start a dolutegravir-containing regimen. The patient's health care professional may discuss other treatment options with them.
- Women of childbearing age who decide to take a dolutegravir-containing regimen should consistently use effective birth control while on HIV treatment. Women should talk to their health care professionals about an effective birth control method to use while taking a dolutegravir-containing regimen.
- Before patients start a dolutegravir-containing regimen they will need a pregnancy test to determine if they are already pregnant.

  Health care professionals should inform women of childbearing age about the potential risk of neural tube defects when a dolutegravir-containing regimen is used at the time of conception and early in pregnancy. In addition:
- **Health care professionals** should weigh the benefits and the risks of dolutegravir when prescribing antiretroviral medicines to women of childbearing age. Alternative antiretroviral medicines should be considered. Discuss the relative risks and benefits of appropriate alternative antiretroviral therapies.
- If the decision is made to use dolutegravir in women of childbearing age, health care professionals should reinforce the consistent use of effective birth control.
- Perform pregnancy testing before initiating a dolutegravir-containing regimen in women of childbearing age to exclude pregnancy.

Ongoing monitoring will continue as part of the observational study in Botswana. Additional birth outcomes are projected from pregnant women who were exposed to dolutegravir at the time of becoming pregnant. We will conduct a comprehensive review of the results and any other data that becomes available. We will update the

public with any new information. To monitor birth outcomes of pregnant women, report pregnancy exposures to the Antiretroviral Pregnancy Registry at 1-800-258-4263.
The FDA urges health care professionals and patients to report side effects involving dolutegravir or other medicines to the FDA MedWatch program.

Safety Announcements

FDA takes important steps to encourage appropriate and rational prescribing of opioids through final approval of new safety measures governing the use of immediate-release opioid analgesic medications

The action places immediate-release opioid analgesic drugs intended for use in an outpatient setting into agency's Opioid Analgesic Risk Evaluation and Mitigation Strategy

[09/18/2018] The FDA took new steps as part of its broader efforts to address the opioid crisis by approving the final Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS). This new plan includes several measures to help better communicate the serious risks about the use of opioid pain medications to patients and health care professionals. This expanded REMS now, for the first time, applies to immediate-release (IR) opioid analgesics intended for use in an outpatient setting. The new REMS also applies to the extended-release and long-acting (ER/LA) opioid analgesics, which have been subject to a REMS since 2012.
The REMS program requires, for the first time, that training be made available to health care providers who are involved in the management of patients with pain, and not only to prescribers. For example, the training provided through the REMS must be made available to nurses and pharmacists. The new REMS also requires that the education cover broader information about appropriate pain management, including alternatives to opioids for the treatment of pain. The agency is also approving new product labeling containing information about the health care provider education available through the new REMS.
Since 2012, manufacturers of ER/LA opioid analgesics have been subject to a REMS that requires as its primary component, that training be made available to prescribers of those products. To meet this requirement, drug companies with approved ER/LA opioid analgesics have been providing unrestricted grants to accredited continuing education providers for the development of education courses for prescribers based on content outlined by the FDA. As part of the final action being taken today, these REMS requirements now also apply to IR opioid analgesic products intended for outpatient use. The IR drugs account for about 90 percent of all opioid pain medications prescribed for outpatient use. Additionally, the entire class of transmucosal immediate-release fentanyl (TIRF) prescription medicines have been subject to a REMS since December 2011.
In addition to expanding the REMS to include IR opioid analgesic products intended for outpatient use, the agency has approved the new FDA Opioid Analgesic REMS Education Blueprint for Health Care Providers Involved in the Treatment and Monitoring of Patients with Pain. This includes updated educational content. The agency believes that all health care providers involved in the management of patients with pain should be educated about the safe use of opioids so that when they write or dispense a prescription for an opioid analgesic, or monitor patients receiving these medications, they can help ensure the proper product is selected for the patient and used with appropriate clinical oversight. It is expected that continuing education training under the modified REMS will be available to health care providers by March 2019.
The action greatly expands the number of products covered by the REMS. Prior to that, the ER/LA Opioid Analgesic REMS included 62 products. But the modified Opioid Analgesic REMS now requires that 347 opioid analgesics intended for outpatient use be subject to these REMS requirements. The REMS program continues to include Medication Guides for patients and caregivers to read, new Patient Counseling Guides to assist health care providers with important discussions with patients, and plans for assessing the program's effectiveness.
The FDA is also approving new safety labeling changes for all opioid analgesic products intended for use in an outpatient setting. For the first time, the FDA is requiring the labeling for those products to include information about the availability of education through the REMS for prescribers and other health care providers who are involved in the treatment and monitoring of patients with pain. The new labeling includes information about REMS-compliant education in the Boxed Warning and Warnings and Precautions sections of labeling and strongly encourages providers to complete a REMS-compliant education program; counsel patients and caregivers on the safe use, risks, and appropriate storage and disposal of these products; emphasize to patients and their caregivers the importance of reading the Medication Guide every time it is provided by their pharmacist; and to consider other tools to improve patient, household and community safety.
There is no mandatory federal requirement that prescribers or other health care providers take the training provided through the REMS and completion of the training is not a precondition to prescribing opioid

analgesics to patients. However, the FDA's Opioid Policy Steering Committee continues to consider whether there are circumstances when the FDA should require some form of mandatory education for health care providers and how the agency would pursue such a goal. The FDA also recently awarded a contract to the National Academies of Sciences, Engineering, and Medicine to help develop a framework to assist medical professional societies in creating evidence-based guidelines on appropriate opioid analgesic prescribing to treat acute pain resulting from specific medical conditions and common surgical procedures for which these drugs are prescribed. The agency's aim is to reduce unnecessary and/or inappropriate exposure to opioids by making certain that prescribers are properly informed about appropriate prescribing recommendations, that providers understand how to identify abuse by individual patients, and know how to get patients with opioid use disorder into treatment. The crisis of opioid addiction is a public health tragedy of enormous proportions. The FDA's goal is to reduce serious adverse outcomes resulting from inappropriate prescribing, misuse and abuse of opioid analgesics, while maintaining patient access to pain medications.

As part of the U.S. Department of Health and Human Services' Five-Point Strategy to Combat the Opioid Crisis, the FDA remains committed to addressing the national crisis of opioid addiction on all fronts, with a significant focus on decreasing unnecessary and/or inappropriate exposure to opioids and preventing new addiction; supporting the treatment of those with opioid use disorder; fostering the development of novel pain treatment therapies and opioids more resistant to abuse and misuse; and taking action against those who contribute to the illegal importation and sale of opioid products. The FDA will also continue to evaluate how drugs currently on the market are used, in both medical and illicit settings, and take regulatory action where needed.

Safety Announcements

FDA analysis finds no new or unexpected safety risks associated with Nuplazid (pimavanserin), a medication to treat the hallucinations and delusions of Parkinson's disease psychosis

[09/18/2018] The FDA has completed a review of all postmarketing reports of deaths and serious adverse events (SAEs) reported with the use of Nuplazid (pimavanserin). Based on an analysis of all available data, FDA did not identify any new or unexpected safety findings with Nuplazid, or findings that are inconsistent with the established safety profile currently described in the drug label. After a thorough review, FDA's conclusion remains unchanged that the drug's benefits outweigh its risks for patients with hallucinations and delusions of Parkinson's disease psychosis.

Nuplazid and other antipsychotics have a Boxed Warning regarding the increased risk of death in elderly patients with dementia-related psychosis associated with the use of these drugs. In view of the numbers of reports of death and other serious adverse events, FDA conducted a comprehensive analysis of all available information. This analysis included information submitted to the FDA Adverse Event Reporting System (FAERS), drug utilization data, safety data from the Nuplazid new drug application, the sponsor's Periodic Adverse Drug Experience Reports, the sponsor's analysis of fatal adverse event reports with Nuplazid and published medical literature.

In assessing the reports of deaths, FDA considered that patients with Parkinson's disease psychosis, for whom Nuplazid is indicated, have a higher mortality (death) rate due to their older age, advanced Parkinson's disease, and other medical conditions. Moreover, Nuplazid is primarily distributed through a patient support program and a specialty pharmacy network, which increases the likelihood that deaths will be reported to the manufacturer. In FAERS reports that included a cause of death (many reports did not provide sufficient information to assess drug cause and effect), there was no evident pattern to suggest a drug effect. Overall, the postmarketing data were consistent with the safety data obtained from the premarketing controlled clinical trials of Nuplazid for Parkinson's disease psychosis.

Although FDA did not identify any new or unexpected safety risks, some potentially concerning prescribing patterns were observed, such as the concomitant use of other antipsychotic drugs or drugs that can cause QT prolongation, a potential cause of heart rhythm disorder. The risk of QT prolongation and serious arrhythmia associated with Nuplazid is noted in the Warnings and Precautions section of the drug label, which warns of the increased risks associated with using Nuplazid together with other drugs known to cause QT interval prolongation. Based on this observation, FDA reminds health care providers to be aware of the risks described in the prescribing information. FDA also reminds heath care providers that none of the other antipsychotic medications are approved for the treatment of Parkinson's disease psychosis.

Patients taking Nuplazid for Parkinson's disease psychosis should continue to use it as prescribed by their health care provider. FDA continues to monitor reports of adverse events associated with Nuplazid. The

agency will communicate any updates to the public as necessary. To help FDA assess potential medication safety issues, the FDA urges health care providers and patients to report suspected side effects involving Nuplazid and other drugs to the FDA MedWatch program.

Current Drug Shortages Index (as of October 2nd, 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***
Aminophylline Injection, USP	***Currently in Shortage***
Asparaginase Erwinia Chrysanthemi (Erwinaze)	***Currently in Shortage***
Atenolol Tablets	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Azithromycin (Azasite) Ophthalmic Solution 1%	***Currently in Shortage***
Belatacept (Nulojix) Lyophilized Powder for Injection	***Currently in Shortage***
Belladonna and Opium Suppository	***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***
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***
Diphenhydramine Injection	***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***
Epinephrine Injection, Auto-Injector	***Currently in Shortage***
Erythromycin Lactobionate for Injection, USP	***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 Injection	***Currently in Shortage***
Fluorescein Sodium and Benoxinate Hydrochloride Ophthalmic Solution	***Currently in Shortage***
Fluorescein Strips	***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***
Isocarboxazid Tablets	***Currently in Shortage***
Ketamine Injection	***Currently in Shortage***
Ketoprofen Capsules	***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***
Lorazepam Injection, USP	***Currently in Shortage***
Magnesium Sulfate Injection	***Currently in Shortage***
Methadone Hydrochloride Injection	***Currently in Shortage***
Methocarbamol Tablets	***Currently in Shortage***
Methotrexate Sodium Injection	***Currently in Shortage***
Methyldopa Tablets	***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***
Penicillamine (Depen) Titratable Tablets	***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***
Scopolamine Transdermal System	***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 Chloride Injection USP, 0.9% Vials and Syringes	***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***
Thiothixene Capsules	***Currently in Shortage***
Trifluoperazine Hydrochloride Tablets	***Currently in Shortage***
Valsartan Tablets	***Currently in Shortage***
Zolpidem Tartrate (Edluar) Sublingual Tablets	***Currently in Shortage***