OKLAHOMA
Health Care Authority

Drug Utilization Review Board

Wednesday,
December 9, 2020
4:00pm

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

Viewing Access Only:
Register for the meeting by clicking on
"Join Meeting as an Attendee" at the following website address:
https://okhca.zoom.us/s/99321236734?pwd=clB4STJmSlBVZklZeDRIVmM3OWozdz09

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

MEMORANDUM

TO: Drug Utilization Review (DUR) Board Members

FROM: Michyla Adams, Pharm.D.

SUBJECT: Packet Contents for DUR Board Meeting – December 9, 2020

DATE: November 23, 2020

NOTE: ***The DUR Board will meet at 4:00pm. For all DUR Board members, College of Pharmacy presenters, and any speakers who sign up in advance for public comment, this meeting will be held in person at the Oklahoma Health Care Authority (OHCA) at 4345 N. Lincoln Blvd in Oklahoma City, Oklahoma. In response to COVID-19, masks, social distancing, and temperature checks will be required for all in person attendees. For additional information on OHCA's COVID-19 precautions and protocols for admittance into the Agency, please go to http://www.okhca.org.***

All non-speaking attendees are encouraged to join this meeting via Zoom access. The Zoom access will be set up in listen-only mode with no voting, speaking, or chat box privileges; however, the Zoom access will allow for viewing of the presentation slides during the meeting.

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Enclosed are the following items related to the December 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

Maintenance Drug List – Appendix B

Update on Medication Coverage Authorization Unit/Pediatric Antipsychotic Monitoring Program Update – Appendix C

Action Item – Vote to Prior Authorize AirDuo® Digihaler® (Fluticasone Propionate/Salmeterol), ArmonAir® Digihaler® (Fluticasone Propionate), and Breztri Aerosphere™ (Budesonide/Glycopyrrolate/Formoterol Fumarate) – Appendix D

Action Item – Vote to Prior Authorize Blenrep (Belantamab Mafodotin-blmf), Darzalex® (Daratumumab), Darzalex Faspro™ (Daratumumab/Hyaluronidase-fihj), Empliciti® (Elotuzumab), Hemady™ (Dexamethasone 20mg Tablet), Ninlaro® (Ixazomib), Sarclisa® (Isatuximab-irfc), and Xpovio® (Selinexor) – Appendix E

Action Item – Vote to Prior Authorize Lenvima® (Lenvatinib) – Appendix F

Action Item – Annual Review of Skin Cancer Medications – Appendix G

Action Item – Annual Review of Antidepressants – Appendix H

Annual Review of Targeted Immunomodulator Agents and 30-Day Notice to Prior Authorize Abrilada™ (Adalimumab-afzb), Avsola™ (Infliximab-axxq), and Hulio® (Adalimumab-fkjp) – Appendix I

Annual Review of Soliris® (Eculizumab) and Ultomiris® (Ravulizumab-cwvz) and 30-Day Notice to Prior Authorize Enspryng™ (Satralizumab-mwge) and Uplizna™ (Inebilizumab-cdon) – Appendix J

Annual Review of Ulcerative Colitis (UC) and Crohn's Disease Medications and 30-Day Notice to Prior Authorize Ortikos™ [Budesonide Extended-Release (ER) Capsule] – Appendix K

Annual Review of Constipation and Diarrhea Medications and 30-Day Notice to Prior Authorize Pizensy™ (Lactitol) – Appendix L

Annual Review of Thrombocytopenia Medications – Appendix M

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

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – December 9, 2020 @ 4:00pm
at the
Oklahoma Health Care Authority (OHCA)
4345 N. Lincoln Blvd.
Oklahoma City, Oklahoma 73105

NOTE: ***For all DUR Board members, College of Pharmacy presenters, and any speakers who sign up in advance for public comment, this meeting will be held in person at OHCA (see address above). In response to COVID-19, masks, social distancing, and temperature checks will be required for all in person attendees. For additional information on OHCA's COVID-19 precautions and protocols for admittance into the Agency, please go to http://www.okhca.org.***

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AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

1. Call to Order
A. Roll Call – Dr. Wilcox

DUR Board Members:

Dr. Stephen Anderson –	participating in person
Dr. Jennifer de los Angeles –	participating in person
Ms. Jennifer Boyett –	participating in person
Dr. Markita Broyles –	participating in person
Dr. Theresa Garton –	participating in person
Dr. Megan Hanner –	participating in person
Dr. Lynn Mitchell –	participating in person
Dr. John Muchmore –	participating in person
Dr. Lee Muñoz –	participating in person
Dr. James Osborne –	participating in person

Public Access to Meeting via Zoom:
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https://okhca.zoom.us/s/99321236734?pwd=clB4STJmSlBVZklZeDRIVmM3OWozdz09

Or join by phone:
Dial: +1-669-900-6833 or +1-253-215-8782
Webinar ID: 993 2123 6734

Public Comment for Meeting:

- Speakers who wish to sign up for public comment at the OHCA DUR Board meeting may do so in writing by visiting www.okhca.org/DUR and completing the Speaker Registration Form. Completed Speaker Registration forms should be submitted to *DURPublicComment@okhca.org*. Forms must be received after the DUR Board agenda has been posted and no later than 24 hours before the meeting.
- The DUR Board meeting will allow public comment and time will be limited to 40 minutes total for all speakers during the meeting. Each speaker will be given 5 minutes to speak at the public hearing. If more than 8 speakers properly request to speak, time will be divided evenly.
- Only 1 speaker per manufacturer will be allowed.
- For the December 2020 DUR Board meeting, any speakers who sign up for public comment must attend the DUR Board meeting in person at OHCA (see address above). Public comment through the OHCA Webinar will not be allowed for the December 2020 DUR Board meeting.

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. November 4, 2020 DUR Minutes – Vote
B. November 4, 2020 DUR Recommendations Memorandum
C. Correspondence

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

4. Maintenance Drug List – See Appendix B

A. Introduction
B. SoonerCare Maintenance Drug List

Items to be presented by Dr. Ha, Dr. Travers, Dr. Muchmore, Chairman:

5. Update on Medication Coverage Authorization Unit/Pediatric Antipsychotic Monitoring Program Update – See Appendix C

A. Pharmacy Helpdesk Activity for November 2020
B. Medication Coverage Activity for November 2020
C. Pediatric Antipsychotic Monitoring Program Update

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

6. Action Item – Vote to Prior Authorize AirDuo® Digihaler® (Fluticasone Propionate/Salmeterol), ArmonAir® Digihaler® (Fluticasone Propionate), and Breztri Aerosphere™ (Budesonide/Glycopyrrolate/Formoterol Fumarate) – See Appendix D

A. New U.S. Food and Drug Administration (FDA) Approval(s)
B. New FDA Expanded Indication(s) and/or Formulation(s)
C. College of Pharmacy Recommendations

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

7. Action Item – Vote to Prior Authorize Blenrep (Belantamab Mafodotin-blmf), Darzalex® (Daratumumab), Darzalex Faspro™ (Daratumumab/Hyaluronidase-fihj), Empliciti® (Elotuzumab), Hemady™ (Dexamethasone 20mg Tablet), Ninlaro® (Ixazomib), Sarclisa® (Isatuximab-irfc), and Xpovio® (Selinexor) – See Appendix E

A. U.S. Food and Drug Administration (FDA) Approval(s) and Indication(s)
B. Product Summaries
C. Recommendations

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

8. Action Item – Vote to Prior Authorize Lenvima® (Lenvatinib) – See Appendix F

A. Lenvima® (Lenvatinib) Product Summary
B. Recommendations

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

9. Action Item – Annual Review of Skin Cancer Medications – See Appendix G

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. Recommendations
G. Utilization Details of Skin Cancer Medications

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

10. Action Item – Annual Review of Antidepressants – See Appendix H

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

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

11. Annual Review of Targeted Immunomodulator Agents and 30-Day Notice to Prior Authorize Abrilada™ (Adalimumab-afzb), Avsola™ (Infliximab-axxq), and Hulio® (Adalimumab-fkjp) – See Appendix I

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

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

12. Annual Review of Soliris® (Eculizumab) and Ultomiris® (Ravulizumab-cwvz) and 30-Day Notice to Prior Authorize Enspryng™ (Satralizumab-mwge) and Uplizna™ (Inebilizumab-cdon) – See Appendix J

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Soliris® (Eculizumab) and Ultomiris® (Ravulizumab-cwvz)
D. Prior Authorization of Soliris® (Eculizumab) and Ultomiris® (Ravulizumab-cwvz)
E. Market News and Updates
F. Enspryng™ (Satralizumab-mwge) Product Summary
G. Uplizna™ (Inebilizumab-cdon) Product Summary
H. College of Pharmacy Recommendations
I. Utilization Details of Soliris® (Eculizumab) and Ultomiris® (Ravulizumab-cwvz)

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

13. Annual Review of Ulcerative Colitis (UC) and Crohn's Disease Medications and 30-Day Notice to Prior Authorize Ortikos™ [Budesonide Extended-Release (ER) Capsule] – See Appendix K

A. Current Prior Authorization Criteria

B. Utilization of UC and Crohn's Disease Medications
C. Prior Authorization of UC and Crohn's Disease Medications
D. Market News and Updates
E. Ortikos™ (Budesonide ER Capsule) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of UC and Crohn's Disease Medications

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

14. Annual Review of Constipation and Diarrhea Medications and 30-Day Notice to Prior Authorize Pizensy™ (Lactitol) – See Appendix L

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. Pizensy™ (Lactitol) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Constipation Medications
H. Utilization Details of Diarrhea Medications

Non-Presentation/Questions Only:

15. Annual Review of Thrombocytopenia Medications – See Appendix M

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

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

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

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

17. Future Business* (Upcoming Product and Class Reviews)
No live meeting scheduled for January 2021. January 2021 will be a packet only meeting.

A. Antiviral Medications
B. Glaucoma Medications
C. Gonadotropin-Releasing Hormone (GnRH) Medications
D. Hyperlipidemia Medications
**Future product and class reviews subject to change.*

18. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW (DUR) BOARD MEETING
MINUTES OF MEETING NOVEMBER 4, 2020

BOARD MEMBERS:	PRESENT	ABSENT
Stephen Anderson, Pharm.D.		x
Jennifer de los Angeles, Pharm.D., BCOP	x	
Jennifer Boyett, MHS; PA-C	x	
Markita Broyles, D.Ph.; MBA	x	
Theresa Garton, M.D.	x	
Megan A. Hanner, D.O.	x	
Lynn Mitchell, M.D.; Vice Chairwoman	x	
John Muchmore, M.D.; Ph.D.; Chairman	x	
Lee Muñoz, D.Ph.	x	
James Osborne, Pharm.D.		x

COLLEGE OF PHARMACY STAFF:	PRESENT	ABSENT
Michyla Adams, Pharm.D.; DUR Manager	x	
Rebekah Bargewell; Administrative Assistant		x
Wendi Chandler, Pharm.D.; Clinical Pharmacist	x	
Andrew Craig; Database Analyst		x
Lisa Daniel, Pharm.D.; Pharmacy Resident	x	
Erin Ford, Pharm.D.; Clinical Pharmacist		x
Mark Fuelling; Client Support Analyst		x
Thomas Ha, Pharm.D.; Clinical Pharmacist	x	
Katrina Harris, Pharm.D.; Clinical Pharmacist		x
Robert Klatt, Pharm.D.; Clinical Pharmacist	x	
Amy Miller; Operations Coordinator		x
Brandy Nawaz, Pharm.D.; Clinical Pharmacist	x	
Karen O'Neill, Pharm.D.; Clinical Pharmacist		x
Wynn Phung, Pharm.D.; Clinical Pharmacist		x
Leslie Robinson, D.Ph.; Pharmacy PA Coordinator		x
Vickie Sams, CPhT.; Quality/Training Coordinator	x	
Grant H. Skrepnek, Ph.D.; Associate Professor	x	
Regan Smith, Pharm.D.; Clinical Pharmacist		x
Ashley Teel, Pharm.D.; Clinical Pharmacist	x	
Jacquelyn Travers, Pharm.D.; Practice Facilitating Pharmacist		x
Devin Wilcox, D.Ph.; Pharmacy Director	x	
Justin Wilson, Pharm.D.; Clinical Pharmacist	x	
PA Oncology Pharmacists: Allison Baxley, Pharm.D., BCOP		x
Emily Borders, Pharm.D., BCOP	x	
Sarah Schmidt, Pharm.D., BCPS, BCOP		x
Graduate Students: Matthew Dickson, Pharm.D.		x
Michael Nguyen, Pharm.D.		x
Corby Thompson, Pharm.D.	x	
Laura Tidmore, Pharm.D.	x	
Visiting Pharmacy Student(s): N/A		

OKLAHOMA HEALTH CARE AUTHORITY STAFF:	PRESENT	ABSENT
Melody Anthony, Chief State Medicaid Director; Chief Operating Officer		x
Ellen Buettner, Chief of Staff		x
Kevin Corbett, C.P.A.; Chief Executive Officer		x
Terry Cothran, D.Ph.; Pharmacy Director	x	
Susan Eads, J.D.; Director of Litigation	x	
Stacey Hale; Drug Rebate Manager		x
Michael Herndon, D.O.; Chief Medical Officer		x
Paula Root, M.D.; Medical Director	x	
Jill Ratterman, D.Ph.; Clinical Pharmacist	x	
Michelle Tahah, Pharm.D.; Clinical Pharmacist	x	
Nathan Valentine, M.D.; Senior Medical Director		x
Kerri Wade; Pharmacy Operations Manager	x	

OTHERS PRESENT:	
Bob Atkins, Biogen	Frances Bauman, Novo Nordisk
Jomy Joseph, Sanofi-Genzyme	Tom Telly, Ascendis Pharmaceuticals
David Prather, Novo Nordisk	Denise Capo, Karyopharm Therapeutics
Dennis Liu, Sanofi-Genzyme	Melanie Curlett, Takeda
Travis Cooper, Chiasma Pharmaceuticals	Antrice Kay, Horizon Therapeutics
Cheryl Gay, Genentech	Brent Hildebrand, Gilead
Kevin Duhrkopf, Sanofi-Genzyme	Bobby White, Eisai
Curt Griffith, Horizon Therapeutics	Roxann Dominquez, AbbVie
Mark Kaiser, Otsuka	Ronald Cain, Pfizer
Robert Greely, Biogen	Nima Nabavi, Amgen
Gina Heinen, Novo Nordisk	Doug Wood, ViiV Health Care
Bart Vleugels, ODOT	James Beal, Karyopharm Therapeutics
Rick Andrews, Chiasma Pharmaceuticals	Gloria Ross, OMES
Sieana Mackiewicz, ODOT	

PRESENT FOR PUBLIC COMMENT:	
Brent Hildebrand	Gilead

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

1A: ROLL CALL

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 2: **PUBLIC COMMENT FORUM**

2A: AGENDA ITEM NO. 8 BRENT HILDEBRAND

ACTION: NONE REQUIRED

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

3A: OCTOBER 14, 2020 DUR MINUTES – VOTE

3B: OCTOBER 14, 2020 DUR RECOMMENDATIONS MEMORANDUM

Materials included in agenda packet; presented by Dr. Muchmore

Dr. Hanner moved to approve; seconded by Dr. Boyett

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: **2021 DUR BOARD MEETING DATES**

4A: 2021 DUR BOARD MEETING DATES

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

AGENDA ITEM NO. 5: **UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/U.S. FOOD AND DRUG ADMINISTRATION (FDA) SAFETY ALERTS**

5A: PHARMACY HELPDESK ACTIVITY FOR OCTOBER 2020
5B: MEDICATION COVERAGE ACTIVITY FOR OCTOBER 2020
5C: U.S. FOOD AND DRUG ADMINISTRATION (FDA) SAFETY ALERTS

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

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE EVRYSDI™ (RISDIPLAM)**

6A: INTRODUCTION
6B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Chandler
Dr. Garton moved to approve; seconded by Dr. Hanner
ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: **VOTE TO PRIOR AUTHORIZE TRIKAFTA® (ELEXACAFTOR/TEZACAFTOR/IVACAFTOR AND IVACAFTOR)**

7A: NEW U.S. FOOD AND DRUG ADMINISTRATION (FDA) APPROVAL(S)
7B: COLLEGE OF PHARMACY RECOMMENDATIONS

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

AGENDA ITEM NO. 8: **VOTE TO PRIOR AUTHORIZE EPCLUSA® (SOFOSBUVIR/VELPATASVIR) 200MG/50MG TABLET**

8A: NEW U.S. FOOD AND DRUG ADMINISTRATION (FDA) APPROVAL(S) AND LABEL UPDATE(S)
8B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Ford
Dr. Garton moved to approve; seconded by Dr. Boyett
ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: **VOTE TO PRIOR AUTHORIZE CYSTADROPS® (CYSTEAMINE 0.37% OPHTHALMIC SOLUTION) AND CYSTARAN™ (CYSTEAMINE 0.44% OPHTHALMIC SOLUTION)**

9A: INTRODUCTION
9B: COLLEGE OF PHARMACY RECOMMENDATIONS

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

AGENDA ITEM NO. 10: **VOTE TO PRIOR AUTHORIZE MYCAPSSA® (OCTREOTIDE)**

10A: INTRODUCTION
10B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Daniel
Dr. Garton moved to approve; seconded by Dr. Muñoz
ACTION: MOTION CARRIED

AGENDA ITEM NO. 11: VOTE TO PRIOR AUTHORIZE ZEJULA® (NIRAPARIB)
11A: MARKET NEWS AND UPDATES
11B: ZEJULA® (NIRAPARIB) PRODUCT SUMMARY
11C: RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Borders
Dr. Garton moved to approve; seconded by Dr. Muñoz
ACTION: MOTION CARRIED

AGENDA ITEM NO. 12: ANNUAL REVIEW OF MULTIPLE MYELOMA MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE BLENREP (BELANTAMAB MAFODOTIN-BLMF), DARZALEX® (DARATUMUMAB), DARZALEX FASPRO™ (DARATUMUMAB/HYALURONIDASE-FIHJ), EMPLICITI® (ELOTUZUMAB), HEMADY™ (DEXAMETHASONE 20MG TABLET), NINLARO® (IXAZOMIB), SARCLISA® (ISATUXIMAB-IRFC), AND XPOVIO® (SELINEXOR)
12A: INTRODUCTION
12B: UTILIZATION OF MULTIPLE MYELOMA MEDICATIONS
12C: PRIOR AUTHORIZATION OF MULTIPLE MYELOMA MEDICATIONS
12D: MARKET NEWS AND UPDATES
12E: PRODUCT SUMMARIES
12F: RECOMMENDATIONS
12G: UTILIZATION DETAILS OF MULTIPLE MYELOMA MEDICATIONS
Materials included in agenda packet; presented by Dr. Borders
ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: 30-DAY NOTICE TO PRIOR AUTHORIZE LENVIMA® (LENVATINIB)
13A: INTRODUCTION
13B: LENVIMA® (LENVATINIB) PRODUCT SUMMARY
13C: RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Borders
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: ANNUAL REVIEW OF MAINTENANCE ASTHMA AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE AIRDUO® DIGIHALER® (FLUTICASONE PROPIONATE/SALMETEROL), ARMONAIR® DIGIHALER® (FLUTICASONE PROPIONATE), AND BREZTRI AEROSPHERE™ (BUDESONIDE/GLYCOPYRROLATE/ FORMOTEROL FUMARATE)
14A: CURRENT PRIOR AUTHORIZATION CRITERIA
14B: UTILIZATION OF MAINTENANCE ASTHMA AND COPD MEDICATIONS
14C: PRIOR AUTHORIZATION OF MAINTENANCE ASTHMA AND COPD MEDICATIONS
14D: MARKET NEWS AND UPDATES
14E: AIRDUO® DIGIHALER® (FLUTICASONE PROPIONATE/SALMETEROL) PRODUCT SUMMARY
14F: ARMONAIR® DIGIHALER® (FLUTICASONE PROPIONATE) PRODUCT SUMMARY

14G: BREZTRI AEROSPHERE™ (BUDESONIDE/GLYCOPYRROLATE/ FORMOTEROL) PRODUCT SUMMARY
14H: COLLEGE OF PHARMACY RECOMMENDATIONS
14I: UTILIZATION DETAILS OF MAINTENANCE ASTHMA AND COPD MEDICATIONS
14J: UTILIZATION DETAILS OF INHALED CORTICOSTEROIDS
Materials included in agenda packet; presented by Dr. Nawaz
ACTION: NONE REQUIRED

AGENDA ITEM NO. 15: ANNUAL REVIEW OF ATOPIC DERMATITIS (AD) MEDICATIONS
15A: CURRENT PRIOR AUTHORIZATION CRITERIA
15B: UTILIZATION OF AD MEDICATIONS
15C: PRIOR AUTHORIZATION OF AD MEDICATIONS
15D: MARKET NEWS AND UPDATES
15E: COLLEGE OF PHARMACY RECOMMENDATIONS
15F: UTILIZATION DETAILS OF AD MEDICATIONS
Materials included in agenda packet; presented by Dr. Wilson
Dr. Garton moved to approve; seconded by Dr. Muñoz
ACTION: MOTION CARRIED

AGENDA ITEM NO. 16: ANNUAL REVIEW OF ANTICOAGULANTS AND PLATELET AGGREGATION INHIBITORS
16A: CURRENT PRIOR AUTHORIZATION CRITERIA
16B: UTILIZATION OF ANTICOAGULANTS AND PLATELET AGGREGATION INHIBITORS
16C: PRIOR AUTHORIZATION OF ANTICOAGULANTS AND PLATELET AGGREGATION INHIBITORS
16D: MARKET NEWS AND UPDATES
16E: COLLEGE OF PHARMACY RECOMMENDATIONS
16F: UTILIZATION DETAILS OF ANTICOAGULANTS
16G: UTILIZATION DETAILS OF PLATELET AGGREGATION INHIBITORS
Materials included in agenda packet; presented by Dr. Daniel
ACTION: NONE REQUIRED

AGENDA ITEM NO. 17: ANNUAL REVIEW OF TEPEZZA® (TEPROTUMUMAB-TRBW)
17A: INTRODUCTION
17B: CURRENT PRIOR AUTHORIZATION CRITERIA
17C: UTILIZATION OF TEPEZZA® (TEPROTUMUMAB-TRBW)
17D: PRIOR AUTHORIZATION OF TEPEZZA® (TEPROTUMUMAB-TRBW)
17E: MARKET NEWS AND UPDATES
17F: COLLEGE OF PHARMACY RECOMMENDATIONS
17G: UTILIZATION DETAILS OF TEPEZZA® (TEPROTUMUMAB-TRBW)
Materials included in agenda packet; Non-presentation/Questions only
ACTION: NONE REQUIRED

AGENDA ITEM NO. 18: U.S. FOOD AND DRUG ADMINISTRATION (FDA) AND DRUG ENFORCEMENT ADMINISTRATION (DEA) UPDATES
Materials included in agenda packet; presented by Dr. Chandler
ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 19:</u> **FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)**

19A: NONDISCRIMINATION IN HEALTH CARE COVERAGE ACT

- **i. DISCUSSION OF THE NONDISCRIMINATION IN HEALTH CARE COVERAGE ACT, WHICH BECAME EFFECTIVE ON NOVEMBER 1, 2020 (63 OKLA. STAT. §§2560-2565), AND THE DUR BOARD'S COMPLIANCE THEREWITH.**

19B: UPCOMING PRODUCT AND CLASS REVIEWS*

- **i. TARGETED IMMUNOMODULATOR AGENTS**
- **ii. ANTIDEPRESSANTS**
- **iii. ULCERATIVE COLITIS (UC) AND CROHN'S DISEASE MEDICATIONS**
- **iv. THROMBOCYTOPENIA MEDICATIONS**

**Future business subject to change.*

Materials included in agenda packet; presented by Susan Eads, Dr. Adams

ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 20:</u> **ADJOURNMENT**

The meeting was adjourned at 5:37pm.

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

Memorandum

Date: November 5, 2020

To: Terry Cothran, D.Ph.
Pharmacy Director
Oklahoma Health Care Authority

From: Michyla Adams, Pharm.D.
Drug Utilization Review (DUR) Manager
Pharmacy Management Consultants

Subject: DUR Board Recommendations from Meeting of November 4, 2020

Recommendation 1: 2021 DUR Meeting Dates

MOTION CARRIED by unanimous approval.

January 13, 2021
February 10, 2021
March 10, 2021
April 14, 2021
May 12, 2021
June 9, 2021
July 14, 2021
August 11, 2021
September 8, 2021
October 13, 2021
November 10, 2021
December 8, 2021

Recommendation 2: U.S. Food and Drug Administration (FDA) Safety Alerts

NO ACTION REQUIRED.

Recommendation 3: Vote to Prior Authorize Evrysdi™ (Risdiplam)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Evrysdi™ (risdiplam) with the following criteria:

Evrysdi™ (Risdiplam) Approval Criteria:

1. An FDA approved diagnosis of spinal muscular atrophy (SMA) in members 2 months of age and older; and
2. Molecular genetic testing to confirm bi-allelic pathogenic variants in the *survival motor neuron 1* (*SMN1*) gene; and
3. Member is not currently dependent on permanent invasive ventilation (defined as ≥16 hours of respiratory assistance per day continuously for >21 days in the absence of an acute, reversible illness or a perioperative state); and
4. Evrysdi™ must be prescribed by a neurologist or specialist with expertise in the treatment of SMA (or an advanced care practitioner with a supervising physician who is a neurologist or specialist with expertise in the treatment of SMA); and
5. Prescriber must agree to monitor member's liver function prior to initiating Evrysdi™ and periodically while receiving Evrysdi™ treatment; and
6. Pharmacy must confirm Evrysdi™ will be constituted to an oral solution by a pharmacist prior to dispensing and must confirm Evrysdi™ will be shipped via cold chain supply to adhere to the storage and handling requirements in the Evrysdi™ *Prescribing Information*; and
7. Prescriber must confirm the member or caregiver has been counseled on the proper storage of Evrysdi™ and has been instructed on how to prepare the prescribed daily dose of Evrysdi™ prior to administration of the first dose; and
8. Female members of reproductive potential must not be pregnant and must have a negative pregnancy test prior to initiation of therapy; and
9. Female members of reproductive potential must be willing to use effective contraception during treatment with Evrysdi™ and for at least 1 month after the last dose; and
10. Prescriber must verify male members of reproductive potential have been counseled on the potential effects on fertility and the potential of compromised male fertility is acceptable; and
11. Member will not be approved for concomitant treatment with Spinraza® (nusinersen); and
12. Member must not have previously received treatment with Zolgensma® (onasemnogene abeparvovec-xioi); and
13. A baseline assessment must be provided using a functionally appropriate exam [e.g., Children's Hospital of Philadelphia Infant Test of

Neuromuscular Disorders (CHOP-INTEND), Hammersmith Functional Motor Scale Expanded (HFMSE), Hammersmith Infant Neurological Exam (HINE), Upper Limb Module (ULM) Test]; and
14. Initial authorizations will be for the duration of 6 months, at which time the prescriber must verify the member is compliant with Evrysdi™ and responding to the medication as demonstrated by clinically significant improvement or maintenance of function from pre-treatment baseline status using the same exam as performed at baseline assessment; and
15. Member's recent weight must be provided to ensure accurate dosing in accordance with Evrysdi™ *Prescribing Information*; and
16. A quantity limit of 240mL per 36 days will apply.

Additionally, the College of Pharmacy recommends the following changes shown in red to the current Spinraza® (nusinersen) and Zolgensma® (onasemnogene abeparvovec-xioi) approval criteria:

Spinraza® (Nusinersen) Approval Criteria:

1. A diagnosis of spinal muscular atrophy (SMA):
   a. Type 1; or
   b. Type 2; or
   c. Type 3 with symptoms; and
2. Molecular genetic testing to confirm bi-allelic pathogenic variants in the *survival motor neuron 1* (*SMN1*) gene; and
3. Member is not currently dependent on permanent invasive ventilation (defined as ≥16 hours of respiratory assistance per day continuously for >21 days in the absence of an acute, reversible illness or a perioperative state); and
4. Spinraza® must be prescribed by a neurologist or specialist with expertise in the treatment of SMA (or an advanced care practitioner with a supervising physician who is a neurologist or specialist with expertise in the treatment of SMA); and
5. Member must not have previously received treatment with Zolgensma® (onasemnogene abeparvovec-xioi); and
6. Member will not be approved for concomitant treatment with Evrysdi™ (risdiplam); and
7. Platelet count, coagulation laboratory testing, and quantitative spot urine protein testing must be conducted at baseline and prior to each dose and verification that levels are acceptable to the prescriber; and
8. Spinraza® must be administered in a health care facility by a specialist experienced in performing lumbar punctures; and
   a. Spinraza® must be shipped to the facility where the member is scheduled to receive treatment; and
9. A baseline assessment must be provided using at least 1 of the following exams as functionally appropriate:
   a. Hammersmith Infant Neurological Exam (HINE); or

   b. Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND); or
   c. Upper Limb Module (ULM) Test; or
   d. Hammersmith Functional Motor Scale Expanded (HFMSE); and
10. Initial authorizations will be for the duration of 6 months, at which time the prescriber must verify the member is responding to the medication as demonstrated by clinically-significant improvement or maintenance of function from pretreatment baseline status using the same exam as performed at baseline assessment:
   a. HINE; or
   b. CHOP-INTEND; or
   c. ULM Test; or
   d. HFMSE; and
11. Approval quantity will be based on Spinraza® *Prescribing Information* and FDA approved dosing regimen(s).
   a. Only (1) 5mL vial of Spinraza® is to be dispensed prior to each scheduled procedure for administration.

Zolgensma® (Onasemnogene Abeparvovec-xioi) Approval Criteria:

1. An FDA approved diagnosis of spinal muscular atrophy (SMA) in pediatric members younger than 2 years of age; and
2. Member must have reached full-term gestational age prior to Zolgensma® infusion; and
3. Molecular genetic testing to confirm bi-allelic mutations in the *survival motor neuron 1* (*SMN1*) gene; and
4. Member is not currently dependent on permanent invasive ventilation (defined as ≥16 hours of respiratory assistance per day continuously for >21 days in the absence of an acute, reversible illness or a perioperative state); and
5. Zolgensma® must be prescribed by a neurologist or specialist with expertise in the treatment of SMA (or an advanced care practitioner with a supervising physician who is a neurologist or specialist with expertise in the treatment of SMA); and
6. Member must have baseline anti-AAV9 antibody titers ≤1:50; and
7. Prescriber must agree to monitor liver function tests, platelet counts, and troponin-I at baseline and as directed by the Zolgensma® *Prescribing Information*; and
8. Prescriber must agree to administer systemic corticosteroids starting 1 day prior to the Zolgensma® infusion and continuing as recommended in the Zolgensma® *Prescribing Information* based on member's liver function; and
9. Zolgensma® must be shipped to the facility where the member is scheduled to receive treatment and must adhere to the storage and handling requirements in the Zolgensma® *Prescribing Information*; and
10. Member will not be approved for concomitant treatment with Evrysdi™ (risdiplam) or Spinraza® (nusinersen) following Zolgensma® infusion

(current authorizations for risdiplam or nusinersen will be discontinued upon Zolgensma® approval); and
11. Member's recent weight must be provided to ensure accurate dosing in accordance with Zolgensma® *Prescribing Information*; and
12. Only 1 Zolgensma® infusion will be approved per member per lifetime.

Recommendation 4: Vote to Prior Authorize Trikafta® (Elexacaftor/Tezacaftor/Ivacaftor and Ivacaftor)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Trikafta® (elexacaftor/tezacaftor/ivacaftor and ivacaftor) and recommends updating the age restriction of Kalydeco® (ivacaftor) based on the FDA-approved age expansion with the following criteria (changes and new criteria shown in red):

Trikafta® (Elexacaftor/Tezacaftor/Ivacaftor and Ivacaftor) Approval Criteria:

1. An FDA approved diagnosis of cystic fibrosis (CF) in members who have at least 1 *F508del* mutation in the CF transmembrane conductance regulator *(CFTR)* gene; and
2. If the member's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of a *CFTR* mutation followed by verification with bi-directional sequencing when recommended by the mutation test's instructions for use; and
3. Member must be 12 years of age or older; and
4. Members using Trikafta® must be supervised by a pulmonary specialist; and
5. If member is currently stabilized on Orkambi® (lumacaftor/ivacaftor) or Symdeko® (tezacaftor/ivacaftor and ivacaftor) and experiencing adverse effects associated with Orkambi® or Symdeko® use, the prescriber must indicate that information on the prior authorization request; and
6. Prescriber must verify that member has been counseled on proper administration of Trikafta® including taking with a fat-containing food; and
7. Prescriber must verify that ALT, AST, and bilirubin will be assessed prior to initiating Trikafta®, every 3 months during the first year of treatment, and annually thereafter; and
8. Prescriber must verify that the member does not have severe hepatic impairment; and
9. Prescriber must verify that pediatric members will receive baseline and follow-up ophthalmological examinations as recommended in the Trikafta® *Prescribing Information*; and
10. Member must not be taking any of the following medications concomitantly with Trikafta®: rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin, and St. John's wort; and

11. A quantity limit of 3 tablets per day or 84 tablets per 28 days will apply; and
12. Initial approval will be for the duration of 3 months, after which time compliance will be required for continued approval. After 6 months of utilization, compliance and information regarding efficacy, such as improvement in forced expiratory volume in 1 second (FEV_1), will be required for continued approval. Additionally after 6 months of utilization, information regarding efficacy as previously mentioned or fewer adverse events than with a previous CFTR therapy must be provided for members who switched from Orkambi® (lumacaftor/ivacaftor) or Symdeko® (tezacaftor/ivacaftor and ivacaftor).

Kalydeco® (Ivacaftor) Approval Criteria:

1. An FDA approved diagnosis of cystic fibrosis (CF) with a mutation in the CF transmembrane conductance regulator *(CFTR)* gene detected by genetic testing that is responsive to ivacaftor based on clinical and/or *in vitro* assay data; and
2. Documentation must be submitted with results of *CFTR* genetic testing; and
3. Member must be 4 ~~6~~ months of age or older; and
4. A quantity limit of 2 tablets or granule packets per day or 56 tablets or granule packets per 28 days will apply; and
5. An age restriction of 4 ~~6~~ months to younger than 6 years of age will apply to Kalydeco® oral granule packets. Members 6 years of age or older will require a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation; and
6. Initial approval will be for the duration of 3 months, after which time compliance will be required for continued approval. After 6 months of utilization, compliance and information regarding efficacy, such as improvement in forced expiratory volume in 1 second (FEV_1), will be required for continued approval.

Recommendation 5: Vote to Prior Authorize Epclusa® (Sofosbuvir/Velpatasvir) 200mg/50mg Tablet

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Epclusa® (sofosbuvir/velpatasvir) 200mg/50mg tablets with criteria similar to the higher strength Epclusa® 400mg/100mg tablets. Additionally, the College of Pharmacy recommends updating the Epclusa® (sofosbuvir/velpatasvir), Harvoni® (ledipasvir/sofosbuvir), and Vosevi® (sofosbuvir/velpatasvir/voxilaprevir) prior authorization criteria based on new FDA label updates. The following criteria will apply (changes and additions noted in red):

Epclusa® (Sofosbuvir/Velpatasvir 400/100mg and 200/50mg Tablets)
Approval Criteria:

1. Member must be ~~18~~ 6 years of age or older or weighing at least 17kg; and
2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) genotype (GT)-1, GT-2, GT-3, GT-4, GT-5, or GT-6; and
3. Requests for the generic formulation will require a patient-specific, clinically significant reason why the member cannot use the brand formulation; and***
4. Epclusa® must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated for hepatitis C treatment by a gastroenterologist, infectious disease specialist, or transplant specialist within the last 3 months; and
5. Hepatitis C Virus (HCV) GT testing must be confirmed and indicated on prior authorization request; and
6. Member has chronic HCV infection defined by:
    a. If the member has a liver fibrosis score ≥F1 (METAVIR equivalent), then only 1 detectable and quantifiable HCV RNA (>15 IU/mL) test within the last 12 months is required (must be within last 3 months if requesting 8-week regimen); or
    b. If the member has a liver fibrosis score <F1 (METAVIR equivalent), then the following must be met:
        i. Positive (i.e., reactive) HCV antibody test that is at least 6 months old and has a detectable and quantifiable HCV RNA (>15 IU/mL) test 6 months after date of positive HCV antibody test; or
        ii. 2 detectable and quantifiable HCV RNA (>15 IU/mL) tests at least 6 months apart; and
7. The following regimens and requirements based on prior treatment experience, baseline viral load, and cirrhosis will apply:
    a. **GT-1, -2, -3, -4, -5, -6:**
        i. Treatment-naïve or treatment-experienced without cirrhosis or with compensated cirrhosis (Child-Pugh A): Epclusa® for 12 weeks; or
        ii. Treatment-naïve or treatment-experienced with decompensated cirrhosis (Child-Pugh B and C): Epclusa® + weight based ribavirin for 12 weeks; or
    b. New regimens will apply as approved by the FDA; and
8. Member must sign and submit the Hepatitis C Intent to Treat contract; and
9. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
10. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Virologic Response (SVR-12); and

11. Prescriber must agree to counsel members on potential harms of illicit intravenous (IV) drug use or alcohol use and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
12. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
13. ~~Member must not have severe renal impairment (estimated Glomerular Filtration Rate [eGFR] <30mL/min/1.73m2); and~~
14. Female members must not be pregnant and must have a negative pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use 2 forms of non-hormonal birth control while on therapy (and for 6 months after therapy completion for ribavirin users); and
15. Member must not be taking the following medications: H2-receptor antagonists at doses >40mg famotidine equivalent, amiodarone, omeprazole or other proton pump inhibitors, topotecan, rifampin, rifabutin, rifapentine, carbamazepine, eslicarbazepine, phenytoin, phenobarbital, oxcarbazepine, efavirenz, tenofovir disoproxil fumarate, tipranavir/ritonavir, St. John's wort, and rosuvastatin doses >10mg; and
16. If member is using antacids, they must agree to separate antacid and Epclusa® administration by 4 hours; and
17. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight-management, severe concurrent medical diseases, such as but not limited to, retinal disease, or autoimmune thyroid disease; and
18. Member must not have a limited life expectancy (<12 months) that cannot be remediated by treating HCV, liver transplantation, or another directed therapy; and
19. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
20. Members must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy; and
21. Approvals for treatment regimen initiation for 12 weeks of therapy will not be granted prior to the 10th of a month in order to prevent prescription limit issues from affecting the member's compliance. ****The brand formulation of Epclusa® is preferred based on net cost after rebates, and products may be moved to non-preferred if the net cost changes in comparison to other available products.*

Harvoni® (Ledipasvir/Sofosbuvir Tablets and Oral Pellets) Approval Criteria:

1. Member must be 3 years of age or older; and

2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) genotype (GT)-1, GT-4, GT-5, or GT-6; and
3. Request for the generic formulation will require a patient-specific, clinically significant reason why the member cannot use the brand formulation; and***
4. Harvoni® must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated for hepatitis C treatment by a gastroenterologist, infectious disease specialist, or transplant specialist within the last 3 months; and
5. Hepatitis C Virus (HCV) GT testing must be confirmed and indicated on prior authorization request; and
6. Member has chronic HCV infection defined by:
    a. If the member has a liver fibrosis score ≥F1 (METAVIR equivalent), then only 1 detectable and quantifiable HCV RNA (>15 IU/mL) test within the last 12 months is required (must be within last 3 months if requesting 8-week regimen); or
    b. If the member has a liver fibrosis score <F1 (METAVIR equivalent), then the following must be met:
        i. Positive (i.e., reactive) HCV antibody test that is at least 6 months old and has a detectable and quantifiable HCV RNA (>15 IU/mL) test 6 months after date of positive HCV antibody test; or
        ii. 2 detectable and quantifiable HCV RNA (>15 IU/mL) tests at least 6 months apart; and
7. The following regimens and requirements based on prior treatment experience, baseline viral load, and cirrhosis will apply:
    a. **GT-1:**
        i. Treatment-naïve without cirrhosis who have a pre-treatment HCV-RNA <6 million IU/mL: Harvoni® for 8 weeks; or
        ii. Treatment-naïve patients who are cirrhotic or have a pre-treatment HCV-RNA >6 million IU/mL: Harvoni® for 12 weeks; or
        iii. Treatment-experienced without cirrhosis: Harvoni® for 12 weeks; or
        iv. Treatment-experienced with compensated cirrhosis:
            1. Harvoni® with weight-based ribavirin for 12 weeks; or
            2. Harvoni® for 24 weeks; or
        v. Treatment-naïve or treatment-experienced with decompensated cirrhosis: Harvoni® with weight-based ribavirin for 12 weeks; or
    b. **GT-1 or GT-4:**
        i. Treatment-naïve or treatment-experienced liver transplant recipients with or without compensated cirrhosis: Harvoni® with weight-based ribavirin for 12 weeks; or
    c. **GT-4, GT-5, or GT-6:**

i. Treatment-naïve or treatment-experienced with or without compensated cirrhosis: Harvoni® for 12 weeks; or

d. New regimens will apply as approved by the FDA; and

8. For members 6 years of age or older who request the oral pellet formulation of Harvoni®, a patient-specific, clinically significant reason to support use of the oral pellet formulation in place of the tablet formulation must be provided; and
9. Member must sign and submit the Hepatitis C Intent to Treat contract; and
10. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
11. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Virologic Response (SVR-12); and
12. Prescriber must agree to counsel members on potential harms of illicit intravenous (IV) drug use or alcohol use and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
13. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
~~14. Member must not have severe renal impairment (estimated Glomerular Filtration Rate [eGFR] <30mL/min/1.73m^2); and~~
15. Female members must not be pregnant and must have a negative pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use 2 forms of non-hormonal birth control while on therapy (and for 6 months after therapy completion for ribavirin users); and
16. Member must not be taking the following medications: rifampin, rifabutin, rifapentine, carbamazepine, eslicarbazepine, phenytoin, phenobarbital, oxcarbazepine, tipranavir/ritonavir, simeprevir, rosuvastatin, St. John's wort, or elvitegravir/cobicistat/emtricitabine in combination with tenofovir disoproxil fumarate; and
17. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight management, severe concurrent medical diseases, such as but not limited to, retinal disease or autoimmune thyroid disease; and
18. Member must not have a limited life expectancy (<12 months) that cannot be remediated by treating HCV, liver transplantation, or another directed therapy; and
19. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
20. Member must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy; and

21. Approvals for treatment regimen initiation for 8 or 12 weeks of therapy will not be granted prior to the 10th of a month, and for 24 weeks of therapy prior to the 15th of a month in order to prevent prescription limit issues from affecting the member's compliance.
****The brand formulation of Harvoni® is preferred based on net cost after rebates, and products may be moved to non-preferred if the net cost changes in comparison to other available products.*

Vosevi® (Sofosbuvir/Velpatasvir/Voxilaprevir Tablets) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) genotype (GT)-1, GT-2, GT-3, GT-4, GT-5, or GT-6; and
3. Vosevi® must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated for hepatitis C treatment by a gastroenterologist, infectious disease specialist, or transplant specialist within the last 3 months; and
4. Hepatitis C Virus (HCV) GT testing must be confirmed and indicated on prior authorization request; and
5. Member has chronic HCV infection defined by:
    a. If the member has a liver fibrosis score ≥F1 (METAVIR equivalent), then only 1 detectable and quantifiable HCV RNA (>15 IU/mL) test within the last 12 months is required (must be within last 3 months if requesting 8-week regimen); or
    b. If the member has a liver fibrosis score <F1 (METAVIR equivalent), then the following must be met:
        i. Positive (i.e., reactive) HCV antibody test that is at least 6 months old and has a detectable and quantifiable HCV RNA (>15 IU/mL) test 6 months after date of positive HCV antibody test; or
        ii. 2 detectable and quantifiable HCV RNA (>15 IU/mL) tests at least 6 months apart; and
6. The following regimens and requirements based on prior treatment experience, baseline viral load, and cirrhosis will apply:
    a. **Adult patients without cirrhosis or with compensated cirrhosis (Child-Pugh A) GT-1, -2, -3, -4, -5, -6:**
        i. **GT-1, -2, -3, -4, -5, -6 patients who were previously treated with an HCV regimen containing an NS5A inhibitor** (e.g., daclatasvir, elbasvir, ledipasvir, ombitasvir, velpatasvir): Vosevi® for 12 weeks; or
        ii. **GT-1a or -3 patients who were previously treated with an HCV regimen containing sofosbuvir without an NS5A inhibitor:** Vosevi® for 12 weeks; or
    b. New regimens will apply as approved by the FDA; and
7. Member must sign and submit the Hepatitis C Intent to Treat contract; and

8. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
9. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Virologic Response (SVR-12); and
10. Prescriber must agree to counsel members on potential harms of illicit intravenous (IV) drug use or alcohol use and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
11. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
12. Member must not have decompensated cirrhosis or moderate or severe hepatic impairment (Child-Pugh B or C); and
13. Member must not have a limited life expectancy (<12 months) that cannot be remediated by treating HCV, liver transplantation, or another directed therapy; and
~~14. Member must not have severe renal impairment (estimated Glomerular Filtration Rate [eGFR] <30mL/min/1.73m2); and~~
15. Female members must not be pregnant and must have a negative pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use 2 forms of non-hormonal birth control while on therapy (and for 6 months after therapy completion for ribavirin users); and
16. Member must not be taking the following medications: H2-receptor antagonists at doses >40mg famotidine twice daily equivalent, omeprazole doses >20mg daily or other proton pump inhibitors, amiodarone, carbamazepine, eslicarbazepine, phenytoin, phenobarbital, oxcarbazepine, rifampin, rifabutin, rifapentine, atazanavir, lopinavir, tipranavir/ritonavir, efavirenz, St. John's wort, pravastatin doses >40mg daily, rosuvastatin, pitavastatin, cyclosporine, methotrexate, mitoxantrone, imatinib, irinotecan, lapatinib, sulfasalazine, topotecan; and
17. If member is using antacids, they must agree to separate antacid and Vosevi® administration by 4 hours; and
18. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight-management, severe concurrent medical diseases, such as but not limited to, retinal disease, or autoimmune thyroid disease; and
19. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
20. Members must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy; and

21. Approvals for treatment regimen initiation for 12 weeks of therapy will not be granted prior to the 10th of a month in order to prevent prescription limit issues from affecting the member's compliance.

Recommendation 6: Vote to Prior Authorize Cystadrops® (Cysteamine 0.37% Ophthalmic Solution) and Cystaran™ (Cysteamine 0.44% Ophthalmic Solution)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Cystadrops® (cysteamine 0.37% ophthalmic solution) and Cystaran™ (cysteamine 0.44% ophthalmic solution) with the following criteria:

Cystadrops® (Cysteamine 0.37% Ophthalmic Solution) and Cystaran™ (Cysteamine 0.44% Ophthalmic Solution) Approval Criteria:

1. An FDA approved indication for the treatment of corneal cystine crystal accumulation in members with cystinosis; and
2. The requested medication must be prescribed by, or in consultation with, an ophthalmologist; and
3. Prescriber must verify that the member has been counseled on the proper storage of the requested medication; and
4. For Cystadrops®, a patient-specific, clinically significant reason (beyond convenience) why the member cannot use Cystaran™ must be provided; and
5. A quantity limit of 4 bottles per month will apply.

Recommendation 7: Vote to Prior Authorize Mycapssa® (Octreotide)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Mycapssa® (octreotide) with the following criteria:

Mycapssa® (Octreotide) Approval Criteria:

1. An FDA approved indication for long-term maintenance treatment in members with acromegaly who have responded to and tolerated treatment with octreotide or lanreotide; and
2. Member has elevated insulin-like growth factor-1 (IGF-1) levels for age and/or gender; and
3. Member has a documented trial with injectable octreotide or lanreotide, and the prescriber must verify that the member responded to and tolerated treatment with octreotide or lanreotide; and
4. A patient-specific, clinically significant reason why the member cannot continue treatment with injectable octreotide or lanreotide must be provided; and

5. Mycapssa® must be prescribed by, or in consultation with, an endocrinologist; and
6. Prescriber must document that the member has had an inadequate response to surgery or is not a candidate for surgery; and
7. Initial approvals will be for the duration of 12 months. Reauthorization may be granted if the prescriber documents the member's IGF-1 level has decreased or normalized since initiating treatment; and
8. A quantity limit of 120 capsules per 30 days will apply.

Recommendation 8: Vote to Prior Authorize Zejula® (Niraparib)

MOTION CARRIED by unanimous approval.

- The prior authorization of Zejula® (niraparib) with the following criteria listed in red:

Zejula® (Niraparib) Approval Criteria [Ovarian, Fallopian Tube, or Primary Peritoneal Cancer Diagnosis]:

1. **Single-Agent Treatment of Advanced Recurrent/Refractory Disease:**
   a. Diagnosis of recurrent or refractory disease; and
   b. Previous treatment with ≥3 prior lines of chemotherapy (prior chemotherapy regimens should be documented on the prior authorization request); and
   c. Diagnosis is associated with homologous recombination deficiency (HRD) positive status defined by either:
      i. A deleterious or suspected deleterious BRCA mutation; or
      ii. Genomic instability and progression >6 months after response to last platinum-based chemotherapy; and
   d. Used as a single-agent; or
2. **Treatment of Advanced Recurrent/Refractory Disease in Combination with Bevacizumab:**
   a. Used in combination with bevacizumab for platinum-sensitive persistent disease or recurrence; and
   b. Meets 1 of the following:
      i. As immediate treatment for serially rising CA-125 in members who previously received chemotherapy, or
      ii. Evidence of radiographic and/or clinical relapse in members with previous complete remission and relapse ≥6 months after completing prior chemotherapy; or
3. **Maintenance Treatment of Advanced Disease:**
   a. Diagnosis of advanced or recurrent disease; and
   b. Disease must be in a complete or partial response to platinum chemotherapy; and
   c. Used as a single-agent.

- Update the current Mekinist® (trametinib) prior authorization criteria based on NCCN Compendium approval (changes noted in red in the following approval criteria; only criteria with changes are listed):

Mekinist® (Trametinib) Approval Criteria [Serous Ovarian Cancer Diagnosis]:

1. Diagnosis of persistent disease or recurrent low-grade serous carcinoma; and
2. Meets 1 of the following:
   a. Immediate treatment for serially rising CA-125 in members who previously received chemotherapy; or
   b. Progression on primary, maintenance, or recurrence therapy; or
   c. Stable or persistent disease (if not on maintenance therapy); or
   d. Complete remission and relapse after receiving prior chemotherapy.

Recommendation 9: Annual Review of Multiple Myeloma Medications and 30-Day Notice to Prior Authorize Blenrep (Belantamab Mafodotin-blmf), Darzalex® (Daratumumab), Darzalex Faspro™ (Daratumumab/Hyaluronidase-fihj), Empliciti® (Elotuzumab), Hemady™ (Dexamethasone 20mg Tablet), Ninlaro® (Ixazomib), Sarclisa® (Isatuximab-irfc), and Xpovio® (Selinexor)

NO ACTION REQUIRED.

Recommendation 10: 30-Day Notice to Prior Authorize Lenvima® (Lenvatinib)

NO ACTION REQUIRED.

Recommendation 11: Annual Review of Maintenance Asthma and Chronic Obstructive Pulmonary Disease (COPD) Medications and 30-Day Notice to Prior Authorize AirDuo® Digihaler® (Fluticasone Propionate/Salmeterol), ArmonAir® Digihaler® (Fluticasone Propionate), and Breztri Aerosphere™ (Budesonide/Glycopyrrolate/Formoterol Fumarate)

NO ACTION REQUIRED.

Recommendation 12: Annual Review of Atopic Dermatitis (AD) Medications

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends updating the approval criteria for Eucrisa® (crisaborole) and Dupixent® (dupilumab injection) for atopic dermatitis diagnosis based on the FDA approved age expansions, with the following changes shown in red:

Eucrisa® (Crisaborole Ointment) Approval Criteria:

1. An FDA approved indication for treatment of mild-to-moderate atopic dermatitis (eczema); and
2. Member must be at least ~~2 years~~ 3 months of age or older; and
3. Member must have a documented trial within the last 6 months for a minimum of 2 weeks that resulted in failure with a topical corticosteroid (or have a contraindication or documented intolerance); and
4. A quantity limit of 1 tube per 30 days will apply; and
5. Initial approvals will be for the duration of 1 month. Reauthorization may be granted if the prescriber documents the member is responding well to treatment; and
6. Clinical exceptions for children not meeting the age restriction for Eucrisa® (crisaborole ointment):
    a. Documented adverse effect, drug interaction, or contraindication to topical corticosteroids; or
    b. Atopic dermatitis of the face or groin where prescriber does not want to use topical corticosteroids; or
    c. Prescribed by a dermatologist.

Dupixent® (Dupilumab Injection) Approval Criteria [Atopic Dermatitis Diagnosis]:

1. An FDA approved diagnosis of moderate-to-severe atopic dermatitis not adequately controlled with topical prescription therapies; and
2. Member must be ~~12~~ 6 years of age or older; and
3. Member must have documented trials within the last 6 months for a minimum of 2 weeks that resulted in failure with both of the following therapies (or have a contraindication or documented intolerance):
    a. 1 medium potency to very-high potency Tier-1 topical corticosteroid; and
    b. 1 topical calcineurin inhibitor [e.g., Elidel® (pimecrolimus), Protopic® (tacrolimus)]; and
4. Dupixent® must be prescribed by a dermatologist, allergist, or immunologist or the member must have been evaluated by a dermatologist, allergist, or immunologist within the last 12 months (or an advanced care practitioner with a supervising physician who is a dermatologist, allergist, or immunologist); and
5. Requests for concurrent use of Dupixent® with other biologic medications will be reviewed on a case-by-case basis and will require patient-specific information to support the concurrent use (Dupixent® has not been studied in combination with other biologic therapies); and

6. Initial approvals will be for the duration of 16 weeks. Reauthorization may be granted if the prescriber documents the member is responding well to treatment. Additionally, compliance will be evaluated for continued approval.

Recommendation 13: Annual Review of Anticoagulants and Platelet Aggregation Inhibitors

NO ACTION REQUIRED.

Recommendation 14: Annual Review of Tepezza® (Teprotumumab-trbw)

NO ACTION REQUIRED.

Recommendation 15: U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates

NO ACTION REQUIRED.

Recommendation 16: Future Business

NO ACTION REQUIRED.

Make today a breakthrough.

November 3, 2020

Oklahoma Drug Utilization Review Board
Oklahoma Health Care Authority
4345 N Lincoln Boulevard
Oklahoma City, OK 73105

Re: Prior Authorize Evrysdi™ (Risdiplam)

Dear Oklahoma Drug Utilization Review Board Members:

On behalf of Oklahoma residents with a neuromuscular disease known as spinal muscular atrophy (SMA), **Cure SMA urges the Oklahoma Drug Utilization Review Board to approve and allow full access to Evrysdi, a new SMA treatment, for all eligible Oklahoma residents with SMA according to the FDA label.** As we wrote in our August 12, 2020 Evrysdi coverage letter to Oklahoma Medicaid (attached), we advocate that **no one impacted by SMA should be denied access to a potentially life-saving treatment**.

SMA is a progressive neurodegenerative disease that can significantly impact an individual's ability to walk, swallow, and—in the most severe cases—even breathe. In Oklahoma, an estimated 5 babies with SMA are born each year and more than 78,000 Oklahoma residents are carriers of the SMA genetic mutation.[i] Cure SMA is the leading national organization dedicated to finding a cure and treatments for SMA. Cure SMA and our Oklahoma supporters are focused on improving lives and removing barriers for Oklahoma residents with SMA and their families.

Every person with SMA in Oklahoma should be able to access the treatment of their choice, based on their individualized needs and in consultation with their health care provider. As we wrote in our August 12, 2020 letter to Oklahoma Medicaid, the U.S. Food and Drug Administration (FDA) approved Evrysdi for the treatment of SMA in all individuals with SMA who are 2 months of age and older.

> ***FDA Prescribing Information for EVRYSDI (August 2020)***[ii]
> *EVRYSDI is a survival of motor neuron 2 (SMN2) splicing modifier indicated for the treatment of spinal muscular atrophy (SMA) in patients 2 months of age and older.*

The FDA's approval and broad label were based on clinical trials that demonstrated Evrysdi's effectiveness in all individuals with SMA who are 2 months of age and older. In our August 12, 2020 letter, Cure SMA highlighted the key data from the FIREFISH (Part 1 & 2), SUNFISH, and JEWELFISH trials. Together, these studies showed individuals with SMA who received Evrysdi achieved unprecedented developmental gains and milestones (i.e., swallowing, sitting, standing) and required fewer hospitalizations and reduced need for permanent ventilation and feeding support. In addition to the efficacy, the FDA thoroughly

reviewed the SMA treatment for safety and concluded that the clinical trials data established that Evrysdi was safe for the treatment of SMA.[ii]

Cure SMA is very concerned by the restrictive Medicaid prior authorization criteria that would prevent access to Evrysdi by those dependent on invasive ventilation and those who have been previously treated with Zolgensma.[iii] Also requiring reauthorization more than annually is a burden on patients and healthcare providers. Currently, Oklahoma does not offer newborn screening for SMA. Thus, every child with SMA is diagnosed due to clinical symptoms. Clinical trials of children with symptomatic SMA during infancy who have received an SMA treatment will have residual symptoms of SMA that may benefit from treatment with gene modifying therapies with an alternative mechanism. In comparison, children identified by newborn screening who receive treatment pre-symptomatically may have minimal to no significant symptoms of SMA. In addition, there is not evidence to exclude people with SMA who are on permanent ventilation.

Cure SMA respectfully asks that this distinguished committee of health care experts approves Medicaid coverage of Evrysdi for all Oklahoma Medicaid beneficiaries with SMA who are 2 months of age and older, as recommended by the FDA. Covering Evrysdi without restrictions, based on the FDA label, will allow individuals with SMA to experience a higher quality of life and greater longevity – leading to better outcomes. **All Oklahoma residents with SMA should be able to access an SMA treatment based on their individual choice and circumstance.**

Thank you for considering Cure SMA's recommendation for full coverage of Evrysdi. Please do not hesitate to contact Cure SMA if you have questions or need additional information. Cure SMA can be reached through Maynard Friesz, Vice President for Policy and Advocacy at Cure SMA, at maynard.friesz@curesma.org or 202-871-8004. Thank you for your consideration.

Sincerely,

Kenneth Hobby
President

Mary Schroth, M.D
Chief Medical Officer

Jill Jarecki, PhD
Chief Scientific Officer

Enclosure:* *August 12, 2020 Oklahoma Medicaid Letter Seeking Coverage of Evrysdi

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[i] Cure SMA Oklahoma Fact Sheet, 2020 https://www.curesma.org/wp-content/uploads/2020/09/SMA-State-Fact-Sheet_Aug2020_OK_v4.pdf

[ii] U.S. Food and Drug Administration, Evrysdi Prescribing Information, 2020, (Page 2), https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/213535s000lbl.pdf

[iii] Oklahoma Healthcare Authority Prior Authorize Evrysdi™ (Risdiplam), http://www.okhca.org/WorkArea/linkit.aspx?LinkIdentifier=id&ItemID=25273&libID=24259

Make today a breakthrough.

August 12, 2020

Melody Anthony
Medicaid Director
State of Oklahoma, Oklahoma Health Care Authority
4345 N. Lincoln Blvd.
Oklahoma City, OK 73105

RE: Evrysdi (risdiplam) for Medicaid Beneficiaries with Spinal Muscular Atrophy

Dear Director Anthony,

On behalf of the largest organization dedicated to finding treatments and a cure for Spinal Muscular Atrophy (SMA), **we are writing to respectfully request that you provide coverage and access to Evrysdi (risdiplam) for Medicaid beneficiaries as indicated by the drug's label.** The U.S. Food and Drug Administration (FDA) approved Evrysdi for the treatment of SMA on August 7, 2020. The treatment was approved for daily oral/enteral route of administration in all individuals with SMA who are two month of age and older. We urge you to ensure that this drug is covered without restriction for all people with SMA over two months old.

SMA is a progressive neurodegenerative disease that impacts 1 in 11,000 births in the US among all races, ethnicities, and genders. An estimated 1 in 50 Americans are genetic carriers. SMA robs people of physical strength by affecting the motor nerve cells in the spinal cord, impeding their ability to walk, swallow, and in the most severe cases, the ability to breathe. The disease is an autosomal recessive genetic disease caused by a mutation in the survival motor neuron gene 1 (SMN1).

As an oral treatment for SMA, the burden of administration is decreased, giving more patients potential access to SMA treatment. Covering this treatment without restrictions will allow individuals with SMA to experience a higher quality of life and greater longevity – leading to better outcomes. At the current time approximately 60% of all US patients are not yet treated. There are ongoing urgent unmet needs in our community, especially for our older patients, which this treatment will meet.

Historically, individuals with SMA have required aggressive medical care to survive, especially as the disease progressed and weakness increased with further loss of function. Because of the complexities of the disease, patients traditionally have needed a multi-disciplinary team of healthcare professionals to provide them with care and support. Without treatment, patients with SMA type 1 require permanent ventilation and feeding tubes, and costly, intensive, around the clock care. Those with type 2 and 3 may also require some of these interventions. All of these services place a tremendous financial burden on both families and insurers.

Evrysdi modifies splicing of the backup gene SMN2 to produce more functional full length SMN protein, a protein that is deficient in SMA and is necessary for motor neuron function and survival. Evrysdi is designed to increase and sustain SMN protein levels both throughout the central nervous system and in the peripheral tissues of the body. Evrysdi is a liquid oral treatment that is given daily at home.

Clinical trials have demonstrated Evrysdi's effectiveness. In the FIREFISH trial Part 1, a pivotal global study evaluating Evrysdi safety and efficacy in infants aged 2-7 months with symptomatic SMA type 1, the study showed that 41% of infants (7/17) sat without support for 5 seconds by month 12, as assessed by the Gross Motor Scale of the Bayley Scales of Infant and Toddler Development Third Edition (BSID-III). No infants achieved this milestone in the natural history of SMA type 1.[1] In addition, after 12 months of treatment with Evrysdi, 90% (19/21) of patients were alive without permanent ventilation. After a minimum of 23 months of treatment with Evrysdi, 81% (17/21) of patients were alive without permanent ventilation and reached an age of 28 months or older compared to average age of 13.5 months for death or permanent ventilation in a natural history study.[1] In this cohort, 88% (15/17) of infants were able to feed by mouth and swallow; 13/17 fed exclusively by mouth. In a natural history study, all infants over 12 months of age with SMA type 1 required feeding support.[1] Motor milestone assessment with the Hammersmith Infant Neurological Exam Module 2 (HINE-2) showed 77% (13/17) of infants had more milestones improve versus decline.

In the FIREFISH trial Part 2, a pivotal global study evaluating Evrysdi in infants aged 2-7 months old with symptomatic SMA type 1, the study met its primary endpoint with 29% of infants (12/41; $p<0.0001$) sitting without support for 5 seconds by month 12, as assessed by the BSID-III. No infants achieve this milestone in the natural history of SMA type 1. In addition, 44% (18/41) of infants were able to hold their head upright, 32% (13/41) were able to roll to the side and 5% (2/41) were able to stand with support, as measured by the HINE-2. Approximately 90% (37/41) had a Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND) score increase of at least 4 points, with 56% (23/41) achieving a score above 40; the median increase was 20 points. Without treatment, infants with SMA type 1 show a decrease in CHOP-INTEND scores over time. Almost half of the infants (49%) treated with Evrysdi did not require hospitalization up to month 12 compared to up to 7.6 hospitalizations per year for untreated patients with SMA type 1.[2] In addition, 93% were alive at month 12 compared to average age of 13.5 months for death or permanent ventilation in a natural history study.[1] Of the surviving infants, swallowing was maintained in 95% (36/38) and the ability to feed by mouth was maintained in 89% (34/38) compared to natural history.[1]

SUNFISH, a two-part, double-blind, placebo-controlled pivotal study in patients aged 2-25 years with SMA type 2 or type 3. Part 1 (n=51), determined the dose for the confirmatory Part 2 study. Part 2 (n=180) evaluated motor function using total score of Motor Function Measure 32 (MFM-32) at 12 months of treatment in non-ambulatory patients with type 2 or type 3. MFM-32 is a validated scale used to evaluate fine and gross motor function in people with neurological disorders including SMA. The study met its primary endpoint and showed that the MFM-32 change from placebo was significant in people treated with Evrysdi (1.55 point mean difference; p=0.0156). The Revised Upper Limb Module (RULM), a key secondary endpoint, also showed improvement (1.59 point difference; p=0.0028) compared to placebo. As anticipated, exploratory subgroup analyses showed that the strongest responses in MFM-32 versus placebo were observed in the youngest age group (2-5 years) with 78.1% vs. 52.9% achieving ≥3 point increase. Importantly, disease stabilization was observed in the 18-25 years age group (57.1% vs. 37.5%, with stabilization defined as a ≥0 point increase), which is the goal of treatment for those with more established disease.

The exploratory efficacy analysis of SUNFISH study Part 1 assessed motor function, using the MFM-32 scale. In a weighted analysis comparing the data with a robust natural history comparator cohort, MFM-32 change from placebo at month 24 was greater in patients receiving Evrysdi (3.99 point difference [95% CI: 2.34, 5.65] p<0.0001). Even small changes in motor function can result in meaningful

differences in daily living. Results also showed that treatment with Evrysdi led to a median two-fold increase in blood SMN protein levels after four weeks, which was sustained for at least 24 months. This is consistent with previously reported results through 12 months of treatment. SMN protein is found throughout the body and is critical for maintaining healthy motor neurons, which transmit movement signals from the central nervous system to the muscles.

JEWELFISH is an open-label study, assessing safety and pharmacodynamic data in people with SMA aged 6 months-60 years who have previously received other SMA-directed treatments and who currently are receiving Evrysdi. Among the patients who completed 12 months of treatment with Evrysdi, a median two-fold increase in SMN protein versus baseline was observed (n=18), consistent with treatment naïve patients. An early assessment of safety showed a consistent safety profile compared to treatment-naïve patients. No patients had drug related adverse events that led to Evrysdi withdrawal.

As individuals with SMA are life-long patients and regular consumers of significant health care resources, treatment with Evrysdi will very likely reduce their need for other health care services, such as inpatient and outpatient visits, emergency care, physical therapy, occupational therapy, and other related care and services. Participants in the clinical trials have already shown less need for costly, invasive interventions and services. In addition, the caregiver burden is dramatically reduced as patients gain or maintain independence.

Therefore, we ask that this life-changing treatment be covered with no restrictions for Medicaid beneficiaries for whom it has been approved. Decisions about care should be made by patients, their families, and their expert clinical care providers, based on what works best for that individual, not on financial or insurance concerns. We believe that no one impacted by SMA should be denied access to a potentially life-saving therapy, intervention, or expert care provider. To that end, we are eager to work with you to ensure that the forthcoming coverage and reimbursement policies associated with Evrysdi adequately address the needs of the eligible SMA community.

For more information, please contact Maynard Friesz, Vice President for Policy and Advocacy at Cure SMA at maynard.friesz@curesma.org or 202.871.8004.

Sincerely,

Kenneth Hobby
President

Jill Jarecki, PhD
Chief Scientific Officer

Mary Schroth, M.D.
Chief Medical Officer

References:

1. Finkel, RS, McDermott, MP, Kaufmann, P, et al. Observational study of spinal muscular atrophy type I and implications for clinical trials*. Neurology.* 2014;83(9):810-817.
2. Chatwin, M, Bush, A, Simonds, AK. Outcome of goal-directed non-invasive ventilation and mechanical insufflation/exsufflation in spinal muscular atrophy type I*. Arch Dis Child.* 2011;96(5):426-432.

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Karyopharm Therapeutics is an innovation-driven pharmaceutical company focused on the discovery, development, and commercialization of medicines with the goal of improving the lives of patients with cancer. Karyopharm is the industry leader in oral Selective Inhibitor of Nuclear Export (SINE) technology, developed to address a fundamental mechanism of oncogenesis. Currently, U.S. Food and Drug Administration (FDA) has approved oral XPOVIO (selinexor), a nuclear export inhibitor, in combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma (RRMM) who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, at least two immunomodulatory agents, and an anti-CD38 monoclonal antibody and for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from follicular lymphoma, after at least two lines of systemic therapy. These indications are approved under accelerated approval based on response rate. Continued approval for these indications may be contingent upon verification and description of clinical benefit in a confirmatory trial. The ongoing, randomized Phase 3 BOSTON study evaluating selinexor in combination with Velcade® (bortezomib) and low-dose dexamethasone will serve as the confirmatory trial. The FDA's Accelerated Approval Program was developed to allow for expedited approval of drugs that treat serious conditions and that fill an unmet medical need.

Phase 2b STORM trial in patients with relapsed-refractory multiple myeloma

The accelerated FDA approval of XPOVIO is based on results from the Phase 2b STORM (Selinexor Treatment of Refractory Myeloma) trial, which was a multicenter, single-arm, open-label study of patients with RRMM. STORM Part 2 included 122 patients with RRMM who had previously received three or more anti-myeloma treatment regimens including an alkylating agent, glucocorticoids, bortezomib, carfilzomib, lenalidomide, pomalidomide, and an anti-CD38 monoclonal antibody; and whose myeloma was documented to be refractory to glucocorticoids, a proteasome inhibitor, an immunomodulatory agent, an anti-CD38 monoclonal antibody, and to the last line of therapy.

In STORM Part 2, a total of 122 patients were treated with XPOVIO (80 mg) in combination with dexamethasone (20 mg) on Days 1 and 3 of every week. Eighty-three patients had RRMM that was documented to be refractory to bortezomib, carfilzomib, lenalidomide, pomalidomide, and daratumumab. Treatment continued until disease progression, death, or unacceptable toxicity.

The major efficacy outcome measure was overall response rate (ORR), as assessed by an Independent Review Committee based on the International Myeloma Working Group (IMWG) Uniform Response Criteria for Multiple Myeloma. The approval of XPOVIO was based upon the efficacy and safety in a prespecified subgroup analysis of the 83 patients whose disease was penta-refractory as the benefit-risk ratio appeared to be greater in this more heavily pretreated population than in the overall trial population.

For the STORM Part 2 study's major efficacy outcome measure, the ORR was 25.3% in the subgroup of 83 patients, which included one stringent complete response, no complete responses, four very good partial responses and 16 partial responses. The median time to first response for these patients was 4 weeks and the median duration of response was 3.8 months.

Amongst the 202 patients enrolled in STORM Parts 1 and 2 who were treated with XPOVIO (80 mg) in combination with dexamethasone (20 mg) on days 1 and 3 weekly, the most common adverse reactions (incidence ≥20%) were thrombocytopenia, fatigue, nausea, anemia, decreased appetite, decreased weight, diarrhea, vomiting, hyponatremia, neutropenia, leukopenia, constipation, dyspnea, and upper respiratory tract infections. The treatment discontinuation rate due to adverse reactions was 27%; 53% of patients had a reduction in the XPOVIO dose, and 65.3% had the dose of XPOVIO interrupted. The most frequent adverse reactions requiring permanent discontinuation in 4% or greater of patients who received XPOVIO included fatigue, nausea, and thrombocytopenia. The rate of fatal adverse reactions was 8.9%.

Phase 2b SADAL trial in patients with relapsed-refractory diffuse large B-cell lymphoma

The U.S. Food and Drug Administration (FDA) has also approved oral XPOVIO® (selinexor), the Company's first-in-class, Selective Inhibitor of Nuclear Export (SINE) compound, for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from follicular lymphoma, after at least two lines of systemic therapy. This indication was approved based on response rate under the FDA's Accelerated Approval Program, which was developed to allow for expedited approval of drugs that treat serious conditions and that fill an unmet medical need. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

The accelerated FDA approval of XPOVIO is based on the results from the multi-center, single-arm Phase 2b SADAL (Selinexor Against Diffuse Aggressive Lymphoma) study (NCT02227251), which evaluated 134 patients (median of 2 prior systemic therapies with a range of 1-5) with relapsed or refractory DLBCL. Patients were administered a fixed 60 mg dose of XPOVIO given orally twice weekly for a four-week cycle. Patients with germinal center B-cell (GCB) or non-GCB subtypes of DLBCL were included in enrollment.

The SADAL study met its primary endpoint of overall response rate (ORR) with an ORR of 29%, including 18 (13%) complete responses (CRs) and 21 (16%) partial responses (PRs). Key secondary endpoints included a median duration of response (DOR) in the responding patients. In the responding patients, 56% maintained a response at 3 months, 38% at 6 months and 15% at 12 months.

All 134 patients were included in the safety analyses. The most common treatment-related adverse events (AEs) were cytopenias along with gastrointestinal and constitutional symptoms and were generally reversible and managed with dose modifications and/or standard supportive care. The most common non-hematologic AEs were fatigue (63%), nausea (57%), decreased appetite (37%), and diarrhea (37%), and were mostly Grade 1 and 2 events. Grade 3 and 4 laboratory abnormalities in ≥15% of patients included thrombocytopenia, lymphopenia, neutropenia, anemia, and hyponatremia. Grade 4 laboratory abnormalities in ≥5% of patients were thrombocytopenia (18%), lymphopenia (5%), and neutropenia (9%).

As part of the FDA accelerated approval, the FDA has agreed that the XPORT-DLBCL-030 study could serve as the confirmatory trial for evaluating selinexor in DLBCL. This trial will assess the effect of selinexor or placebo added to a standard backbone immunochemotherapy of rituximab-gemcitabine-dexamethasone-platinum (R-GDP) in patients with 1-3 prior treatments for DLBCL. The rationale for this study is based on data from the ongoing Phase 1B study being conducted by the French Lymphoma Academic Research Organization (LYSARC) (NCT02741388). Karyopharm anticipates the XPORT-DLBCL-030 study will begin by the end of 2020.

Phase 3 BOSTON trial in patients with relapsed-refractory multiple myeloma

The pivotal Phase-3 BOSTON study was presented at the American Society of Clinical Oncology (ASCO) 2020 Virtual Scientific Program on May 29, 2020. The presentation can be found at the following URL: Weekly Selinexor, Bortezomib, and Dexamethasone (SVd) Versus Twice Weekly Bortezomib and Dexamethasone (Vd) in Patients with Multiple Myeloma (MM) After 1-3 Prior Therapies: Initial Results of the Phase 3 BOSTON Study

XPOVIO is a first-in-class, oral Selective Inhibitor of Nuclear Export (SINE) compound. XPOVIO functions by selectively binding to and inhibiting the nuclear export protein exportin 1 (XPO1, also called CRM1). XPOVIO blocks the nuclear export of tumor suppressor, growth regulatory and anti-inflammatory proteins, leading to accumulation of these proteins in the nucleus and enhancing their anti-cancer activity in the cell. The forced nuclear retention of these proteins can counteract a multitude of the oncogenic pathways that, unchecked, allow cancer cells with severe DNA damage to continue to grow and divide in an unrestrained fashion. Karyopharm received accelerated U.S. Food and Drug Administration (FDA) approval of XPOVIO in July 2019 in combination with dexamethasone for the treatment of adult patients with relapsed refractory multiple myeloma (RRMM) who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, at least two immunomodulatory agents, and an anti-CD38 monoclonal antibody. Karyopharm has also submitted a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) with a request for conditional approval of selinexor. A supplemental New Drug Application was accepted by the FDA seeking accelerated approval for selinexor as a new treatment for patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), and selinexor has received Fast Track and Orphan designation and Priority Review from the FDA with a scheduled PDUFA date of June 23, 2020 for this patient population. Selinexor is also being evaluated in several other mid-and later-phase clinical trials across multiple cancer indications, including in multiple myeloma in a pivotal, randomized Phase 3 study in combination with Velcade® (bortezomib) and low-dose dexamethasone (BOSTON), for which Karyopharm announced positive top-line results in March 2020. In May 2020, Karyopharm submitted a supplemental New Drug Application based on data from the Phase 3 BOSTON study. Additional, ongoing trials for selinexor include as a potential backbone therapy in combination with approved myeloma therapies (STOMP), in liposarcoma (SEAL) and in endometrial cancer (SIENDO), among others. Additional Phase 1, Phase 2 and Phase 3 studies are ongoing or currently planned, including multiple studies in combination with approved therapies in a variety of tumor types to further inform Karyopharm's clinical development priorities for selinexor. Additional clinical trial information for selinexor is available at www.clinicaltrials.gov.

Appendix B

Maintenance Drug List

Oklahoma Health Care Authority
December 2020

Introduction[1]

Most adult SoonerCare members have a 6 prescription limit each month; therefore, prescribing for and dispensing 90-day supplies of chronic maintenance medications will help members who are on multiple medications obtain the maintenance medications necessary. Dispensing of 90-day supplies of chronic maintenance medications has been shown to increase medication adherence and persistence, compared to dispensing of 30-day supplies. Additionally, a 90-day supply will reduce the SoonerCare member's financial burden as they will pay the same copay for a 90-day or 30-day supply.

In November 2019, the Oklahoma Health Care Authority (OHCA) Board voted to update the current policy and rules regarding dispensing limitations. Previously, medications could only be dispensed and reimbursed by SoonerCare up to a 34-day supply or if the quantity did not exceed 100 units. The newly voted OHCA policy and rules state the following regarding dispensing limitations and a maintenance drug list (317:30-5-77.1):

> "Prescription quantities shall be limited to a 34-day supply, except in the following situations:
> 1. The Drug Utilization Review (DUR) Board has recommended a different day supply or quantity limit based on published medical data, including the manufacturer's package insert;
> 2. The product is included on the Maintenance List of medications which are exempted from this limit and may be dispensed up to a 90-day supply;
> 3. The manufacturer of the drug recommends a dispensing quantity less than a 34-day supply…."
>
> "The DUR Board shall develop a Maintenance List of medications which are used in general practice on a continuing basis. These drugs shall be made available through the Vendor Drug Program in quantities up to a 90-day supply when approved by the prescriber. The DUR Board shall review the Maintenance List at least annually."

The DUR Board recommended and voted on categories of medications for inclusion on the maintenance drug list in December 2019, and the SoonerCare Maintenance Drug List was implemented in January 2020. The

purpose of this report is to provide the DUR Board with the current maintenance drug list for review, which is to be maintained by the DUR Board. Medications included in the maintenance drug list are set up to allow a 90-day supply of medications in the claims processing system without the need for an override. Action by the DUR Board is not required unless the DUR Board recommends changes to the current maintenance drug list.

SoonerCare Maintenance Drug List

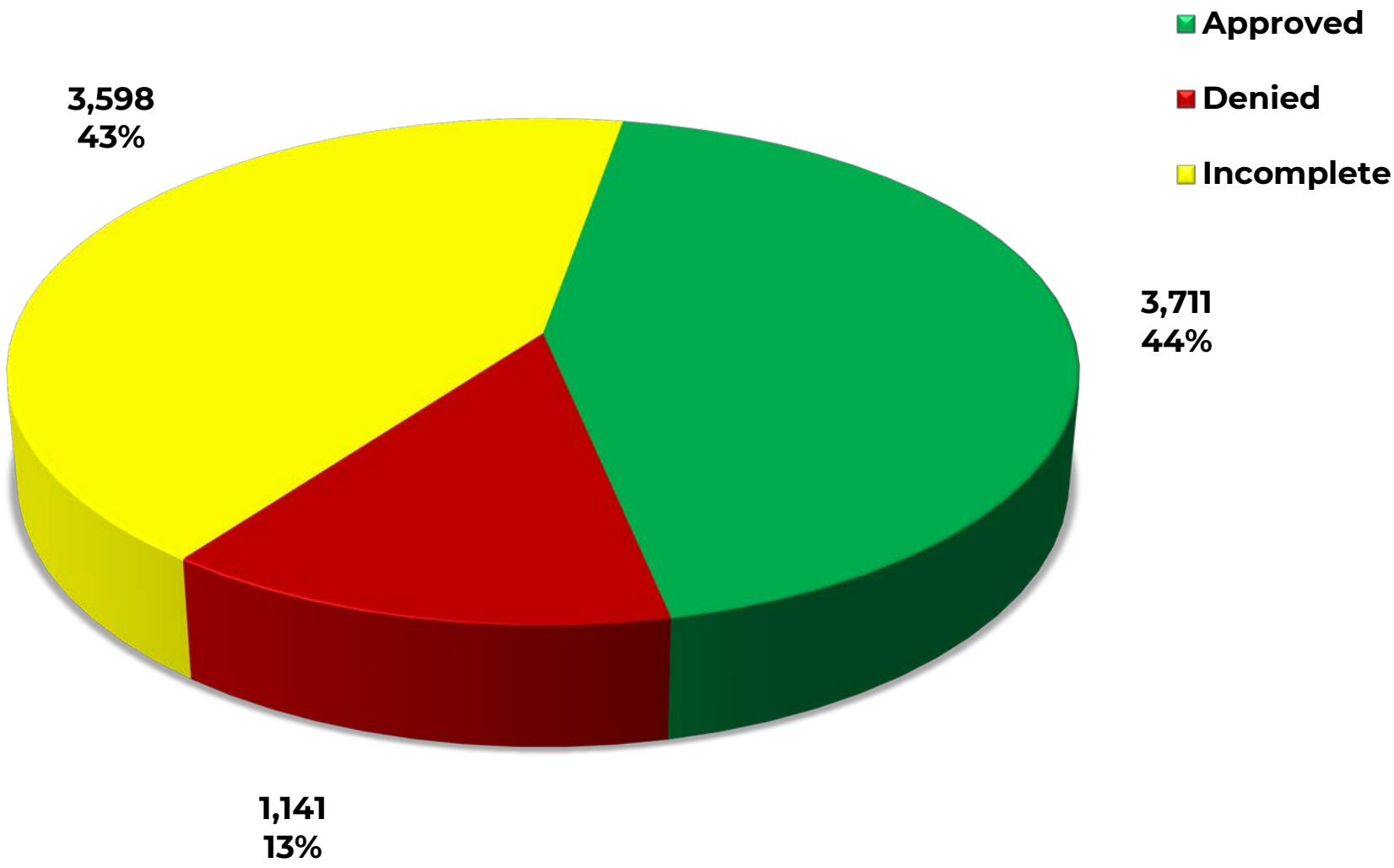
The current SoonerCare Maintenance Drug List is available on the OHCA website (www.okhca.org/rx) and includes the following categories of medications:

- Alzheimer's Medications
- Anticonvulsants
- Antidepressants
- Antihypertensive Medications
- Antipsychotic Medications
- Anti-Ulcer Medications
- Bladder Control Medications
- Benign Prostate Hyperplasia (BPH) Medications
- Cardiovascular Medications
- Chronic Obstructive Pulmonary Disease (COPD) Medications
- Diabetes Medications
- Glaucoma Medications
- Hyperlipidemia Medications
- Parkinson's Medications

[1] Taitel M, Fensterheim L, Kirkham H, et al. Medication Days' Supply, Adherence, Wastage, and Cost Among Chronic Patients in Medicaid. *MMRR* 2012; 2(3): E1-E13. doi: dx.doi.org/10.5600/mmrr.002.03.a04.

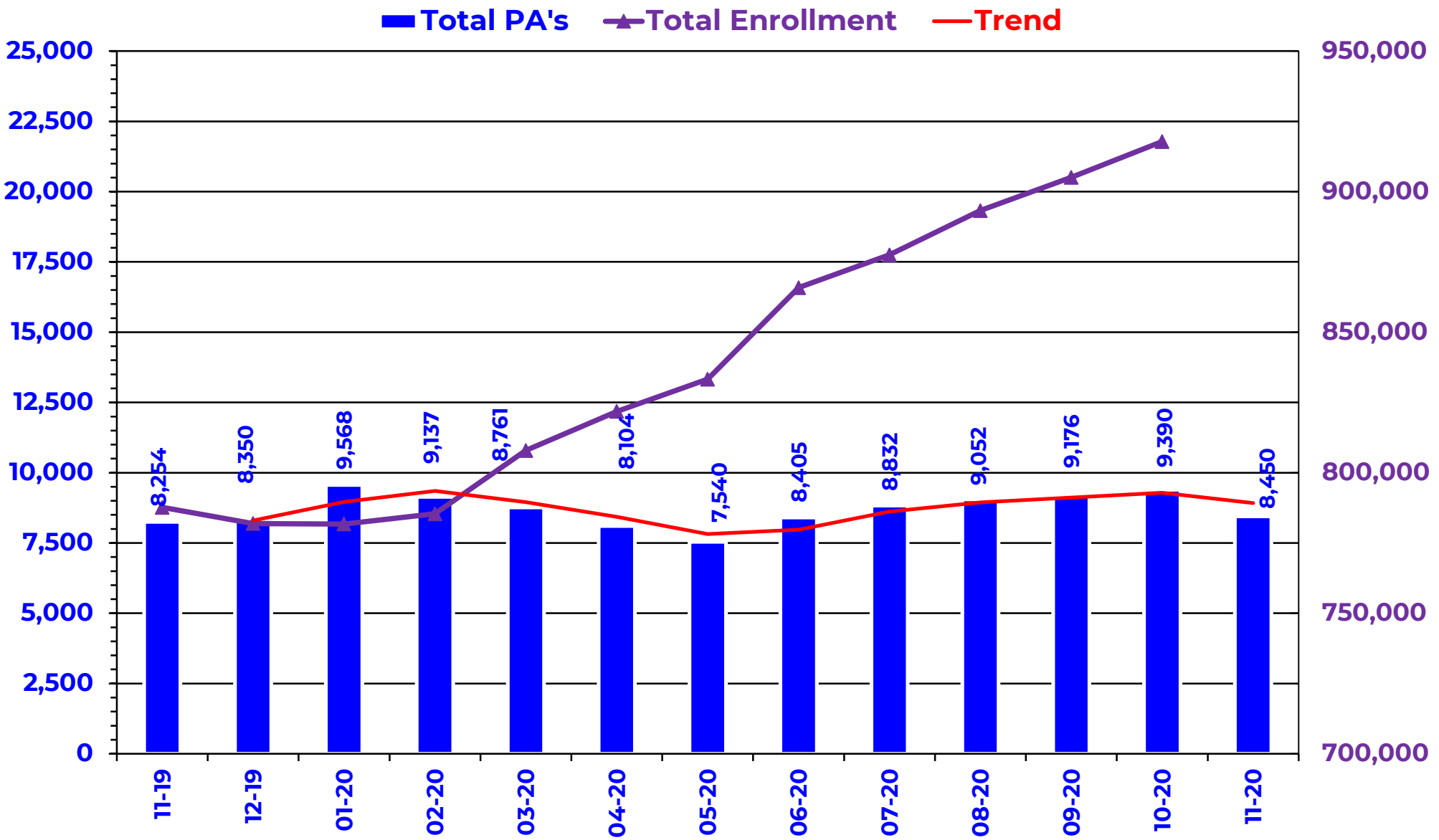
Appendix C

PRIOR AUTHORIZATION ACTIVITY REPORT: NOVEMBER 2020



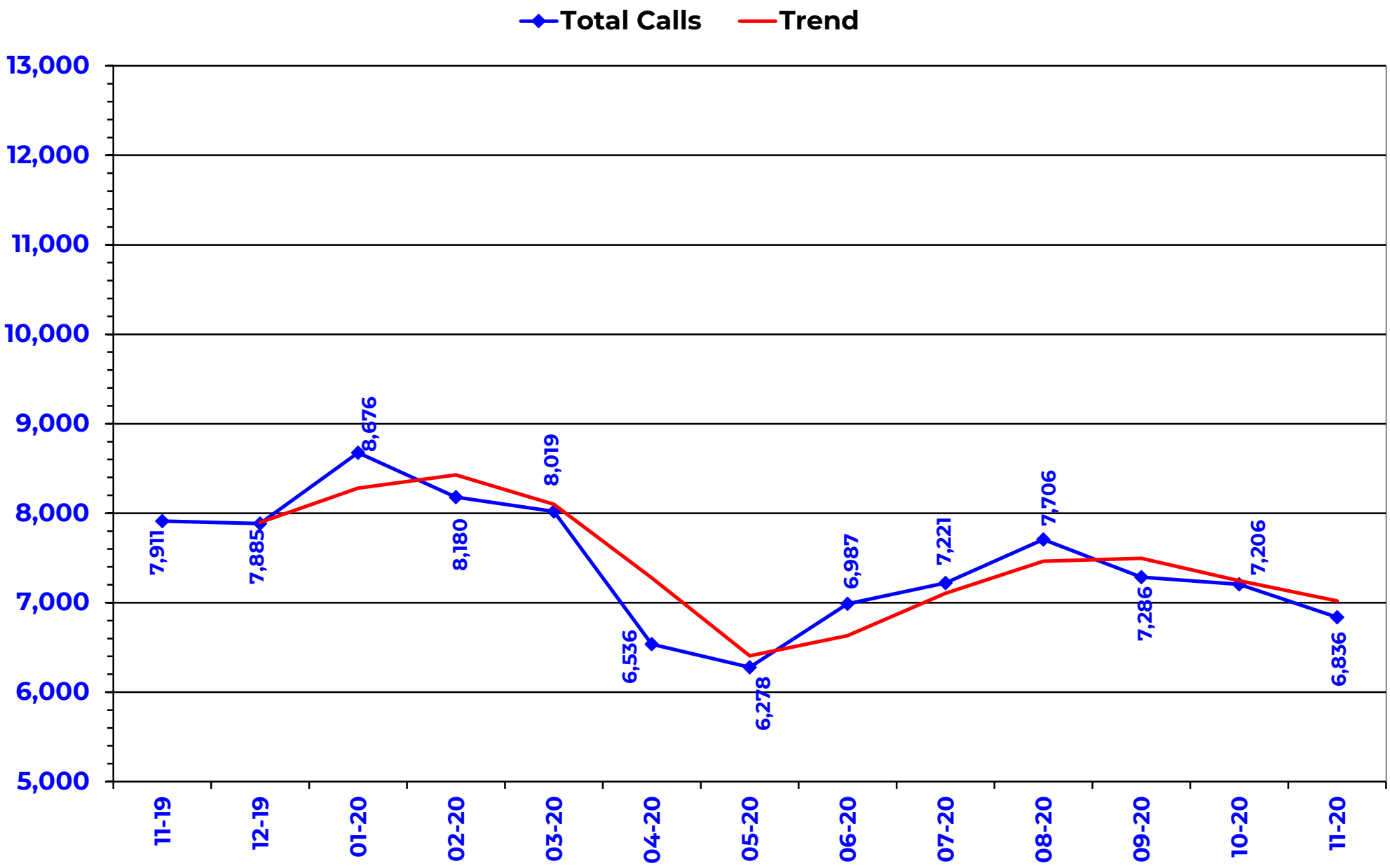
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: NOVEMBER 2019 – NOVEMBER 2020



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT: NOVEMBER 2019 – NOVEMBER 2020



Prior Authorization Activity

11/1/2020 Through 11/30/2020

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	73	4	9	60	359
Analgesic - NonNarcotic	18	0	2	16	0
Analgesic, Narcotic	280	99	36	145	152
Angiotensin Receptor Antagonist	13	3	3	7	359
Anorectal	10	1	7	2	36
Antiasthma	66	17	17	32	310
Antibiotic	63	28	7	28	205
Anticonvulsant	148	68	8	72	312
Antidepressant	162	42	17	103	350
Antidiabetic	333	115	65	153	349
Antigout	24	7	8	9	303
Antihistamine	28	5	7	16	357
Antimigraine	221	22	91	108	227
Antineoplastic	88	53	6	29	162
Antiparasitic	13	2	2	9	2
Antiulcers	59	5	15	39	125
Anxiolytic	30	1	2	27	84
Atypical Antipsychotics	264	119	19	126	347
Biologics	157	78	20	59	288
Bladder Control	35	7	9	19	314
Blood Thinners	330	183	12	135	323
Botox	48	31	10	7	271
Buprenorphine Medications	63	10	3	50	64
Cardiovascular	80	34	8	38	284
Chronic Obstructive Pulmonary Disease	163	26	38	99	346
Constipation/Diarrhea Medications	145	26	36	83	191
Contraceptive	25	8	2	15	357
Dermatological	312	87	82	143	156
Diabetic Supplies	664	299	66	299	208
Endocrine & Metabolic Drugs	70	35	8	27	150
Erythropoietin Stimulating Agents	10	2	4	4	110
Fibromyalgia	1	0	0	1	0
Gastrointestinal Agents	115	28	15	72	205
Genitourinary Agents	11	2	2	7	359
Growth Hormones	121	68	14	39	138
Hematopoietic Agents	22	7	2	13	111
Hepatitis C	112	63	15	34	9
HFA Rescue Inhalers	16	1	0	15	25
Insomnia	55	4	15	36	220
Insulin	145	55	10	80	339
Miscellaneous Antibiotics	25	5	4	16	13
Multiple Sclerosis	57	23	7	27	227
Muscle Relaxant	42	4	14	24	69
Nasal Allergy	67	10	20	37	112
Neurological Agents	80	32	12	36	256
NSAIDs	25	0	10	15	0
Ocular Allergy	20	4	4	12	86
Ophthalmic Anti-infectives	29	7	4	18	15
Ophthalmic Corticosteroid	10	0	1	9	0
Osteoporosis	6	4	0	2	357
Other*	287	71	58	158	278

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Otic Antibiotic	17	3	1	13	14
Pediculicide	16	1	4	11	7
Respiratory Agents	53	35	0	18	195
Statins	25	2	10	13	267
Stimulant	820	355	92	373	346
Synagis	202	87	53	62	141
Testosterone	56	17	11	28	331
Thyroid	48	43	1	4	358
Topical Antifungal	32	7	6	19	31
Topical Corticosteroids	58	0	39	19	0
Vitamin	76	20	36	20	95
Pharmacotherapy	40	39	0	1	260
Emergency PAs	0	0	0	0	
Total	**6,684**	**2,414**	**1,079**	**3,191**	
Overrides					
Brand	32	16	2	14	302
Compound	8	8	0	0	70
Cumulative Early Refill	1	1	0	0	180
Diabetic Supplies	10	9	0	1	222
Dosage Change	323	291	1	31	13
High Dose	1	1	0	0	355
Ingredient Duplication	3	3	0	0	11
Lost/Broken Rx	99	90	2	7	16
MAT Override	266	196	1	69	67
NDC vs Age	301	202	20	79	259
NDC vs Sex	5	5	0	0	79
Nursing Home Issue	51	39	3	9	11
Opioid MME Limit	58	26	3	29	142
Opioid Quantity	33	29	1	3	153
Other*	60	52	2	6	11
Quantity vs. Days Supply	455	285	24	146	222
STBS/STBSM	17	10	1	6	69
Stolen	16	13	2	1	71
Temporary Unlock	2	2	0	0	28
Third Brand Request	25	19	0	6	15
Overrides Total	**1,766**	**1,297**	**62**	**407**	
Total Regular PAs + Overrides	**8,450**	**3,711**	**1,141**	**3,598**	

Denial Reasons	
Unable to verify required trials.	2,890
Does not meet established criteria.	1,163
Lack required information to process request.	678
Other PA Activity	
Duplicate Requests	737
Letters	14,701
No Process	9
Changes to existing PAs	582
Helpdesk Initiated Prior Authorizations	745
PAs Missing Information	10

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

Pediatric Antipsychotic Monitoring Program Update

Oklahoma Health Care Authority
December 2020

Background[1]

The Oklahoma Health Care Authority (OHCA) is responsible for establishing and maintaining a program to monitor and manage appropriate utilization of antipsychotic medications for all children, including children in the foster care system, as part of a requirement by the Centers for Medicare and Medicaid (CMS). To accomplish these purposes, the College of Pharmacy developed the Pediatric Antipsychotic Monitoring Program (PAMP) in October 2019. The PAMP is updated twice per year, and includes providers with pediatric members receiving antipsychotic medications. Specific provider focus alternates on a semi-annual basis between all children and those children in the foster care system. The PAMP evaluates prescribing patterns and medical claims across 4 topics: medication adherence, target diagnosis, polypharmacy, and metabolic monitoring as described below:

- Adherence: Poor medication adherence is defined as members whose proportion of days covered (PDC), or adherence, was <80%. Adherence is calculated from pharmacy claims history for antipsychotic medications.

- Diagnosis: Inappropriate diagnosis is defined as members whose recent 12-month medical claims history does not include a diagnosis with a strong indication for prescribing an antipsychotic medication. These diagnoses include:
  - Schizophrenia
  - Bipolar disorder
  - Delusional disorders
  - Other nonorganic psychoses
  - Autism spectrum disorder
  - Mood disorder
  - Obsessive-compulsive disorder
  - Severe depression with or without psychotic features

- Polypharmacy: Polypharmacy is defined as members whose pharmacy claims history indicated concurrent use of 2 or more antipsychotic medications for >90 days.

- Metabolic Monitoring: Poor metabolic monitoring is defined as members whose recent 12-month medical claims history does not include glucose testing. Metabolic monitoring also evaluates the recent 12-month medical claims history for lipid testing for members with a diagnosis of hyperlipidemia.

PAMP inclusion criteria was limited to providers whose prescribing of antipsychotic medications for pediatric SoonerCare members varied significantly when compared to other SoonerCare providers in 1 or more of the topics listed above.

Providers received an educational mailing and member list if they were the last prescriber of record for an antipsychotic medication and were in the most concerning cohort of prescribers. Following receipt of the PAMP mailings, providers were offered an in-person or virtual visit by an academic detailing pharmacist and/or a consultation with an OHCA child psychiatrist. Providers were encouraged to participate in the pediatric psychiatry Project ECHO (Extension for Community Health Care Outcomes) for medical education and care management. Additional services through OHCA Care Management and Behavioral Health Care Management were also encouraged. Providers meeting criteria for pediatric members receive mailings and educational offerings each December. Providers meeting criteria for pediatric members in the foster care system receive mailings and educational offerings each June.

PAMP Trends

The following tables show the 2019 baseline values as determined in October 2019 and the resultant changes observed through November 2020. Provider numbers have been assigned to preserve the privacy of providers. In all tables, a lower number indicates improvement. Across all topics, at least 1 provider was able to improve to the degree that they no longer met criteria for the next mailing's cohort. Additionally, summative improvement was seen across all categories, with the possible exception of adherence. Medication adherence appeared to worsen from 224 total members to 247 members with PDC <80%. However, the PAMP educational materials emphasize the appropriate use of antipsychotic medications for appropriate diagnoses. Lowering the dose and/or frequency (i.e., tapering) of these medications with eventual discontinuation is suggested for members who do not meet diagnostic criteria. With this in mind, some intentional medication tapering may be represented as poor adherence.

The following table shows the number of pediatric members having poor adherence (PDC <80%) to antipsychotic medication(s) for each cohort provider.

PAMP Trends: Adherence

Provider #	2019 Adherence	2020 Adherence
1	29	65
2	29	42
3	32	*
4	47	50
5	87	49
20	*	41
Total◊	**224**	**247**

*Did not meet cohort criteria ◊ Lower number indicates improvement

The following table shows the number of pediatric members without a diagnosis supporting the use of antipsychotic medications for each cohort provider.

PAMP Trends: Diagnosis

Provider #	2019 Diagnosis	2020 Diagnosis
1	74	79
3	52	44
4	59	65
5	133	80
6	37	*
20	*	45
Total◊	**355**	**313**

*Did not meet cohort criteria ◊ Lower number indicates improvement

The following table shows the number of members receiving 2 or more antipsychotic medications for >90 days for each cohort provider.

PAMP Trends: Polypharmacy

Provider #	2019 Polypharmacy	2020 Polypharmacy
5	41	*
8	9	*
10	9	*
11	9	10
12	11	14
14	*	8
18	*	8
20	*	8
Total◊	**79**	**48**

*Did not meet cohort criteria ◊ Lower number indicates improvement

The following table shows the number of pediatric members receiving antipsychotic medication(s) with no metabolic monitoring for each cohort provider.

PAMP Trends: Metabolic Monitoring

Provider #	2019 Metabolic Monitoring	2020 Metabolic Monitoring
1	*	4
2	6	*
5	4	*
7	4	*
8	5	*
9	5	*
12	*	4
13	*	3
17	*	4
19	*	4
Total◊	**24**	**19**

*Did not meet cohort criteria ◊ Lower number indicates improvement

Conclusions

The first year of PAMP trends indicate overall improvements in the areas of diagnosis, metabolic monitoring, and polypharmacy. Improvements in the area of adherence are more difficult to determine, owing to the likely co-occurrences of true poor adherence and intentional tapering. The greatest improvements were seen in the areas of metabolic monitoring and polypharmacy. In the case of metabolic monitoring, none of the original cohort met the inclusion criteria at the end of the first year. Polypharmacy improvements also resulted in 3 providers no longer meeting cohort criteria at the end of the first year. Overall results indicate the PAMP targeted mailing and educational offerings are likely leading to improvements in antipsychotic medication management resulting in a lower risk of overprescribing and increased rates of recommended metabolic monitoring. The College of Pharmacy will continue to work with OHCA to identify providers who may benefit from PAMP activities with the goal of promoting evidence-based use of antipsychotic medications for pediatric members. Future results of the PAMP activities will be reviewed with the DUR Board as they become available.

[1] 115th U.S. Congress (2017-2018). H.R.6 – SUPPORT for Patients and Communities Act. Available online at: https://www.congress.gov/115/bills/hr6/BILLS-115hr6enr.pdf. Issued 10/24/2018. Last accessed 11/23/2020.

Appendix D

Vote to Prior Authorize AirDuo® Digihaler® (Fluticasone Propionate/Salmeterol), ArmonAir® Digihaler® (Fluticasone Propionate), and Breztri Aerosphere™ (Budesonide/Glycopyrrolate/Formoterol Fumarate)

Oklahoma Health Care Authority
December 2020

New U.S. Food and Drug Administration (FDA) Approval(s)[1,2,3,4,5,6]

- **AirDuo® Digihaler® (fluticasone propionate/salmeterol inhalation powder)**, a combination therapy digital inhaler with built-in sensors that connect to a companion mobile application (app) to provide information on inhaler use to patients with asthma, was FDA approved in July 2019. AirDuo® Digihaler® is indicated for the treatment of asthma in patients 12 years of age and older. AirDuo® Digihaler® is not indicated for the relief of acute bronchospasm. AirDuo® Digihaler® contains a built-in electronic module which detects, records, and stores data on inhaler events for transmission to a mobile app. Use of the mobile app is not required for administration of medication to the patient. The starting dosage is based on prior asthma therapy and disease severity. The recommended dose is 1 inhalation of AirDuo® Digihaler® 55/14mcg, 113/14mcg, or 232/14mcg twice daily. The approval of AirDuo® Digihaler® is based on the review of the supplemental New Drug Application (sNDA) submitted by Teva to the FDA, and efficacy was based primarily on the dose-ranging trials and the confirmatory trials for AirDuo RespiClick®. AirDuo® Digihaler® was approved in a low, medium, and high dose (55/14mcg, 113/14mcg, and 232/14mcg). As a fixed dose combination asthma therapy containing an inhaled corticosteroid (ICS) and a long-acting beta$_2$ agonist (LABA), AirDuo® Digihaler® contains the same active ingredients as Advair Diskus®, which is also FDA approved in low, medium, and high doses: 100/50mcg, 250/50mcg, and 500/50mcg. The annual estimated cost for AirDuo® Digihaler® is $5,388.00.
- **ArmonAir® Digihaler® (fluticasone propionate inhalation powder)**, an ICS delivered via Teva's Digihaler® device (*refer to AirDuo® Digihaler® above for additional information on the Digihaler® device*) was FDA approved in February 2020. ArmonAir® Digihaler® is indicated for the maintenance treatment of asthma in patients 12 years of age and older. ArmonAir® Digihaler® is not indicated for the relief of acute bronchospasm. The starting dose of ArmonAir® Digihaler® is based on prior asthma therapy and disease severity. The recommended dosage

for the treatment of asthma in patients 12 years of age and older is 1 inhalation of ArmonAir® Digihaler® 55mcg, 113mcg, or 232mcg twice daily. ArmonAir® Digihaler® should not be used with a spacer or volume holding chamber. The approval of ArmonAir® Digihaler® is based on the review of the sNDA submitted by Teva to the FDA, and efficacy was based primarily on the dose-ranging trials and the confirmatory trials for ArmonAir™ RespiClick®. ArmonAir® Digihaler® was approved in a low, medium, and high dose (55mcg, 113mcg, and 232mcg). The annual estimated cost of ArmonAir® Digihaler® is $3,588.00.

- **Breztri Aerosphere™ (budesonide/glycopyrrolate/formoterol aerosol)** was FDA approved in July 2020 for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD). Breztri Aerosphere™ is not indicated for the relief of acute bronchospasm or for the treatment of asthma. Breztri Aerosphere™ is supplied as an inhalation aerosol pressurized metered dose inhaler (MDI) containing 160mcg budesonide/9mcg glycopyrrolate/4.8mcg formoterol fumarate per actuation. The recommended dosage of Breztri Aerosphere™ for the maintenance treatment of COPD is 2 inhalations twice daily. The FDA approval was based on positive results from the Phase 3 ETHOS trial in which Breztri Aerosphere™, a triple-combination therapy, showed a statistically significant reduction in the rate of moderate or severe exacerbations compared with dual-combination therapies glycopyrrolate/formoterol fumarate and PT009 (budesonide/formoterol fumarate). The approval was also supported by efficacy and safety data from the Phase 3 KRONOS trial. Results from the Phase 3 ETHOS trial were published in *The New England Journal of Medicine* in June 2020, and results from the Phase 3 KRONOS trial were published in *The Lancet Respiratory Medicine* in September 2018. In both trials, the safety and tolerability of Breztri Aerosphere™ were consistent with the profiles of the dual comparators. The estimated annual cost of Breztri Aerosphere™ is $7,084.80.

New FDA Expanded Indication(s) and/or Formulation(s)[7,8,9,10,11,12,13,14]

- **Dulera® (mometasone/formoterol inhalation aerosol)** was approved by the FDA in August 2019 for a new strength, 50mcg/5mcg, and an age expansion to treat asthma in patients 5 years of age and older. The approval was based on findings from a trial evaluating the efficacy of Dulera® 50mcg/5mcg in pediatric patients 5 years of age to younger than 12 years of age compared with mometasone furoate MDI 50mcg. Patients included in the trial were adequately controlled on an ICS/LABA for at least 4 weeks and had no symptoms of asthma worsening during a 2-week run-in on mometasone furoate MDI 50mcg. Results showed that patients on Dulera® 50mcg/5mcg had a

statistically significant change from baseline to week 12 in 60-minute morning post-dose percent predicted forced expiratory volume per 1 second ($ppFEV_1$) compared with mometasone furoate MDI 50mcg [primary end point: 5.21; 95% confidence interval (CI): 3.22, 7.20]. With regard to safety, patients in this age group demonstrated safety results similar to those seen in patients 12 years of age and older. Dulera® was previously FDA approved for patients 12 years of age and older and is also available as 100mcg/5mcg and 200mcg/5mcg strengths.

- **Asmanex® HFA (mometasone furoate)** was FDA approved in August 2019 for a new strength, 50mcg, and an age expansion to treat asthma in patients 5 years of age and older. The approval was based on data from a 12-week, double-blind, placebo-controlled trial in 583 patients 5 years of age to younger than 12 years of age with persistent asthma (mean baseline FEV_1: 79% of predicted) who had been using a low-to-medium dose of an ICS with or without a LABA for at least 12 weeks prior to study entry. After an approximate 2-week run-in period, patients were randomized to receive Asmanex® HFA 50mcg, 2 other doses of Asmanex® HFA, Asmanex® dry-powder inhaler (DPI), or placebo. Results showed that after 12 weeks of treatment, Asmanex® HFA 50mcg was statistically superior to placebo as measured by improvement from baseline in morning pre-dose $ppFEV_1$ at the end of the dosing interval (primary end point: 6.29%; 95% CI: 3.05, 9.53). The safety profile and overall effectiveness in this age group were consistent with that observed in patients 12 years of age and older who also received Asmanex® HFA. Asmanex® HFA was previously FDA approved for patients 12 years of age and older and is also available as 100mcg and 200mcg strengths.
- **Nucala® (mepolizumab)** was FDA approved in September 2020 for adults and children 12 years of age and older with hypereosinophilic syndrome (HES) for 6 months or longer without another identifiable non-blood related cause of the disease. The new indication for Nucala® is the first approval for HES patients in nearly 14 years. HES is a heterogeneous group of rare disorders associated with persistent eosinophilia with evidence of organ damage. HES is defined as an absolute eosinophil count (AEC) >1,500 cells/mcL in the peripheral blood on 2 examinations separated in time by at least 1 month and/or pathologic confirmation of tissue hypereosinophilia. Symptoms include skin rashes, itching, asthma, difficulty breathing, abdominal pain, vomiting, diarrhea, arthritis, muscle inflammation, congestive heart failure, deep venous thrombosis (DVT), and anemia. Nucala® was evaluated in a randomized, double-blind, multicenter, placebo-controlled trial in 108 patients with HES. Patients entering the trial had experienced at least 2 HES flares within the past 12 months and had a blood eosinophil count of 1,000 cells/mcL or higher during screening. In

the trial, patients were randomly assigned to receive Nucala® or placebo by injection every 4 weeks. The trial compared the proportion of patients who experienced an HES flare during the 32-week treatment period. An HES flare was defined as worsening of clinical signs and symptoms of HES or increasing eosinophils on at least 2 occasions. The trial compared the proportion of patients with at least 1 flare over a 32-week treatment period, as well as the time to the first flare. Fewer patients in the Nucala® treatment group (28%) had HES flares compared to patients in the placebo group (56%), with a 50% relative reduction. In addition, the time to the first HES flare was later, on average, for patients treated with Nucala® vs. placebo. Nucala® is also FDA approved for patients 6 years of age and older with severe asthma with an eosinophilic phenotype and for adult patients with eosinophilic granulomatosis with polyangiitis (EGPA), a rare autoimmune condition that causes blood vessel inflammation.

- **Trelegy Ellipta (fluticasone furoate/umeclidinium/vilanterol)** was FDA approved in September 2020 for the treatment of asthma in patients 18 years of age and older, adding to its current indication for the treatment of patients with COPD. Trelegy Ellipta is not indicated for the relief of acute bronchospasm. The FDA approved strength for both COPD and asthma is fluticasone furoate/umeclidinium/vilanterol 100/62.5/25mcg. There is an additional strength for asthma alone, which is fluticasone furoate/umeclidinium/vilanterol 200/62.5/25mcg.

Recommendations

The College of Pharmacy recommends the prior authorization of AirDuo® Digihaler® (fluticasone propionate/salmeterol inhalation powder) and ArmonAir® Digihaler® (fluticasone propionate inhalation powder) with the following criteria (new criteria is shown in red):

AirDuo® Digihaler® (Fluticasone Propionate/Salmeterol Inhalation Powder) Approval Criteria:

1. An FDA approved diagnosis of asthma; and
2. Member must be 12 years of age or older; and
3. A patient-specific, clinically significant reason why the member requires AirDuo® Digihaler® over AirDuo RespiClick® and all preferred Tier-1 inhaled corticosteroid and long-acting beta$_2$-agonist (ICS/LABA) products (Advair®, Dulera®, and Symbicort®) must be provided; and
4. Failure of Advair®, Dulera®, and Symbicort® or a reason why Advair®, Dulera®, and Symbicort® are not appropriate for the member must be provided; and
5. Member must have used an ICS for at least 1 month immediately prior; and

6. Member must be considered uncontrolled by provider [required rescue medication >2 days a week (not for prevention of exercise induced bronchospasms) and/or needed oral systemic corticosteroids]; or
7. A clinical situation warranting initiation with combination therapy due to severity of asthma; and
8. The prescriber agrees to closely monitor member adherence; and
9. The member should be capable and willing to use the Companion Mobile App and to follow the Instructions for Use, and member must ensure the Digihaler® Companion Mobile App is compatible with their specific smartphone; and
10. The member's phone camera must be functional and able to scan the inhaler QR code and register the AirDuo® Digihaler® inhaler; and
11. Approvals will be for the duration of 3 months. For continuation consideration, documentation demonstrating positive clinical response and member compliance >80% with prescribed maintenance therapy must be provided. In addition, a patient-specific, clinically significant reason why the member cannot transition to Tier-1 medications must be provided. Tier structure rules continue to apply.

ArmonAir® Digihaler® (Fluticasone Propionate Inhalation Powder) Approval Criteria:

1. An FDA approved diagnosis of asthma; and
2. Member must be 12 years of age or older; and
3. A patient-specific, clinically significant reason why Flovent® (fluticasone propionate) or other preferred monotherapy inhaled corticosteroid (ICS) is not appropriate for the member must be provided; and
4. The prescriber agrees to closely monitor member adherence; and
5. The member should be capable and willing to use the Companion Mobile App and to follow the Instructions for Use, and member must ensure the Digihaler® Companion Mobile App is compatible with their specific smartphone; and
6. The member's phone camera must be functional and able to scan the inhaler QR code and register the ArmonAir® Digihaler® inhaler; and
7. Approvals will be for the duration of 3 months. For continuation consideration, documentation demonstrating positive clinical response and member compliance >80% with prescribed maintenance therapy must be provided. In addition, a patient-specific, clinically significant reason why the member cannot transition to Tier-1 medications must be provided. Tier structure rules continue to apply.

Additionally, the College of Pharmacy recommends the prior authorization of Breztri Aerosphere™ (budesonide/glycopyrrolate/formoterol aerosol) and recommends updating the current approval criteria for Trelegy Ellipta (fluticasone furoate/umeclidinium/vilanterol) and Nucala® (mepolizumab)

based on the newly FDA approved indications, with the following criteria (new criteria and changes are shown in red):

Breztri Aerosphere™ (Budesonide/Glycopyrrolate/Formoterol) and Trelegy Ellipta (Fluticasone Furoate/Umeclidinium/Vilanterol) Approval Criteria:

1. An FDA approved diagnosis ~~of chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema, or to reduce exacerbations of COPD in patients with a history of exacerbations~~; and
2. Member must be 18 years of age or older; and
3. A 4-week trial of at least 1 long-acting beta$_2$ agonist (LABA) and a 4-week trial of 1 long-acting muscarinic antagonist (LAMA) within the past 90 days used concomitantly with an inhaled corticosteroid (ICS); and
4. A patient-specific, clinically significant reason why the member requires the triple combination therapy in place of the individual components or use of a LABA/ICS combination with a LAMA must be provided.

Nucala® (Mepolizumab Injection) Approval Criteria [Hypereosinophilic Syndrome (HES) Diagnosis]:

1. An FDA approved diagnosis of hypereosinophilic syndrome (HES) for ≥6 months without an identifiable non-hematologic secondary cause; and
2. Member must be 12 years of age or older; and
3. Member must have a past history of at least 2 confirmed HES flares [requiring increase in oral corticosteroid (OCS) dose, initiation/increased dose of cytotoxic or immunosuppressive therapy, or hospitalization] within the past 12 months; and
4. Member must have a baseline blood eosinophil count of 1,000 cells/mcL or higher in the last 4 weeks prior to initiating Nucala®; and
5. Diagnosis of FIP1L1-PDGFRα kinase-positive HES will not be approved; and
6. Failure to achieve remission despite corticosteroid therapy (oral prednisone equivalent ≥10mg/day) for a minimum of 4 weeks duration or member is unable to tolerate corticosteroid therapy due to significant side effects from glucocorticoid therapy; and
7. Nucala® must be prescribed by a hematologist or a specialist with expertise in treatment of HES (or an advanced care practitioner with a supervising physician who is a hematologist or a specialist with expertise in treatment of HES); and
8. For authorization of Nucala® vial, prescriber must verify the injection will be administered in a health care setting by a health care professional prepared to manage anaphylaxis; or

9. For authorization of Nucala® prefilled autoinjector or prefilled syringe, prescriber must verify the member or caregiver has been trained by a health care professional on subcutaneous administration, monitoring for any allergic reactions, and storage of Nucala®; and
10. A quantity limit of 3 vials, prefilled autoinjectors, or prefilled syringes per 28 days will apply; and
11. Initial approvals will be for the duration of 6 months after which time compliance will be evaluated for continued approval. For continued approval, member must be compliant and prescriber must verify the member is responding to Nucala® as demonstrated by fewer HES flares from baseline or a decrease in daily OCS dosing from baseline.

Lastly, the College of Pharmacy recommends the prior authorization of Asmanex® HFA (mometasone furoate) 50mcg and Dulera® (mometasone/formoterol) 50mcg/5mcg based on net costs with the following criteria (new criteria and changes are shown in red):

Inhaled Corticosteroids (ICS) and Combination Products	
Tier-1	**Tier-2***
budesonide (Pulmicort®)	beclomethasone dipropionate (QVAR® RediHaler™)
budesonide/formoterol (Symbicort®)⁺	fluticasone furoate (Arnuity® Ellipta®)
ciclesonide (Alvesco®)	fluticasone furoate/vilanterol (Breo® Ellipta®)
flunisolide (Aerospan®)	fluticasone propionate (ArmonAir™ RespiClick®)
fluticasone propionate (Flovent®)	fluticasone propionate/salmeterol (AirDuo RespiClick®)
fluticasone/salmeterol (Advair®)	**mometasone furoate 50mcg (Asmanex® HFA)**
mometasone furoate (Asmanex®)¥	**mometasone furoate/formoterol 50mcg/5mcg (Dulera®)**
mometasone furoate/formoterol (Dulera®)◊	

Tier-1 products indicated for the member's age are covered with no prior authorization required.
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
¥Includes all strengths and formulations other than Asmanex® HFA 50mcg.
◊ Includes all strengths other than Dulera® 50mcg/5mcg.
*Unique criteria applies to each medication.

Asmanex® HFA (Mometasone Furoate) 50mcg and QVAR® RediHaler™ (Beclomethasone Dipropionate) Approval Criteria:

1. An FDA approved diagnosis of asthma; and
2. Member must be ~~4 years of age or older~~ at the age indicated for the requested product:

   a. Asmanex® HFA 50mcg: Member must be between 5 and 11 years of age; or
   b. QVAR® RediHaler™: Member must be 4 years of age or older; and
3. A trial of all available Tier-1 inhaled corticosteroids or a patient-specific, clinically significant reason why they are not appropriate for the member must be provided.

Dulera® (Mometasone Furoate/Formoterol) 50mcg/5mcg Approval Criteria:

1. An FDA approved diagnosis of asthma; and
2. Member must be between 5 and 11 years of age; and
3. Failure of Advair® and Symbicort® or a reason why Advair® and Symbicort® are not appropriate for the member must be provided; and
4. Member must have used an inhaled corticosteroid for at least 1 month immediately prior; and
5. Member must be considered uncontrolled by provider [required rescue medication >2 days a week (not for prevention of exercise induced bronchospasms) and/or needed oral systemic corticosteroids]; or
6. A clinical situation warranting initiation with combination therapy due to severity of asthma.

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Appendix E

Vote to Prior Authorize Blenrep (Belantamab Mafodotin-blmf), Darzalex® (Daratumumab), Darzalex Faspro™ (Daratumumab/Hyaluronidase-fihj), Empliciti® (Elotuzumab), Hemady™ (Dexamethasone 20mg Tablet), Ninlaro® (Ixazomib), Sarclisa® (Isatuximab-irfc), and Xpovio® (Selinexor)

Oklahoma Health Care Authority
December 2020

U.S. Food and Drug Administration (FDA) Approval(s) and Indication(s)[1,2,3]

- **November 2015:** The FDA approved Ninlaro® (ixazomib) for use in combination with lenalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received at least 1 prior therapy.
- **November 2015:** The FDA approved Empliciti® (elotuzumab) for use in combination with lenalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received 1 to 3 prior therapies.
- **June 2019:** The FDA approved Darzalex® (daratumumab) for intravenous (IV) use in combination with lenalidomide and dexamethasone for patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant (ASCT).
- **July 2019:** The FDA granted accelerated approval to Xpovio® (selinexor) for use in combination with dexamethasone for adult patients with relapsed or refractory multiple myeloma (RRMM) who have received ≥4 prior therapies and whose disease is refractory to ≥2 proteasome inhibitors (PIs), ≥2 immunomodulatory agents, and an anti-cluster of differentiation 38/cyclic adenosine diphosphate ribose hydrolase (anti-CD38) monoclonal antibody.
- **September 2019:** The FDA approved Darzalex® (daratumumab) for adult patients with multiple myeloma for use in combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for ASCT.
- **October 2019:** The FDA approved Hemady™ (dexamethasone 20mg tablet) for use in combination with other anti-myeloma therapies for the treatment of adults with multiple myeloma.
- **March 2020:** The FDA approved Sarclisa® (isatuximab-irfc) for use in combination with pomalidomide and dexamethasone for adult

patients with multiple myeloma who have received ≥2 prior therapies including lenalidomide and a PI.

- **May 2020:** The FDA approved Darzalex Faspro™ (daratumumab/ hyaluronidase-fihj) for adult patients with newly diagnosed RRMM. This new product allows for subcutaneous (sub-Q) dosing of daratumumab.
- **June 2020:** The FDA granted accelerated approval to Xpovio® (selinexor) for adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from follicular lymphoma, after ≥2 lines of systemic therapy.
- **August 2020:** The FDA approved Blenrep (belantamab mafodotin-blmf) for adult patients with RRMM who have received ≥4 prior therapies, including an anti-CD38 monoclonal antibody, a PI, and an immunomodulatory agent.
- **August 2020:** The FDA approved Kyprolis® (carfilzomib) and Darzalex® (daratumumab) in combination with dexamethasone for adult patients with RRMM who have received 1 to 3 prior therapies.

Product Summaries[4,5,6,7,8,9,10]

Blenrep (Belantamab Mafodotin-blmf):

- **Therapeutic Class:** B-cell maturation antigen (BCMA)-directed antibody and microtubule inhibitor conjugate

- **Boxed Warning: Ocular Toxicity**
  - In clinical trials in the pooled safety population (patients who received up to 1.4 times the recommended dose), Blenrep caused changes in the corneal epithelium resulting in severe vision loss, corneal ulcer, blurred vision, and dry eyes.
  - Ophthalmic exams at baseline, prior to each dose, and promptly for worsening symptoms are recommended. Blenrep should be withheld until improvement and then resumed or permanently discontinued, based on the severity of symptoms.
  - Blenrep is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Blenrep REMS.

- **Indication(s):** Treatment of adult patients with RRMM who have received ≥4 prior therapies
- **How Supplied:** 100mg lyophilized powder for reconstitution and further dilution in single-dose vials (SDVs)
- **Dose:** 2.5mg/kg (based on actual body weight) via IV infusion over approximately 30 minutes once every 3 weeks
- **Cost:** The Wholesale Acquisition Cost (WAC) is $8,277.00 per SDV; cost will vary due to weight-based dosing

Darzalex® (Daratumumab):

- **Therapeutic Class:** CD38-directed cytolytic antibody
- **Indication(s):** Treatment of adult patients with multiple myeloma in combination with other medications or monotherapy as follows:
  - In combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for ASCT and in patients with RRMM who have received at least 1 prior therapy
  - In combination with bortezomib, melphalan, and prednisone in newly diagnosed patients who are ineligible for ASCT
  - In combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for ASCT
  - In combination with bortezomib and dexamethasone in patients who have received at least 1 prior therapy
  - In combination with carfilzomib and dexamethasone in patients who have received 1 to 3 prior therapies
  - In combination with pomalidomide and dexamethasone in patients who have received ≥2 prior therapies including lenalidomide and a PI
  - As monotherapy, in patients who have received ≥3 prior therapies including a PI and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent
- **How Supplied:** 100mg/5mL and 400mg/20mL solution in SDVs
- **Dose:** 16mg/kg (based on actual body weight) administered via IV infusion; dosing schedule varies based on regimen recommended for monotherapy or for use in combination with other medication(s)
- **Cost:** The WAC is $111.14 per milliliter (mL), resulting in a cost of $555.70 per 100mg/5mL SDV and $2,222.80 per 400mg/20mL SDV; cost will vary due to weight-based dosing and dosing regimen

Darzalex Faspro™ (Daratumumab/Hyaluronidase-fihj):

- **Therapeutic Class:** Combination of a CD38-directed cytolytic antibody (daratumumab) and an endoglycosidase (hyaluronidase)
- **Indication(s):** Treatment of adult patients with multiple myeloma in combination with other medications or monotherapy as follows:
  - In combination with bortezomib, melphalan, and prednisone in newly diagnosed patients who are ineligible for ASCT
  - In combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for ASCT and in patients with RRMM who have received at least 1 prior therapy
  - In combination with bortezomib and dexamethasone in patients who have received at least 1 prior therapy
  - As monotherapy, in patients who have received ≥3 prior therapies including a PI and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent

- **How Supplied:** 1,800mg daratumumab/30,000 units hyaluronidase/15mL (120mg/2,000 units/mL) solution in SDVs
- **Dose:** 1,800mg/30,000 units via sub-Q injection over 3 to 5 minutes; dosing schedule varies based on regimen recommended for monotherapy or for use in combination with other medication(s)
- **Cost:** The WAC is $504.93 per mL, resulting in a cost of $7,573.95 per SDV; cost will vary based on dosing regimen

Empliciti® (Elotuzumab):

- **Therapeutic Class:** Signaling lymphocytic activation molecule family member 7 (SLAMF7)-directed immunostimulatory antibody
- **Indication(s):**
  - For use in combination with lenalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received 1 to 3 prior therapies
  - For use in combination with pomalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received ≥2 prior therapies including lenalidomide and a PI
- **How Supplied:** 300mg or 400mg lyophilized powder for reconstitution in SDVs
- **Dose:**
  - With lenalidomide and dexamethasone: 10mg/kg (based on actual body weight) administered IV every week for the first 2 cycles, followed by every 2 weeks thereafter
  - With pomalidomide and dexamethasone: 10mg/kg administered IV every week for the first 2 cycles, followed by 20mg/kg every 4 weeks thereafter
- **Cost:** The WAC is $1,941.96 per 300mg SDV and $2,589.27 per 400mg SDV; cost will vary due to weight-based dosing and dosing regimen

Hemady™ (Dexamethasone 20mg Tablet):

- **Therapeutic Class:** Glucocorticoid
- **Indication(s):** For use in combination with other anti-myeloma therapies for the treatment of adults with multiple myeloma
- **How Supplied:** 20mg oral tablets
- **Dose:** 20mg or 40mg once daily, on specific days depending on the protocol regimen
- **Cost Comparison:**

Product	Cost Per Unit	Cost Per 20mg Dose	Cost Per 40mg Dose
Hemady™ (dexamethasone) 20mg tablet	**$24.85**	**$24.85**	**$49.70**
dexamethasone 4mg tablet	$0.62	$3.10	$6.20

Unit = tablet; costs will vary due to variable dosing regimens
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.

Ninlaro® (Ixazomib):

- **Therapeutic Class:** Proteasome inhibitor (PI)
- **Indication(s):** For use in combination with lenalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received at least 1 prior therapy
- **How Supplied:** 2.3mg, 3mg, and 4mg oral capsules
- **Dose:** 4mg once a week on days 1, 8, and 15 of a 28-day treatment cycle; alternative strengths available for dose reductions/modifications if needed
- **Cost:** The WAC is $3,491.67 per capsule for all available strengths, resulting in a cost of $10,475.01 per 28 days based on the recommended dosing of 4mg on days 1, 8, and 15 of a 28-day cycle

Sarclisa® (Isatuximab-irfc):

- **Therapeutic Class:** CD38-directed cytolytic antibody
- **Indication(s):** For use in combination with pomalidomide and dexamethasone, for the treatment of adult patients with multiple myeloma who have received ≥2 prior therapies including lenalidomide and a PI
- **How Supplied:** 100mg/5mL and 500mg/25mL (20mg/mL) solution in SDVs
- **Dose:** 10mg/kg (based on actual body weight) via IV infusion every week for 4 weeks followed by 10mg/kg every 2 weeks in combination with pomalidomide and dexamethasone
- **Cost:** The WAC is $130.00 per mL, resulting in a cost of $650.00 per 100mg/5mL SDV and $3,250.00 per 500mg/25mL SDV; cost will vary due to weight-based dosing

Xpovio® (Selinexor):

- **Therapeutic Class:** Nuclear export inhibitor
- **Indication(s):**
  - For use in combination with dexamethasone for the treatment of adult patients with RRMM who have received ≥4 prior therapies and whose disease is refractory to ≥2 PIs, ≥2 immunomodulatory agents, and an anti-CD38 monoclonal antibody
  - For the treatment of adult patients with relapsed or refractory DLBCL, not otherwise specified, including DLBCL arising from follicular lymphoma, after ≥2 lines of systemic therapy
- **How Supplied:** 20mg oral tablets packaged in 7 dose presentations (allowing for dose reduction based on adverse effects and diagnosis being treated); each dosing option is available in a 28-day supply carton containing 4 weekly blister packs

- **Dose:**
  - RRMM: 80mg [(4) 20mg tablets] in combination with 20mg dexamethasone taken on days 1 and 3 of each week
  - DLBCL: 60mg [(3) 20mg tablets] taken on days 1 and 3 of each week
- **Cost:** The WAC per tablet ranges from $687.50 to $2,750.00, resulting in an approximate cost of $22,000.00 per 28-day supply carton

Recommendations

- The prior authorization of Blenrep (belantamab mafodotin-blmf), Darzalex® (daratumumab), Darzalex Faspro™ (daratumumab/ hyaluronidase-fihj), Empliciti® (elotuzumab), Hemady™ (dexamethasone 20mg tablet), Ninlaro® (ixazomib), Sarclisa® (isatuximab-irfc), and Xpovio® (selinexor) with the following criteria (shown in red):

Blenrep (Belantamab Mafodotin-blmf) Approval Criteria [Multiple Myeloma Diagnosis]:

1. Diagnosis of relapsed or refractory multiple myeloma (RRMM) in adults; and
2. Member has received ≥4 prior therapies including an anti-CD38 monoclonal antibody, a proteasome inhibitor (PI), and an immunomodulatory agent; and
3. Prescriber must verify the member will receive eye exams, including visual acuity and slit lamp ophthalmic examinations, with each cycle (every 3 weeks).

Darzalex® (Daratumumab) Approval Criteria [Multiple Myeloma Diagnosis]:

1. Diagnosis of multiple myeloma; and
2. Used in 1 of the following settings:
   a. In combination with lenalidomide and dexamethasone as primary therapy in members who are ineligible for autologous stem cell transplant (ASCT) or in members who have received at least 1 prior therapy; or
   b. In combination with bortezomib, melphalan, and prednisone as primary therapy in members who are ineligible for ASCT; or
   c. In combination with bortezomib, thalidomide, and dexamethasone as primary therapy in members who are eligible for ASCT; or
   d. In combination with carfilzomib and dexamethasone in members with relapsed or progressive disease; or
   e. In combination with bortezomib and dexamethasone in members who have received at least 1 prior therapy; or

f. In combination with pomalidomide and dexamethasone in members who have received ≥2 prior therapies including a proteasome inhibitor (PI) and an immunomodulatory agent; or
g. As a single-agent in members who have received ≥3 prior therapies, including a PI and an immunomodulatory agent, or who are double refractory to a PI and an immunomodulatory agent.

Darzalex Faspro™ (Daratumumab/Hyaluronidase-fihj) Approval Criteria [Multiple Myeloma Diagnosis]:

1. Diagnosis of multiple myeloma; and
2. Used in 1 of the following settings:
   a. In combination with lenalidomide and dexamethasone as primary therapy in members who are ineligible for autologous stem cell transplant (ASCT) or in members who have received at least 1 prior therapy; or
   b. In combination with bortezomib, melphalan, and prednisone as primary therapy in members who are ineligible for ASCT; or
   c. In combination with bortezomib and dexamethasone in members who have received at least 1 prior therapy; or
   d. As a single-agent in members who have received ≥3 prior therapies, including a proteasome inhibitor (PI) and an immunomodulatory agent, or in members who are double refractory to a PI and an immunomodulatory agent.

Empliciti® (Elotuzumab) Approval Criteria [Multiple Myeloma Diagnosis]:

1. Diagnosis of previously treated multiple myeloma with relapsed or progressive disease; and
2. Used in combination with 1 of the following regimens:
   a. Lenalidomide and dexamethasone in members who have received 1 to 3 prior therapies; or
   b. Bortezomib and dexamethasone; or
   c. Pomalidomide and dexamethasone in members who have received ≥2 prior therapies, including an immunomodulatory agent and a proteasome inhibitor (PI).

Hemady™ (Dexamethasone 20mg Tablet) Approval Criteria [Multiple Myeloma Diagnosis]:

1. Diagnosis of multiple myeloma; and
2. A patient-specific, clinically significant reason (beyond convenience) why the member cannot use dexamethasone 4mg tablets to achieve the required dose in place of Hemady™ must be provided.

Ninlaro® (Ixazomib) Approval Criteria [Multiple Myeloma Diagnosis]:

1. Diagnosis of symptomatic multiple myeloma; and
2. Used as primary therapy; or

3. Used following disease relapse after 6 months following primary induction therapy with the same regimen; and
4. Used in combination with 1 of the following regimens:
    a. Lenalidomide and dexamethasone; or
    b. Cyclophosphamide and dexamethasone for transplant candidates only; or
    c. Pomalidomide and dexamethasone if member has failed ≥2 prior therapies and demonstrated disease progression within 60 days; or
5. Used as a single-agent for the maintenance treatment of disease.

Sarclisa® (Isatuximab-irfc) Approval Criteria [Multiple Myeloma Diagnosis]:

1. Diagnosis of relapsed or refractory multiple myeloma (RRMM) after ≥2 prior therapies; and
2. Previous treatment must have included lenalidomide and a proteasome inhibitor (PI); and
3. Used in combination with pomalidomide and dexamethasone.

Xpovio® (Selinexor) Approval Criteria [Multiple Myeloma Diagnosis]:

1. Diagnosis of relapsed or refractory multiple myeloma (RRMM); and
2. Member has received ≥4 prior therapies including refractory disease to ≥2 proteasome inhibitors (PIs), ≥2 immunomodulatory agents, and an anti-CD38 monoclonal antibody; and
3. Used in combination with dexamethasone.

Xpovio® (Selinexor) Approval Criteria [Diffuse Large B-Cell Lymphoma (DLBCL) Diagnosis]:

1. Diagnosis of relapsed/refractory DLBCL, not otherwise specified, including DLBCL arising from follicular lymphoma; and
2. Member has received ≥2 prior lines of systemic therapy.

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Appendix F

Vote to Prior Authorize Lenvima® (Lenvatinib)

Oklahoma Health Care Authority
December 2020

Lenvima® (Lenvatinib) Product Summary[1]

Lenvima® (Lenvatinib):

- **Therapeutic Class:** Kinase inhibitor
- **Indication(s):**
  - Treatment of patients with locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer (DTC)
  - In combination with everolimus, for the treatment of patients with advanced renal cell carcinoma (RCC) following 1 prior anti-angiogenic therapy
  - First-line treatment of patients with unresectable hepatocellular carcinoma (HCC)
  - In combination with pembrolizumab, for the treatment of patients with advanced endometrial carcinoma that is microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR), with disease progression following prior systemic therapy, and who are not candidates for curative surgery or radiation
- **How Supplied:** 4mg and 10mg oral capsules supplied in cartons of (6) 5-day blister cards as follows:
  - 24mg/day: (10) 10mg capsules and (5) 4mg capsules per card
  - 20mg/day: (10) 10mg capsules per card
  - 18mg/day: (5) 10mg capsules and (10) 4mg capsules per card
  - 14mg/day: (5) 10mg capsules and (5) 4mg capsules per card
  - 12mg/day: (15) 4mg capsules per card
  - 10mg/day: (5) 10mg capsules per card
  - 8mg/day: (10) 4mg capsules per card
  - 4mg/day: (5) 4mg capsules per card
- **Dose:**
  - DTC: 24mg once daily
  - RCC: 18mg once daily with everolimus 5mg once daily
  - HCC: Based on actual body weight:
    - 8mg once daily for patients <60kg
    - 12mg once daily for patients ≥60kg
  - Endometrial carcinoma: 20mg once daily with pembrolizumab 200mg via intravenous (IV) infusion every 3 weeks

- **Cost:** The Wholesale Acquisition Cost (WAC) ranges from $211.34 to $634.03 per capsule, resulting in an approximate cost of $19,000.00 per 30-day supply dose pack

Recommendations

- The prior authorization of Lenvima® (lenvatinib) with the following criteria shown in red:

Lenvima® (Lenvatinib) Approval Criteria [Differentiated Thyroid Cancer (DTC) Diagnosis]:

1. Locally recurrent or metastatic disease; and
2. Disease progression on prior treatment; and
3. Radioactive iodine-refractory disease.

Lenvima® (Lenvatinib) Approval Criteria [Renal Cell Carcinoma (RCC) Diagnosis]:

1. Advanced disease; and
2. Following 1 prior anti-angiogenic therapy; and
3. Used in combination with everolimus.

Lenvima® (Lenvatinib) Approval Criteria [Hepatocellular Carcinoma (HCC) Diagnosis]:

1. Unresectable disease; and
2. First-line treatment.

Lenvima® (Lenvatinib) Approval Criteria [Endometrial Carcinoma Diagnosis]:

1. Advanced disease with progression on prior systemic therapy; and
2. Member is not a candidate for curative surgery or radiation; and
3. Disease is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR); and
4. Used in combination with pembrolizumab.

[1] Lenvima® Prescribing Information. Eisai, Inc. Available online at: http://www.lenvima.com/pdfs/prescribing-information.pdf. Last revised 09/2020. Last accessed 11/10/2020.

Appendix G

Fiscal Year 2020 Annual Review of Skin Cancer Medications

Oklahoma Health Care Authority
December 2020

Introduction[1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16]

Skin cancers are commonly divided into 2 different types: non-melanoma 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 increase. More people are diagnosed with BCC than all other cancers combined. The incidence of SCC is approximately half that 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 2020, an estimated 100,350 new cases of melanoma skin cancer will be diagnosed in the United States, and an estimated 6,850 deaths will occur 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 of the following agents in the last 5 years: encorafenib, binimetinib, 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 [Renal Cell Carcinoma (RCC) Diagnosis]:

1. Diagnosis of advanced RCC; and
2. Used as first-line treatment; and
3. Used in combination with axitinib.

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.

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.

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; and
3. Member meets 1 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. Diagnosis of unresectable cutaneous, subcutaneous, or nodal lesions that are recurrent after initial surgery; and
    a. Not indicated in members with visceral metastases; and
2. Member is not immunocompromised or pregnant.

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

1. Diagnosis of recurrent or metastatic cervical cancer; and
2. Member has had disease progression on or after chemotherapy; and
3. Tumors must express programmed death ligand 1 (PD-L1) [combined positive score (CPS) ≥1]; and
4. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Opdivo® (nivolumab)].

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

1. Diagnosis of advanced endometrial cancer that is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR); and
2. Progressive disease following prior systemic therapy; and
3. Member is not a candidate for curative surgery or radiation; and
4. Used in combination with lenvatinib; and
5. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Opdivo® (nivolumab)].

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

1. Diagnosis of locally advanced or metastatic esophageal carcinoma; and
2. Must be used following disease progression after 1 or more prior lines of systemic therapy; and
3. Tumor must be squamous cell histology; and
4. Tumor must have positive programmed death ligand 1 (PD-L1) expression [combined positive score (CPS) ≥10]; and
5. Used as monotherapy; and
6. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Opdivo® (nivolumab)].

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

1. Diagnosis of recurrent, locally advanced or metastatic gastric or gastroesophageal junction adenocarcinoma; and
2. Tumors must express programmed death ligand 1 (PD-L1); and
3. Disease progression on or after 2 or more prior systemic therapies [including fluoropyrimidine- and platinum-containing chemotherapy, and if appropriate, human epidermal growth factor receptor 2 (HER2)/neu-targeted therapy]; and
4. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Opdivo® (nivolumab)].

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

1. First-line or recurrent setting; and
2. Squamous cell histology; and
3. If used in the recurrent setting, member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Opdivo® (nivolumab)].

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

1. Diagnosis of relapsed or progressive HCC; and
2. Member must have been previously treated with sorafenib; and
3. Member has not previously failed other programmed death 1 (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; and
2. Pembrolizumab must be used as a single-agent; and
3. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Opdivo® (nivolumab)].

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

1. Member meets 1 of the following:
    a. Adjuvant treatment of members with melanoma with involvement of lymph node(s) following complete resection; or
    b. Diagnosis of unresectable or metastatic melanoma; and
2. Used as a single-agent; and
3. Member meets 1 of the following:
    a. Used as first-line therapy; or
    b. Used as second-line therapy or subsequent therapy for disease progression if not previously used; and

4. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Opdivo® (nivolumab)]; and
    a. For adjuvant treatment of melanoma, approvals will be for a maximum duration of 1 year.

Keytruda® (Pembrolizumab) Approval Criteria [Merkel Cell Carcinoma (MCC) Diagnosis]:

1. Diagnosis of recurrent, locally advanced, or metastatic MCC; and
2. No history of prior systemic chemotherapy; and
3. Used as a single-agent; and
4. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Opdivo® (nivolumab)].

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

1. Diagnosis of metastatic NSCLC; and
2. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Opdivo® (nivolumab)]; and
3. Tumor proportion scores for programmed death ligand 1 (PD-L1) expression as follows:
    a. As a single-agent, first-line: ≥1%; or
    b. First-line in combination: No expression required; or
    c. As a single-agent, second-line: ≥1%; and
4. Member meets 1 of the following:
    a. Previously untreated, metastatic squamous NSCLC in combination with carboplatin and either paclitaxel or nab-paclitaxel; or
    b. Previously untreated, metastatic non-squamous NSCLC in combination with pemetrexed and carboplatin; or
    c. New diagnosis as first-line therapy (member has not received chemotherapy to treat disease) if: tumor does not express sensitizing epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) translocations; or
    d. Used as a 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 FDA-approved therapy for these aberrations prior to receiving pembrolizumab. *This does not apply if tumors do not have these mutations* (*examples of drugs for EGFR-mutation-positive tumors: osimertinib, erlotinib, afatinib, or gefitinib);* and
        ii. Members with ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving pembrolizumab. *This does not apply if tumors do not have these mutations (examples of*

drugs for ALK-mutation-positive tumors: crizotinib, ceritinib, or alectinib).

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

1. Member must have 1 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; and
2. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Opdivo® (nivolumab)].

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

1. Diagnosis of stage III NSCLC; and
2. Ineligible for surgery or definitive chemoradiation; and
3. Tumor proportion scores for programmed death ligand 1 (PD-L1) expression ≥1%; and
4. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Opdivo® (nivolumab)].

Keytruda® (Pembrolizumab) Approval Criteria [Non-Muscle Invasive Bladder Cancer (NMIBC) Diagnosis]:

1. A diagnosis of high-risk, NMIBC; and
2. Member must have failed therapy with Bacillus Calmette-Guerin (BCG)-therapy; and
3. Member must be ineligible for or has elected not to undergo cystectomy.

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

1. Diagnosis of PMBCL; and
2. Member must have refractory disease or relapsed after 2 or more prior lines of therapy; and
3. Authorizations will not be granted for members who require urgent cytoreduction; and
4. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Opdivo® (nivolumab)].

Keytruda® (Pembrolizumab) Approval Criteria [Renal Cell Carcinoma (RCC) Diagnosis]:

1. Newly diagnosed or recurrent stage IV clear-cell RCC; and
2. No previous systemic therapy for advanced disease; and

3. Used in combination with axitinib; and
4. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Opdivo® (nivolumab)].

Keytruda® (Pembrolizumab) Approval Criteria [Small Cell Lung Cancer (SCLC) Diagnosis]:

1. Diagnosis of metastatic SCLC; and
2. Progressed on or following a platinum-based regimen and at least 1 other regimen; and
3. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Opdivo® (nivolumab)].

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

1. Member must have 1 of the following:
    a. Locally advanced or metastatic urothelial carcinoma with 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 for members with locally advanced or metastatic urothelial carcinoma who are ineligible for cisplatin-containing chemotherapy; and
        i. Cisplatin ineligibility is defined as:
            1. Baseline creatinine clearance of <60mL/min; or
            2. ECOG performance status of 2; or
            3. Class III heart failure; or
            4. Grade 2 or greater peripheral neuropathy; or
            5. Grade 2 or greater hearing loss; and
2. Member has not previously failed other programmed death 1 (PD-1) inhibitors [i.e., Opdivo® (nivolumab)].

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

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

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

1. Diagnosis of ATC; and
2. Locally advanced or metastatic disease; and
3. BRAF V600E mutation; and

4. No satisfactory locoregional treatment options.

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; and
3. Must meet 1 of the following:
    a. Used as first-line therapy in combination with dabrafenib; or
    b. Used as second-line 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. Diagnosis of refractory or metastatic NSCLC; and
2. BRAF V600E or V600K mutation; and
    a. Trametinib is not indicated for wild-type BRAF NSCLC; and
3. Used in combination with dabrafenib.

Mekinist® (Trametinib) Approval Criteria [Serous Ovarian Cancer Diagnosis]:

1. Diagnosis of persistent disease or recurrent low-grade serous carcinoma; and
2. Meets 1 of the following:
    a. Immediate treatment for serially rising CA-125 in members who previously received chemotherapy; or
    b. Progression on primary, maintenance, or recurrence therapy; or
    c. Stable or persistent disease (if not on maintenance therapy); or
    d. Complete remission and relapse after completing chemotherapy.

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.

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 [Adjuvant Treatment of Melanoma Diagnosis]:

1. Member has had complete resection of melanoma; and
2. Diagnosis of stage III B/C melanoma following complete resection; and
3. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Keytruda® (pembrolizumab)]; and
4. Used as a single-agent; and
5. Dose as follows:
    a. Single-agent: 240mg every 2 weeks or 480mg every 4 weeks; and
    b. Maximum duration of 1 year.

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

1. 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. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Keytruda® (pembrolizumab)]; and
5. Dose as follows: 240mg every 2 weeks or 480mg every 4 weeks.

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

1. Diagnosis of relapsed or progressive HCC; and
2. Member must have been previously treated with sorafenib; and
3. Member has not previously failed other programmed death 1 (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; and
2. Used as a single-agent; and
3. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Keytruda® (pembrolizumab)].

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

1. Diagnosis of MSI-H or dMMR mCRC; and
2. Progression following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan; and
3. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Keytruda® (pembrolizumab)].

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

1. Diagnosis of metastatic NSCLC; and
2. Tumor histology is 1 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. Used as a single-agent; and
5. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Keytruda® (pembrolizumab)]; and
6. Dose as follows: 240mg every 2 weeks or 480mg every 4 weeks.

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 1 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. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Keytruda® (pembrolizumab)]; and
4. Dose as follows:
    a. Single-agent: 240mg every 2 weeks or 480mg every 4 weeks; or
    b. In combination with ipilimumab: Nivolumab 3mg/kg followed by ipilimumab 1mg/kg on the same day, every 3 weeks for a maximum of 4 doses, then nivolumab 240mg every 2 weeks or 480mg every 4 weeks.

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

1. Must meet 1 of the following criteria:
    a. Disease relapsed within 6 months of initial chemotherapy; or
    b. Disease is progressive on initial chemotherapy; and
2. Used as a single-agent or in combination with ipilimumab; and

3. Member has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Keytruda® (pembrolizumab)].

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

1. Diagnosis of unresectable or metastatic melanoma; and
2. 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 programmed death 1 (PD-1) inhibitors [e.g., Keytruda® (pembrolizumab)]; and
3. Dose as follows:
    a. Single-agent: 240mg every 2 weeks or 480mg every 4 weeks; or
    b. In combination with ipilimumab: Nivolumab 1mg/kg, followed by ipilimumab on the same day, every 3 weeks for 4 doses, then 240mg every 2 weeks or 480mg every 4 weeks.

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

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

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

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

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; and
3. Used as a single-agent or in combination with trametinib; and
4. Must meet 1 of the following:
    a. Used as first-line therapy; or
    b. Used as second-line or subsequent therapy.

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

1. Diagnosis of refractory or metastatic NSCLC; and
2. BRAF V600E or V600K mutation; and
    a. Dabrafenib is not indicated for wild-type BRAF NSCLC; and
3. Used as a single-agent or in combination with trametinib.

Tecentriq® (Atezolizumab) Approval Criteria [Melanoma Diagnosis]:

1. Diagnosis of unresectable or metastatic melanoma; and
2. BRAF V600 mutation-positive; and
3. In combination with cobimetinib and vemurafenib.

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

1. Member has had 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. Used as a single-agent; and
4. Maximum dose of 10mg/kg will apply.

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

1. 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. Used in combination with nivolumab; and
3. Member has not failed previous programmed death 1 (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 3 weeks for a maximum of 4 doses, then nivolumab 240mg every 2 weeks or 480mg every 4 weeks.

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

1. Diagnosis of SCLC; and
2. Must meet 1 of the following criteria:
    a. Disease relapsed within 6 months of initial chemotherapy; or
    b. Disease is progressive on initial chemotherapy; and
3. Used in combination with nivolumab.

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

1. Diagnosis of unresectable or metastatic melanoma; and
2. 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
3. Used as a single-agent for 1 of the following:
    a. First-line therapy as a single course of 4 treatments; or
    b. Second-line or subsequent lines of therapy as a single course of 4 treatments; or
    c. Retreatment, consisting of a 4-dose limit, for a member who had:
        i. No significant systemic toxicity during prior ipilimumab therapy; and
        ii. Whose disease progressed after being stable >6 months following completion of a prior course of ipilimumab; and
        iii. For whom no intervening therapy has been administered; and
4. Maximum dose of 3mg/kg will apply.

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

1. Diagnosis of ECD; and
2. BRAF V600E or V600K mutation; and
3. Used as a single-agent.

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

1. Diagnosis of hairy-cell leukemia; and
2. Used as a single-agent; and
3. Disease progression following failure of purine analog therapy (i.e., pentostatin, cladribine).

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; and
3. Must meet 1 of the following:
    a. Used as first-line therapy; or
    b. Used as second-line or subsequent therapy; and
4. Used as a single-agent or in combination with cobimetinib.

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

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

Approval criteria for Tecentriq® (atezolizumab) for indications other than skin cancer diagnoses can be found in the April 2020 Drug Utilization Review (DUR) Board packet. Atezolizumab approval criteria are reviewed annually with the lung cancer medications.

Utilization of Skin Cancer Medications: Fiscal Year 2020

The following utilization data includes medications indicated for skin cancer; the data does not differentiate between skin cancer diagnoses and other diagnoses, for which use may be appropriate.

Fiscal Year Comparison: Pharmacy Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	13	110	$970,103.34	$8,819.12	$300.16	9,121	3,232
2020	11	60	$536,080.53	$8,934.68	$303.56	5,076	1,766
% Change	**-15.40%**	**-45.50%**	**-44.70%**	**1.30%**	**1.10%**	**-44.30%**	**-45.40%**
Change	**-2**	**-50**	**-$434,022.81**	**$115.56**	**$3.40**	**-4,045**	**-1,466**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2019 = 07/01/2018 to 06/30/2019; Fiscal Year 2020 = 07/01/2019 to 06/30/2020

Fiscal Year Comparison: Medical Claims

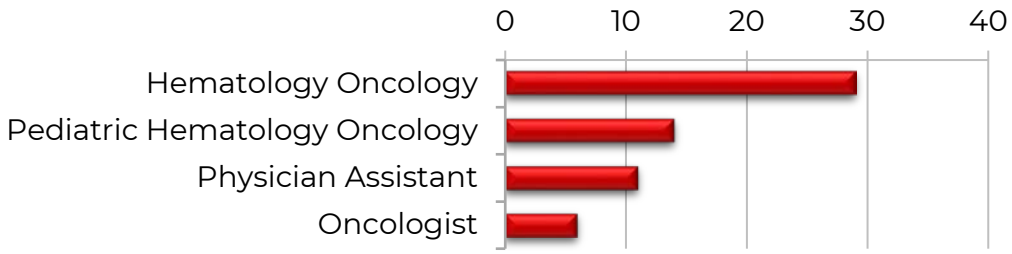
Fiscal Year	*Total Members	†Total Claims	Total Cost	Cost/ Claim	Total Units
2019	139	673	$7,409,976.85	$11,010.37	206,349
2020	173	829	$9,258,902.82	$11,168.76	209,544
% Change	**24.46%**	**23.18%**	**24.95%**	**1.44%**	**1.55%**
Change	**34**	**156**	**$1,848,925.97**	**$158.39**	**3,195**

*Total number of unduplicated members.
†Total number of unduplicated claims.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2019 = 07/01/2018 to 06/30/2019; Fiscal Year 2020 = 07/01/2019 to 06/30/2020

Demographics of Members Utilizing Skin Cancer Medications: Pharmacy Claims

- Due to the small number of members utilizing skin cancer medications during fiscal year 2020, detailed demographic information could not be provided.

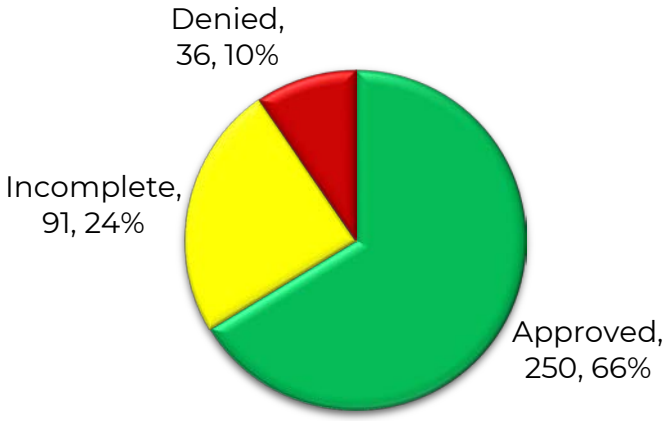
Top Prescriber Specialties of Skin Cancer Medications By Number of Claims: Pharmacy Claims



Prior Authorization of Skin Cancer Medications

There were 377 prior authorization requests submitted for skin cancer medications during fiscal year 2020. The following chart shows the status of the submitted petitions for fiscal year 2020.

Status of Petitions



Market News and Updates[17,18]

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

- **March 2020:** The FDA granted accelerated approval to the combination of Opdivo® (nivolumab) and Yervoy® (ipilimumab) for the treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.
- **April 2020:** The FDA approved Braftovi® (encorafenib) in combination with cetuximab for the treatment of adult patients with metastatic colorectal cancer (mCRC) with a BRAF V600E mutation.
- **April 2020:** The FDA granted accelerated approval to a new dosing regimen of 400mg every 6 weeks for Keytruda® (pembrolizumab) across all currently approved adult indications, in addition to the

current 200mg every 3 weeks dosing regimen. This new dosing regimen was approved under accelerated approval based on pharmacokinetic data, the relationship of exposure to efficacy, and the relationship of exposure to safety.

- **May 2020:** The FDA approved the combination of Opdivo® (nivolumab) and Yervoy® (ipilimumab) as first-line treatment for patients with metastatic non-small cell lung cancer (NSCLC) whose tumors express programmed death ligand 1 (PD-L1) ≥1% with no epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) genomic tumor aberrations.
- **May 2020:** The FDA approved the combination of Opdivo® (nivolumab) and Yervoy® (ipilimumab) and 2 cycles of platinum-doublet chemotherapy as first-line treatment for patients with metastatic or recurrent NSCLC, with no EGFR or ALK genomic tumor aberrations.
- **June 2020:** The FDA approved Opdivo® (nivolumab) for the treatment of patients with unresectable advanced, recurrent, or metastatic esophageal squamous cell carcinoma (ESCC) after prior fluoropyrimidine- and platinum-based chemotherapy.
- **June 2020:** The FDA granted accelerated approval to Keytruda® (pembrolizumab) for the treatment of adult and pediatric patients with unresectable or metastatic tumor mutational burden-high (TMB-H) [≥10 mutations/megabase (mut/Mb)] solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options.
- **June 2020:** The FDA approved Keytruda® (pembrolizumab) for the treatment of patients with recurrent or metastatic cutaneous squamous cell carcinoma (cSCC) that is not curable by surgery or radiation.
- **June 2020:** The FDA approved Keytruda® (pembrolizumab) for the first-line treatment of patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer (CRC).
- **June 2020:** The FDA approved Bavencio® (avelumab) for maintenance treatment of patients with locally advanced or metastatic urothelial carcinoma that has not progressed with first-line platinum-containing chemotherapy.
- **July 2020*:** The FDA approved Tecentriq® (atezolizumab) in combination with cobimetinib and vemurafenib for the treatment of patients with BRAF V600 mutation-positive unresectable or metastatic melanoma. **This new FDA approved indication was previously reviewed with the breast cancer medications at the September 2020 DUR Board meeting*.

- **October 2020:** The FDA approved the combination of Opdivo® (nivolumab) and Yervoy® (ipilimumab) as first-line treatment for adult patients with unresectable malignant pleural mesothelioma.
- **October 2020:** The FDA extended the approval of Keytruda® (pembrolizumab) for adult patients with relapsed or refractory classical Hodgkin lymphoma (cHL) and for pediatric patients with refractory cHL or cHL that has relapsed after ≥2 therapies.
- **November 2020:** The FDA granted accelerated approval to Keytruda® (pembrolizumab) in combination with chemotherapy for the treatment of patients with locally recurrent, unresectable or metastatic triple-negative breast cancer (TNBC) whose tumors express PD-L1 with a combined positive score (CPS) ≥10.

Guideline Update(s)*:

- A recent change in the National Comprehensive Cancer Network (NCCN) Compendium guidelines involved the inclusion of several oral targeted therapies for the treatment of recurrent ovarian cancer. This change included the use of Mekinist® (trametinib) as an option for patients with low-grade serous carcinomas. **This compendium approval was previously reviewed with the ovarian cancer medications at the October 2020 DUR Board meeting.*

Recommendations

- Update the prior authorization criteria for Bavencio® (avelumab), Braftovi® (encorafenib), Keytruda® (pembrolizumab), Opdivo® (nivolumab), and Yervoy® (ipilimumab) to reflect the new FDA approved indications; changes and new criteria noted in red (only criteria with updates are listed):

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

1. A 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; or
3. Used as maintenance therapy for members not progressing on first-line platinum-containing regimen.

Braftovi® (Encorafenib) Approval Criteria [Colorectal Cancer (CRC) Diagnosis]:

1. Diagnosis of advanced or metastatic CRC; and
2. BRAF V600E mutation positive; and
3. Used in combination with cetuximab or panitumumab; and
4. Disease must have progressed following adjuvant therapy within 12 months; or

5. Used following progression of any line of metastatic therapy.

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

1. Diagnosis of locally recurrent unresectable or metastatic triple-negative breast cancer; and
2. Tumors express programmed death ligand 1 (PD-L1) with a combined positive score (CPS) ≥10.

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

1. First-line treatment; and
2. Metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR); or
3. Unresectable disease.

Keytruda® (Pembrolizumab) Approval Criteria [Cutaneous Squamous Cell Carcinoma (cSCC) Diagnosis]:

1. Diagnosis of recurrent or metastatic disease; and
2. Not curable by radiation or surgery.

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

1. Used as a single-agent; and
2. The member has not previously failed other programmed death 1 (PD-1) inhibitors [i.e. Opdivo® (nivolumab)]; and
3. For adult members:
    a. Diagnosis of relapsed or refractory classical Hodgkin lymphoma (cHL); and
        i. Exception: Lymphocyte-predominant Hodgkin lymphoma; or
4. For pediatric members:
    a. Diagnosis of refractory cHL; or
    b. Relapsed disease after ≥2 therapies.

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

1. Member has not previously failed other programmed death 1 (PD-1) inhibitors [i.e., Opdivo® (nivolumab)]; and
2. ~~Member must have 1 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 [Tumor Mutational Burden-High (TMB-H) Solid Tumors Diagnosis]:

1. Unresectable or metastatic TMB-H [≥10 mutations/megabase (mut/Mb)] solid tumors; and
2. Used following disease progression after prior treatment; and
3. No satisfactory alternative treatment options.

Opdivo® (Nivolumab) Approval Criteria [Esophageal Squamous Cell Carcinoma (ESCC) Diagnosis]:

1. Diagnosis of unresectable, advanced, recurrent, or metastatic disease; and
2. Used following prior fluoropyrimidine- and platinum-based chemotherapy.

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

~~1. Relapsed or progressive disease; and~~
~~2. The patient has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Keytruda® (pembrolizumab)]; and~~
~~3. Member must have been previously treated with sorafenib.~~
1. Member must have unresectable disease and is not a transplant candidate; or
2. Metastatic disease or extensive liver tumor burden; and
3. Must meet 1 of the following:
    a. If used as first-line therapy, must be used as single-agent; and
        i. Ineligible for tyrosine kinase inhibitors or anti-angiogenic agents; or
    b. If used as second-line or greater therapy, may be used as single-agent or in combination with ipilimumab; and
        i. Must not have failed other checkpoint inhibitors.

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

1. Diagnosis of malignant pleural mesothelioma that cannot be surgically removed; and
2. Used as first-line therapy; and
3. Used in combination with ipilimumab.

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

1. For first-line therapy for recurrent, advanced, or metastatic disease, meets the following:
    a. No epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) genomic tumor aberrations; and
    b. Used in combination with ipilimumab; and
    c. Expresses programmed death ligand 1 (PD-L1) ≥1%; or

    d. Given in combination with 2 cycles of platinum-doublet chemotherapy.
2. For second-line therapy for metastatic disease, meets the following:
    a. Tumor histology is 1 of the following:
        i. Adenocarcinoma; or
        ii. Squamous cell; or
        iii. Large cell; and
    b. Disease progression on or after platinum-containing chemotherapy (e.g., cisplatin, carboplatin); and
    c. The patient has not previously failed other programmed death 1 (PD-1) inhibitors [e.g., Keytruda® (pembrolizumab)]; and
    d. Used as a single-agent; and
    e. Dose as follows: 240mg every 2 weeks or 480mg every 4 weeks.

Yervoy® (Ipilimumab) Approval Criteria [Hepatocellular Carcinoma (HCC) Diagnosis]:

1. Member must have unresectable disease and is not a transplant candidate; or
2. Metastatic disease or extensive liver tumor burden; and
3. Used as second-line or greater therapy; and
4. Used in combination with nivolumab; and
5. Must not have failed other checkpoint inhibitors.

Yervoy® (Ipilimumab) Approval Criteria [Mesothelioma Diagnosis]:

1. Diagnosis of malignant pleural mesothelioma that cannot be surgically removed; and
2. Used as first-line therapy; and
3. Used in combination with nivolumab.

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

1. Diagnosis of recurrent, advanced, or metastatic non-small cell lung cancer (NSCLC); and
    a. First-line therapy for metastatic disease; and
    b. No epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) genomic tumor aberrations; and
    c. Given in combination with nivolumab; and
    d. Expresses programmed death ligand 1 (PD-L1) ≥1%; or
    e. Given in combination with 2 cycles of platinum-doublet chemotherapy.

Utilization Details of Skin Cancer Medications: Fiscal Year 2020

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
BINIMETINIB PRODUCTS					
MEKTOVI TAB 15MG	3	1	$35,899.11	3	$11,966.37
SUBTOTAL	**3**	**1**	**$35,899.11**	**3**	**$11,966.37**
COBIMETINIB PRODUCTS					
COTELLIC TAB 20MG	8	1	$56,097.96	8	$7,012.25
SUBTOTAL	**8**	**1**	**$56,097.96**	**8**	**$7,012.25**
DABRAFENIB PRODUCTS					
TAFINLAR CAP 75MG	5	3	$37,748.88	1.67	$7,549.78
SUBTOTAL	**5**	**3**	**$37,748.88**	**1.67**	**$7,549.78**
ENCORAFENIB PRODUCTS					
BRAFTOVI CAP 75MG	3	1	$36,589.05	3	$12,196.35
SUBTOTAL	**3**	**1**	**$36,589.05**	**3**	**$12,196.35**
TRAMETINIB PRODUCTS					
MEKINIST TAB 0.5MG	17	3	$97,568.47	5.67	$5,739.32
MEKINIST TAB 2MG	7	3	$82,437.15	2.33	$11,776.74
SUBTOTAL	**24**	**6**	**$180,005.62**	**4**	**$7,500.23**
VEMURAFENIB PRODUCTS					
ZELBORAF TAB 240MG	8	1	$86,864.68	8	$10,858.09
SUBTOTAL	**8**	**1**	**$86,864.68**	**8**	**$10,858.09**
VISMODEGIB PRODUCTS					
ERIVEDGE CAP 150MG	9	2	$102,875.23	4.5	$11,430.58
SUBTOTAL	**9**	**2**	**$102,875.23**	**4.5**	**$11,430.58**
TOTAL	**60**	**11***	**$536,080.53**	**5.45**	**$8,934.68**

CAP = capsule; TAB = tablet
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020

Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS+	TOTAL MEMBERS*	TOTAL COST	COST/ CLAIM
J9271 PEMBROLIZUMAB INJ	409	89	$4,287,819.21	$10,483.67
J9299 NIVOLUMAB INJ	256	44	$2,735,692.45	$10,686.30
J9022 ATEZOLIZUMAB INJ	135	29	$1,246,531.08	$9,233.56
J9228 IPILIMUMAB INJ	25	9	$960,069.08	$38,402.76
J9119 CEMIPLIMAB-RWLC INJ	4	2	$28,791.00	$7,197.75
TOTAL	**829**	**173**	**$9,258,902.82**	**$11,168.76**

INJ = injection
+Total number of unduplicated claims.
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020

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Appendix H

Fiscal Year 2020 Annual Review of Antidepressants

Oklahoma Health Care Authority
December 2020

Current Prior Authorization Criteria

Antidepressants*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
Selective Serotonin Reuptake Inhibitors (SSRIs)			
citalopram (Celexa®)			citalopram 20mg/10mL soln (UDC)
escitalopram (Lexapro®)			escitalopram 10mg/10mL soln (UDC)
fluoxetine caps (Prozac®)			fluoxetine 20mg/5mL soln (UDC)
fluvoxamine (Luvox®)			fluoxetine tabs
paroxetine (Paxil®)			fluoxetine DR (Prozac® Weekly™)
sertraline (Zoloft®)			fluvoxamine CR (Luvox CR®)
			paroxetine CR (Paxil CR®)
			paroxetine (Pexeva®)
Dual-Acting Antidepressants			
bupropion (Wellbutrin®, Wellbutrin SR®, XL®)	desvenlafaxine (Pristiq®)	desvenlafaxine (Khedezla®)	bupropion ER (Aplenzin®)
duloxetine (Cymbalta®)		levomilnacipran (Fetzima®)	bupropion ER (Forfivo XL®)
mirtazapine (Remeron®, Remeron SolTab®)		nefazodone (Serzone®)	duloxetine 40mg (Irenka™)
trazodone 50mg, 100mg, & 150mg tabs (Desyrel®)		vilazodone (Viibryd®)	duloxetine (Drizalma Sprinkle™)
venlafaxine (Effexor®, Effexor XR® caps)			trazodone 300mg tabs (Desyrel®)

Antidepressants*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
			venlafaxine ER tabs (Effexor XR® tabs)
Monoamine Oxidase Inhibitors (MAOIs)			
		phenelzine (Nardil®)	isocarboxazid (Marplan®)
		selegiline (Emsam®)	
		tranylcypromine (Parnate®)	
Unique Mechanisms of Action			
		vortioxetine (Trintellix®)	esketamine nasal spray (Spravato®)

*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
PA = prior authorization; CR = controlled-release; DR = delayed-release; ER = extended-release; tabs = tablets; caps = capsules; soln = solution; UDC = unit dose cups

Antidepressant Tier-2 Approval Criteria:

1. Member must have a documented, recent (within 6 months) trial of 2 Tier-1 medications at least 4 weeks in duration each and titrated to recommended dosing, that did not provide an adequate response. Tier-1 selection must include at least 1 medication from the SSRI category and 1 trial with duloxetine; or
2. Prior stabilization on the Tier-2 medication documented within the last 100 days. A past history of success on the Tier-2 medication will also be considered with adequate documentation; or
3. A unique FDA-approved indication not covered by Tier-1 medications or other medications from a different therapeutic class; or
4. A petition may be submitted for consideration whenever a unique patient-specific situation exists.

Antidepressant Tier-3 Approval Criteria:

1. Member must have a documented, recent (within 6 months) trial with 2 Tier-1 medications (1 medication from the SSRI category and 1 trial with duloxetine) and a trial of a Tier-2 medication at least 4 weeks in duration each and titrated to recommended dosing, that did not provide an adequate response; or
2. Prior stabilization on the Tier-3 medication documented within the last 100 days. A past history of success on the Tier-3 medication will also be considered with adequate documentation; or
3. A unique FDA-approved indication not covered by a lowered tiered medication or other medications from a different therapeutic class; or
4. A petition may be submitted for consideration whenever a unique patient-specific situation exists.

Antidepressant Special Prior Authorization (PA) Approval Criteria:

1. Use of any Special PA medication will require a patient-specific, clinically significant reason why the member cannot use other available generic Tier-1 medications; or
2. A petition may be submitted for consideration whenever a unique patient-specific situation exists; and
3. Tier structure rules still apply.
4. **Irenka™ (Duloxetine 40mg Capsule) Approval Criteria [Non-Depression Diagnosis]:**
    a. An FDA approved diagnosis of diabetic peripheral neuropathy or chronic musculoskeletal pain; and
    b. A patient-specific, clinically significant reason why the member cannot use 2 duloxetine 20mg capsules in place of Irenka™ 40mg capsules must be provided; and
    c. A quantity limit of 30 capsules per 30 days will apply; and
    d. Tier structure rules still apply.
5. **Drizalma Sprinkle™ (Duloxetine Delayed-Release Capsule) Approval Criteria [Diabetic Peripheral Neuropathic Pain/Chronic Musculoskeletal Pain Diagnosis]:**
    a. An FDA approved diagnosis of diabetic peripheral neuropathy or chronic musculoskeletal pain; and
    b. A patient-specific, clinically significant reason why the member cannot use generic duloxetine 20mg, 30mg, or 60mg capsules, which are available without prior authorization, in place of Drizalma Sprinkle™ must be provided; and
    c. A quantity limit of 30 capsules per 30 days will apply.
6. **Marplan® (Isocarboxazid) Approval Criteria:**
    a. A patient-specific, clinically significant reason why the member cannot use any of the Tier-3 monoamine oxidase inhibitors (MAOIs) or other cost-effective, lower tiered alternatives in place of Marplan® must be provided. Tier structure rules still apply.
7. **Desyrel® (Trazodone 300mg Tablet) Approval Criteria:**
    a. A patient-specific, clinically significant reason why the member cannot use other available generic Tier-1 products including 2 trazodone 150mg tablets or 3 trazodone 100mg tablets to achieve a 300mg dose must be provided.
8. **Fluoxetine Tablet Approval Criteria:**
    a. Fluoxetine capsules are available without a prior authorization. The tablet formulation will require prior authorization and a patient-specific, clinically significant reason why the tablet formulation is required in place of the capsule formulation.

9. **Citalopram 20mg/10mL Solution, Escitalopram 10mg/10mL Solution, and Fluoxetine 20mg/5mL Solution Unit Dose Cup (UDC) Approval Criteria:**
    a. An FDA approved indication; and
    b. A patient-specific, clinically significant reason why the member cannot use the bulk medication must be provided.

Spravato® (Esketamine Nasal Spray) Approval Criteria:

1. An FDA approved indication of treatment-resistant depression in adults; and
2. Member must be 18 years of age or older; and
3. Spravato® must be used in conjunction with an oral antidepressant; and
4. Member must have had an inadequate response to at least 2 different antidepressants from different classes at least 4 weeks in duration each and titrated to recommended dosing during the current depressive episode, unless contraindicated or clinically significant adverse effects; and
5. Prescriber must agree that member will be monitored by a health care provider for at least 2 hours after each administration; and
6. Prescriber must agree that member's blood pressure will be monitored prior to and after administration of Spravato® in accordance with the Spravato® *Prescribing Information*; and
7. Member must not have any contraindications to therapy [e.g., aneurysmal vascular disease (including thoracic and abdominal aorta, intracranial, and peripheral arterial vessels) or arteriovenous malformation; intracerebral hemorrhage; hypersensitivity to esketamine, ketamine, or any of the excipients]; and
8. Member must not have severe hepatic impairment (Child Pugh C); and
9. Prescriber must verify that female members are not currently pregnant and will use effective contraception while receiving treatment with Spravato®; and
10. Prescriber must verify female member is not breastfeeding; and
11. Pharmacy and health care setting must be certified in the Spravato® Risk Evaluation and Mitigation Strategy (REMS) program; and
12. Member must be enrolled in the Spravato® REMS program; and
13. Spravato® must be administered under the direct observation of a health care provider in a REMS certified health care setting; and
14. Initial approvals will be for the duration of the induction phase. For continued authorization, prescriber must verify member demonstrated an adequate response during the induction phase and verify member is using Spravato® in combination with an oral antidepressant; and
15. A quantity limit of 4 kits per 28 days will apply. A quantity limit override will be approved for induction of therapy upon meeting Spravato® approval criteria.

Utilization of Antidepressants: Fiscal Year 2020

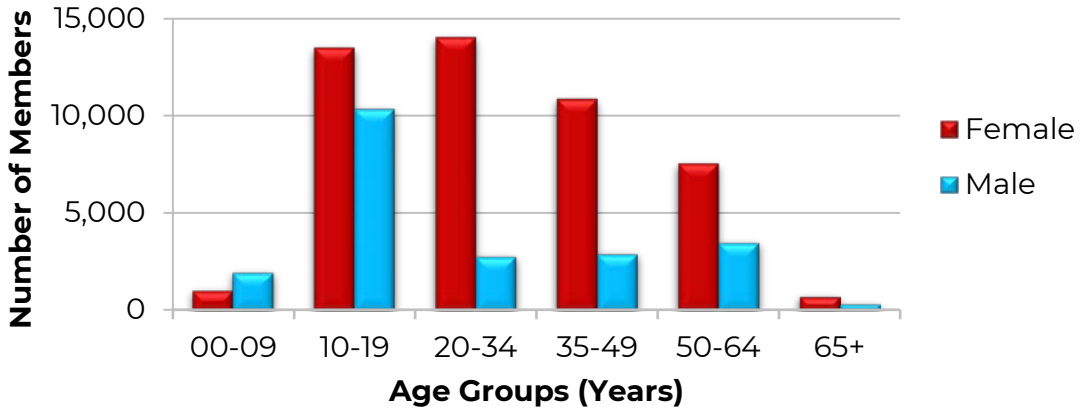
Comparison of Fiscal Years: Pharmacy Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	71,665	394,421	$6,171,449.84	$15.65	$0.45	15,865,848	13,692,346
2020	69,534	390,909	$6,436,380.02	$16.47	$0.46	16,275,577	14,052,584
% Change	**-3.00%**	**-0.90%**	**4.30%**	**5.20%**	**2.20%**	**2.60%**	**2.60%**
Change	**-2,131**	**-3,512**	**$264,930.18**	**$0.82**	**$0.01**	**409,729**	**360,238**

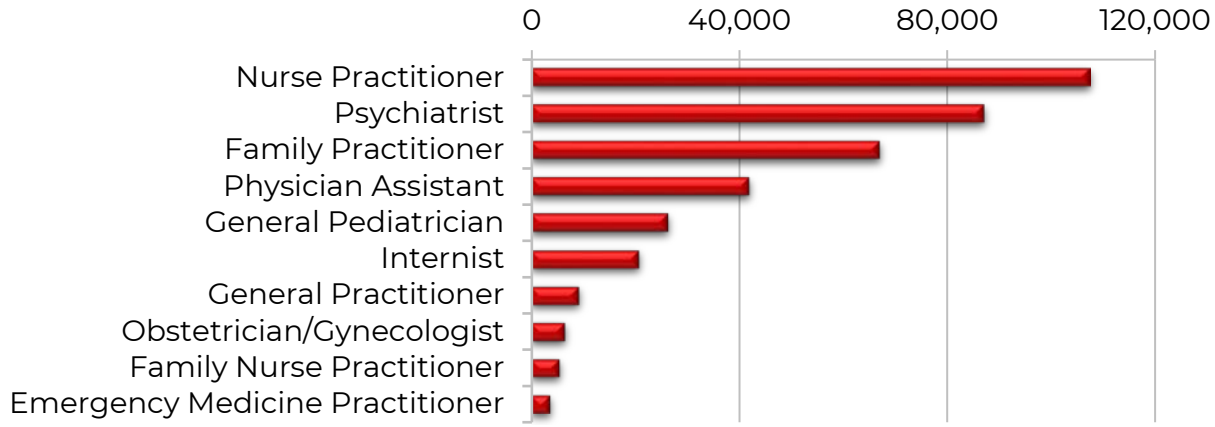
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2019 = 07/01/2018 to 06/30/2019; Fiscal Year 2020 = 07/01/2019 to 06/30/2020

- There were no paid medical claims for antidepressants during fiscal year 2020.

Demographics of Members Utilizing Antidepressants

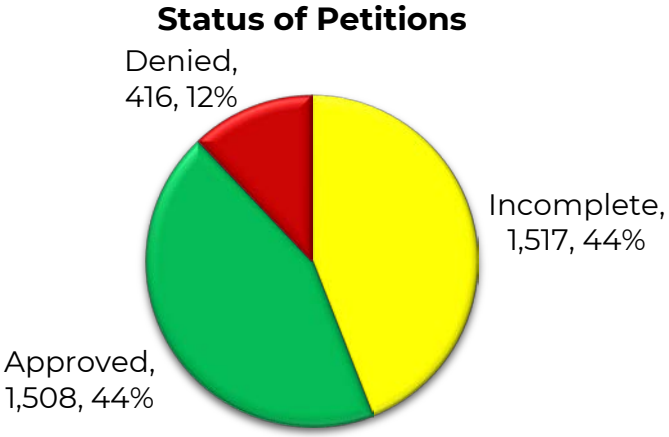


Top Prescriber Specialties of Antidepressants by Number of Claims



Prior Authorization of Antidepressants

There were 3,441 prior authorization requests submitted for antidepressants during fiscal year 2020. Computer edits are in place to detect lower tiered medications in the member's recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions for fiscal year 2020.



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

Anticipated Patent Expiration(s):

- Pexeva® (paroxetine tablets): May 2025
- Aplenzin® [bupropion extended-release (ER) tablets]: June 2026
- Forfivo XL® (bupropion ER tablets): June 2027
- Spravato® (esketamine nasal spray): July 2031
- Trintellix® (vortioxetine tablets): March 2032
- Fetzima® (levomilnacipran ER capsules): May 2032
- Drizalma Sprinkle™ [duloxetine delayed-release (DR) capsules]: April 2037

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

- **July 2020:** The FDA approved a supplemental New Drug Application (sNDA) for Spravato® (esketamine nasal spray), in conjunction with an oral antidepressant, to treat depressive symptoms in adults with major depressive disorder (MDD) with acute suicidal ideation or behavior. The sNDA approval was based on 2 identical Phase 3 clinical studies in which Spravato® (84mg twice weekly) plus comprehensive standard of care (SOC) demonstrated a statistically significant, rapid reduction of depressive symptoms within 24 hours, with some patients responding as early as 4 hours. The primary efficacy measure was the change from baseline in the Montgomery-Åsberg Depression Rating Scale (MADRS) total score at 24 hours after first dose. MADRS is a tool used to assess

severity of depressive symptoms. Spravato® plus comprehensive SOC demonstrated statistical superiority with a 15.9 and 16 point decrease on the MADRS in the 2 studies at 24 hours after the first dose of study medication (P=0.006 in both studies). Comparatively, in the placebo plus comprehensive SOC group, there was a decrease of 12 and 12.2 points in the 2 studies. The comprehensive SOC included initial hospitalization and a newly initiated or optimized oral antidepressant. The recommended dosage of Spravato® for the treatment of depressive symptoms in adults with MDD with acute suicidal ideation or behavior is 84mg twice weekly for 4 weeks in conjunction with an oral antidepressant. The dosage may be reduced to 56mg twice weekly based on tolerability. After 4 weeks of treatment with Spravato®, evidence of therapeutic benefit should be evaluated to determine need for continued treatment. The use of Spravato®, in conjunction with an oral antidepressant, beyond 4 weeks has not been systematically evaluated in the treatment of depressive symptoms in patients with MDD with acute suicidal ideation or behavior. Due to the risks of serious adverse outcomes resulting from sedation, dissociation, abuse, and misuse, Spravato® is only available through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Spravato® REMS program. The Wholesale Acquisition Cost (WAC) for Spravato® is $309.46 per 28mg nasal spray device, resulting in a cost of $7,427.04 per 28 days at the recommended dose of 84mg twice weekly for patients with MDD with acute suicidal ideation or behavior.

News:

- **July 2020:** Although patients with bipolar disorder commonly experience depressive symptoms, clinicians should be very cautious about treating them with antidepressants, especially as monotherapy, experts asserted in a recent debate on the topic as part of the European Psychiatric Association (EPA) 2020 Congress. At the Congress, psychiatric experts advised that clinicians should also screen patients for mixed symptoms that are better treated with mood stabilizers. These same experts also raised concerns over long-term antidepressant use, recommending continued use only in patients who relapse after stopping antidepressants.
- **July 2020:** A number of studies have begun looking into the presence of inflammation in the blood and brains of patients with depression, which could lead to new treatment approaches. With inflammation as a potential cause of depression, researchers have started looking into whether existing drugs can be repurposed to treat depression. One study found minocycline could stop mice from developing depressive behavior and depression-related cognitive deficits. Minocycline may be able to prevent depressive behaviors in humans, as it is able to suppress

the inflammatory response of microglia. Another study showed minocycline stops both the microglia and the brain neurons from releasing a stress-induced inflammatory protein called high mobility group box 1 (HMGB1) into the brain. It has also shown promise in modifying the immune system's response and acting as an anti-inflammatory. Further, minocycline has been found to have neuroprotective properties and is shown to be useful in reducing the severity of diseases such as Huntington's disease and amyotrophic lateral sclerosis (ALS), as it can easily cross the blood-brain barrier. Although few large-scale human studies have been conducted evaluating the effects of minocycline on depression, those that have been conducted appear to confirm the antidepressant effects. More studies are needed to evaluate adverse effects, whether relapse occurs after use, and whether it can be effective in treating depression where brain inflammation is not observed.

- **August 2020:** Patients with obesity, chronic illnesses like diabetes, and elderly patients have an increased risk for vitamin D deficiency, as well as an increased risk for depression. As a result, vitamin D supplementation has been hypothesized as a strategy to reduce depressive symptoms in at-risk populations. A recent randomized controlled study found vitamin D supplementation was not associated with a reduced risk of depression or any secondary outcomes involving mood among middle age and older adults. Among the 18,353 patients 50 years of age and older in the study, there was no significant difference in the risk of incident or recurrent depression or in clinically relevant depressive symptoms, between groups assigned to 2,000IU/day of cholecalciferol (vitamin D) supplementation or placebo at 5.3 years [hazard ratio (HR): 0.97; 95% confidence interval (CI): 0.87, 1.09; P=0.62]. Additionally, there were no significant differences in the change in Patient Health Questionnaire depression scale (PHQ-8) scores across the study period between groups (difference: 0.01; 95% CI: −0.04, 0.05; P=0.72).
- **November 2020:** *The Lancet Psychiatry* published findings from a cohort study that utilized an electronic health record network to assess whether a diagnosis of COVID-19 (compared with other health events) was associated with increased rates of subsequent psychiatric diagnoses, and whether patients with a history of psychiatric illness are at a higher risk of being diagnosed with COVID-19. This study used electronic health records from 69 million patients, 62,354 of whom had a diagnosis of COVID-19 between January 20, 2020 and August 1, 2020. Cohorts of patients were created who had been diagnosed with COVID-19 or a range of other health events. Propensity score matching was used to control for confounding risk factors for COVID-19 and for severity of illness. HRs and the incidence of psychiatric disorders,

dementia, and insomnia were measured during the first 14 to 90 days after a diagnosis of COVID-19. In patients with no previous psychiatric history, a diagnosis of COVID-19 was associated with increased incidence of a first psychiatric diagnosis in the following 14 to 90 days compared with 6 other health events [HR: 2.1, 95% CI: 1.8, 2.5 vs. influenza; HR: 1.7, 95% CI: 1.5, 1.9 vs. other respiratory tract infections; HR: 1.6, 95% CI: 1.4, 1.9 vs. skin infection; HR: 1.6, 95% CI: 1.3, 1.9 vs. cholelithiasis; HR: 2.2, 95% CI: 1.9, 2.6 vs, urolithiasis; HR: 2.1, 95% CI: 1.9, 2.5 vs. fracture of a large bone; all P<0.0001]. The most frequent psychiatric diagnosis after COVID-19 diagnosis was anxiety disorder, with a probability of outcome within 90 days of 4.7%. The probability of a first diagnosis of mood disorder within 14 to 90 days after COVID-19 diagnosis was 2% with depressive episode being the most common. The findings indicated a low probability of being newly diagnosed with a psychiatric disorder in the 14 to 90 days after COVID-19 diagnosis (0.1%). Having a diagnosis of a psychiatric disorder in the year before the COVID-19 outbreak was associated with a 65% increased risk of COVID-19 [relative risk (RR): 1.65; 95% CI: 1.59, 1.71; P<0.0001] compared with a cohort matched for established physical risk factors for COVID-19 but without a psychiatric diagnosis.

Pipeline:

- **Psilocybin:** The effect of psilocybin therapy in patients with MDD was studied in a randomized, waiting list–controlled clinical study. Adults 21 to 75 years of age with an MDD diagnosis, not currently using antidepressant medications, and without history of psychotic disorder, serious suicide attempt, or hospitalization were eligible to participate. A total of 27 patients were randomized to an immediate treatment condition group (N=15) or delayed treatment condition group (waiting list-controlled; N=12). Two psilocybin sessions (session 1: 20mg/70kg; session 2: 30mg/70kg) were given in the context of supportive psychotherapy (approximately 11 hours). Psilocybin was administered orally as a gelatin capsule. Participants were randomized to begin treatment immediately or after an 8-week delay. The primary outcome, depression severity, was assessed with the GRID-Hamilton Depression Rating Scale (GRID-HAMD, scored 0 to ≥24 where 0 is no depression and ≥24 is severe depression) scores at baseline (score of ≥17 required for enrollment) and at weeks 5 and 8 after enrollment for the delayed treatment group, which corresponded to weeks 1 and 4 after the intervention for the immediate treatment group. Of the randomized participants, 24 of 27 (89%) completed the intervention and the week 1 and week 4 post-session assessments. The mean GRID-HAMD scores at weeks 1 and 4 in the immediate treatment group were statistically significantly lower than the scores at the comparable time points of

weeks 5 and 8 in the delayed treatment group. In the overall sample, 16 participants (67%) at week 1 and 17 (71%) at week 4 had a clinically significant response to the intervention (≥50% reduction in GRID-HAMD score), and 14 participants (58%) at week 1 and 13 participants (54%) at week 4 were in remission (defined as GRID-HAMD score ≤7).

- **Zuranolone:** Topline results from SHORELINE, an ongoing Phase 3 open-label study, demonstrated zuranolone was well tolerated in patients taking 30mg, and among patients treated with 50mg after the study protocol was changed to include the 50mg dose. Zuranolone is an oral once-daily, 2-week therapy being developed as a potential treatment for MDD and for postpartum depression (PPD). As a neuroactive steroid $GABA_A$ receptor positive allosteric modulator, its pharmacology is similar to the intravenous (IV) drug Zulresso™ (brexanolone), approved by the FDA in 2019 for the treatment of PPD. SHORELINE studied the safety, tolerability, and need for repeat dosing with zuranolone in adults 18 to 75 years of age who have MDD, defined by a baseline total score of ≥20 on the Hamilton Depression Rating Scale (HAMD-17). The initial 725 patients had an average baseline score of 25.3 ± 4.1. After the first 14-day course of once-nightly zuranolone 30mg, patients had a mean change from baseline of -14.9 ± 7.1 (N=640); 458 (71.6%) patients showed a response and 255 (39.8%) achieved remission, defined as a HAMD-17 score of ≤7. During the course of the study, a new cohort of patients started treatment with an increased dose of 50mg. The 52 patients in the new cohort had a mean HAMD-17 baseline score of 25.1 ± 3.1. At day 15, the mean change was -15.9 ± 6.6 (slightly higher than in the initial cohort). A total of 39 (75%) patients responded to a 14-day treatment course and 25 (48.1%) achieved remission, also both higher than among the 30mg cohort. Among the 494 patient responders from the initial treatment cycle continuing in the study, 274 (55.5%) of patients used zuranolone in retreatment 1 or more times, while the remaining 220 (44.5%) were not retreated during their participation in the study.

Recommendations

The College of Pharmacy recommends updating the Spravato® (esketamine nasal spray) criteria based on the new FDA approved indication with the following criteria (new criteria and changes are shown in red):

Spravato® (Esketamine Nasal Spray) Approval Criteria [Depressive Symptoms in Adults with Major Depressive Disorder (MDD) with Acute Suicidal Ideation or Behavior Diagnosis]:

1. An FDA approved indication of depressive symptoms in adults with MDD with acute suicidal ideation or behavior; and
2. Member must be 18 years of age or older; and

3. Spravato® must be used in conjunction with an oral antidepressant; and
4. Prescriber must agree that member will be monitored by a health care provider for at least 2 hours after each administration; and
5. Prescriber must agree that member's blood pressure will be monitored prior to and after administration of Spravato® in accordance with the Spravato® *Prescribing Information*; and
6. Member must not have any contraindications to therapy [i.e., aneurysmal vascular disease (including thoracic and abdominal aorta, intracranial, and peripheral arterial vessels) or arteriovenous malformation; intracerebral hemorrhage; hypersensitivity to esketamine, ketamine, or any of the excipients]; and
7. Member must not have severe hepatic impairment (Child Pugh C); and
8. Prescriber must verify that female members are not currently pregnant and will use effective contraception while receiving treatment with Spravato®; and
9. Prescriber must verify female member is not breastfeeding; and
10. Pharmacy and health care setting must be certified in the Spravato® Risk Evaluation and Mitigation Strategy (REMS) program; and
11. Member must be enrolled in the Spravato® REMS program; and
12. Spravato® must be administered under the direct observation of a health care provider in a REMS certified health care setting; and
13. For initial approval, the number of doses the member received while hospitalized, if applicable, and the dates of these doses must be provided to allow authorization of the appropriate quantity for the initial 4 weeks of treatment; and
14. For continued authorization, prescriber must verify member demonstrated an adequate response during the initial 4 weeks of treatment, verify member is using Spravato® in combination with an oral antidepressant, and provide patient-specific, clinically significant information to support continued use of Spravato®; and
15. A quantity limit of 8 kits per 28 days will apply.

Spravato® (Esketamine Nasal Spray) Approval Criteria [Treatment-Resistant Depression Diagnosis]:

1. An FDA approved indication of treatment-resistant depression in adults; and
2. Member must be 18 years of age or older; and
3. Spravato® must be used in conjunction with an oral antidepressant; and
4. Member must have had an inadequate response to at least 2 different antidepressants from different classes at least 4 weeks in duration each and titrated to recommended dosing during the current depressive episode, unless contraindicated or clinically significant adverse effects; and

5. Prescriber must agree that member will be monitored by a health care provider for at least 2 hours after each administration; and
6. Prescriber must agree that member's blood pressure will be monitored prior to and after administration of Spravato® in accordance with the Spravato® *Prescribing Information*; and
7. Member must not have any contraindications to therapy [e.g., aneurysmal vascular disease (including thoracic and abdominal aorta, intracranial, and peripheral arterial vessels) or arteriovenous malformation; intracerebral hemorrhage; hypersensitivity to esketamine, ketamine, or any of the excipients]; and
8. Member must not have severe hepatic impairment (Child Pugh C); and
9. Prescriber must verify that female members are not currently pregnant and will use effective contraception while receiving treatment with Spravato®; and
10. Prescriber must verify female member is not breastfeeding; and
11. Pharmacy and health care setting must be certified in the Spravato® Risk Evaluation and Mitigation Strategy (REMS) program; and
12. Member must be enrolled in the Spravato® REMS program; and
13. Spravato® must be administered under the direct observation of a health care provider in a REMS certified health care setting; and
14. Initial approvals will be for the duration of the induction phase. For continued authorization, prescriber must verify member demonstrated an adequate response during the induction phase and verify member is using Spravato® in combination with an oral antidepressant; and
15. A quantity limit of 4 kits per 28 days will apply for maintenance dosing. ~~A quantity limit override will be approved for induction of therapy upon meeting Spravato® approval criteria.~~

Utilization Details of Antidepressants: Fiscal Year 2020

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
TIER-1 MEDICATIONS						
SERTRALINE PRODUCTS						
SERTRALINE TAB 50MG	29,989	10,455	$366,729.84	$12.23	2.87	5.70%
SERTRALINE TAB 100MG	29,672	6,852	$362,720.28	$12.22	4.33	5.64%
SERTRALINE TAB 25MG	17,131	6,130	$207,634.19	$12.12	2.79	3.23%
SERTRALINE 20MG/ML	707	190	$39,994.35	$56.57	3.72	0.62%
SUBTOTAL	**77,499**	**23,627**	**$977,078.66**	**$12.61**	**3.28**	**15.19%**
TRAZODONE PRODUCTS						
TRAZODONE TAB 50MG	28,642	8,309	$317,130.25	$11.07	3.45	4.93%
TRAZODONE TAB 100MG	21,995	5,630	$260,308.87	$11.83	3.91	4.04%
TRAZODONE TAB 150MG	12,526	2,912	$167,407.16	$13.36	4.3	2.60%
SUBTOTAL	**63,163**	**16,851**	**$744,846.28**	**$11.79**	**3.75**	**11.57%**
FLUOXETINE PRODUCTS						
FLUOXETINE CAP 20MG	29,740	8,727	$317,128.64	$10.66	3.41	4.93%
FLUOXETINE CAP 10MG	15,791	5,415	$189,664.37	$12.01	2.92	2.95%
FLUOXETINE CAP 40MG	15,203	3,848	$184,710.06	$12.15	3.95	2.87%
FLUOXETINE 20MG/5ML	1,534	371	$54,914.27	$35.80	4.13	0.85%
PROZAC CAP 20MG	20	3	$26,812.46	$1,340.62	6.67	0.42%
PROZAC CAP 40MG	5	2	$6,478.06	$1,295.61	2.5	0.10%
SUBTOTAL	**62,293**	**18,366**	**$779,707.86**	**$12.52**	**3.39**	**12.12%**
ESCITALOPRAM PRODUCTS						
ESCITALOPRAM TAB 10MG	18,364	6,636	$227,024.96	$12.36	2.77	3.53%
ESCITALOPRAM TAB 20MG	18,235	4,311	$237,788.97	$13.04	4.23	3.69%
ESCITALOPRAM TAB 5MG	3,892	1,506	$49,073.00	$12.61	2.58	0.76%
ESCITALOPRAM 5MG/5ML	238	63	$24,819.67	$104.28	3.78	0.39%
LEXAPRO TAB 20MG	16	4	$5,921.75	$370.11	4	0.09%
SUBTOTAL	**40,745**	**12,520**	**$544,628.35**	**$13.37**	**3.25**	**8.46%**
BUPROPION PRODUCTS						
BUPROPION TAB 150MG XL	9,466	3,393	$171,142.41	$18.08	2.79	2.66%
BUPROPION TAB 300MG XL	7,613	1,952	$152,235.44	$20.00	3.9	2.37%
BUPROPION TAB 150MG SR	6,104	1,989	$99,211.51	$16.25	3.07	1.54%
BUPROPION TAB 100MG SR	2,454	860	$39,653.14	$16.16	2.85	0.62%
BUPROPION TAB 75MG	1,603	539	$28,306.39	$17.66	2.97	0.44%
BUPROPION TAB 200MG SR	1,254	305	$23,701.92	$18.90	4.11	0.37%
BUPROPION TAB 100MG	1,144	382	$22,682.41	$19.83	2.99	0.35%
WELLBUTRIN TAB XL 150MG	19	2	$45,316.73	$2,385.09	9.5	0.70%
SUBTOTAL	**29,657**	**9,422**	**$582,249.95**	**$19.63**	**3.15**	**9.05%**
DULOXETINE PRODUCTS						
DULOXETINE CAP 60MG	17,030	4,190	$266,215.81	$15.63	4.06	4.14%
DULOXETINE CAP 30MG	10,245	3,661	$154,093.51	$15.04	2.8	2.39%
DULOXETINE CAP 20MG	2,159	835	$33,683.23	$15.60	2.59	0.52%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
CYMBALTA CAP 60MG	6	1	$2,463.13	$410.52	6	0.04%
SUBTOTAL	**29,440**	**8,687**	**$456,455.68**	**$15.50**	**3.39**	**7.09%**
CITALOPRAM PRODUCTS						
CITALOPRAM TAB 20MG	12,855	4,343	$127,815.64	$9.94	2.96	1.99%
CITALOPRAM TAB 40MG	7,538	2,085	$75,850.03	$10.06	3.62	1.18%
CITALOPRAM TAB 10MG	6,535	2,301	$67,861.52	$10.38	2.84	1.05%
CITALOPRAM 10MG/5ML	176	50	$8,202.86	$46.61	3.52	0.13%
SUBTOTAL	**27,104**	**8,779**	**$279,730.05**	**$10.32**	**3.09**	**4.35%**
MIRTAZAPINE PRODUCTS						
MIRTAZAPINE TAB 15MG	10,927	3,153	$134,434.88	$12.30	3.47	2.09%
MIRTAZAPINE TAB 30MG	6,025	1,591	$80,100.50	$13.29	3.79	1.24%
MIRTAZAPINE TAB 45MG	2,371	512	$36,222.60	$15.28	4.63	0.56%
MIRTAZAPINE TAB 7.5MG	1,620	500	$69,416.62	$42.85	3.24	1.08%
MIRTAZAPINE 15MG ODT	294	94	$9,189.54	$31.26	3.13	0.14%
MIRTAZAPINE 30MG ODT	190	48	$6,896.59	$36.30	3.96	0.11%
MIRTAZAPINE 45MG ODT	117	27	$4,384.45	$37.47	4.33	0.07%
SUBTOTAL	**21,544**	**5,925**	**$340,645.18**	**$15.81**	**3.64**	**5.29%**
VENLAFAXINE PRODUCTS						
VENLAFAXINE CAP 150MG ER	7,643	1,863	$123,937.67	$16.22	4.1	1.93%
VENLAFAXINE CAP 75MG ER	6,437	2,179	$99,826.52	$15.51	2.95	1.55%
VENLAFAXINE CAP 37.5MG ER	3,093	1,412	$44,297.71	$14.32	2.19	0.69%
VENLAFAXINE TAB 75MG	1,514	416	$25,879.12	$17.09	3.64	0.40%
VENLAFAXINE TAB 37.5MG	539	245	$8,792.64	$16.31	2.2	0.14%
VENLAFAXINE TAB 100MG	424	99	$8,636.82	$20.37	4.28	0.13%
VENLAFAXINE TAB 50MG	180	52	$3,867.17	$21.48	3.46	0.06%
VENLAFAXINE TAB 25MG	166	45	$3,239.12	$19.51	3.69	0.05%
EFFEXOR XR CAP 75MG	16	3	$18,727.05	$1,170.44	5.33	0.29%
EFFEXOR XR CAP 150MG	15	3	$13,025.87	$868.39	5	0.20%
EFFEXOR XR CAP 37.5MG	1	1	$385.22	$385.22	1	0.01%
SUBTOTAL	**20,028**	**6,318**	**$350,614.91**	**$17.51**	**3.17**	**5.45%**
PAROXETINE PRODUCTS						
PAROXETINE TAB 20MG	4,214	1,522	$46,772.39	$11.10	2.77	0.72%
PAROXETINE TAB 40MG	3,043	782	$42,055.11	$13.82	3.89	0.65%
PAROXETINE TAB 10MG	2,161	876	$27,456.56	$12.71	2.47	0.43%
PAROXETINE TAB 30MG	1,345	388	$17,286.16	$12.85	3.47	0.27%
PAXIL 10MG/5ML	50	10	$9,124.79	$182.50	5	0.14%
SUBTOTAL	**10,813**	**3,578**	**$142,695.01**	**$13.20**	**3.02**	**2.22%**
FLUVOXAMINE PRODUCTS						
FLUVOXAMINE TAB 100MG	1,344	227	$41,394.12	$30.80	5.92	0.64%
FLUVOXAMINE TAB 50MG	921	204	$20,356.78	$22.10	4.51	0.32%
FLUVOXAMINE TAB 25MG	368	102	$6,488.83	$17.63	3.61	0.10%
SUBTOTAL	**2,633**	**533**	**$68,239.73**	**$25.92**	**4.94**	**1.06%**
TIER-1 SUBTOTAL	**384,919**	**69,126***	**$5,266,891.66**	**$13.68**	**5.57**	**81.84%**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
TIER-2 MEDICATIONS						
DESVENLAFAXINE PRODUCTS						
DESVENLAFAXINE TAB 50MG ER	1,205	344	$42,320.82	$35.12	3.5	0.66%
DESVENLAFAXINE TAB 100MG ER	914	206	$27,505.07	$30.09	4.44	0.43%
DESVENLAFAXINE TAB 25MG ER	246	108	$8,594.24	$34.94	2.28	0.13%
PRISTIQ TAB 100MG	7	2	$2,767.55	$395.36	3.5	0.04%
SUBTOTAL	**2,372**	**531***	**$81,187.68**	**$34.23**	**4.47**	**1.26%**
TIER-2 SUBTOTAL	**2,372**	**531***	**$81,187.68**	**$34.23**	**4.47**	**1.26%**
TIER-3 MEDICATIONS						
VILAZODONE PRODUCTS						
VIIBRYD TAB 40MG	610	94	$167,442.01	$274.50	6.49	2.60%
VIIBRYD TAB 20MG	291	86	$80,225.79	$275.69	3.38	1.25%
VIIBRYD TAB 10MG	44	16	$12,265.97	$278.77	2.75	0.19%
SUBTOTAL	**945**	**196**	**$259,933.77**	**$275.06**	**4.82**	**4.04%**
VORTIOXETINE PRODUCTS						
TRINTELLIX TAB 20MG	846	148	$323,453.66	$382.33	5.72	5.03%
TRINTELLIX TAB 10MG	569	157	$248,325.17	$436.42	3.62	3.86%
TRINTELLIX TAB 5MG	112	38	$42,415.27	$378.71	2.95	0.66%
SUBTOTAL	**1,527**	**343**	**$614,194.10**	**$402.22**	**4.45**	**9.55%**
LEVOMILNACIPRAN PRODUCTS						
FETZIMA CAP 80MG	37	7	$14,577.88	$394.00	5.29	0.22%
FETZIMA CAP 120MG	26	6	$10,276.84	$395.26	4.33	0.16%
FETZIMA CAP 40MG	7	5	$2,737.39	$391.06	1.4	0.04%
SUBTOTAL	**70**	**18**	**$27,592.11**	**$394.17**	**3.89**	**0.43%**
NEFAZODONE PRODUCTS						
NEFAZODONE TAB 100MG	21	4	$1,524.18	$72.58	5.25	0.02%
NEFAZODONE TAB 150MG	21	3	$2,796.95	$133.19	7	0.04%
NEFAZODONE TAB 200MG	12	2	$1,004.88	$83.74	6	0.02%
NEFAZODONE TAB 50MG	4	3	$169.60	$42.40	1.33	0.00%
NEFAZODONE TAB 250MG	3	1	$324.60	$108.20	3	0.01%
SUBTOTAL	**61**	**13**	**$5,820.21**	**$95.41**	**4.69**	**0.09%**
DESVENLAFAXINE PRODUCTS						
DESVENLAFAXINE TAB 50MG ER	10	6	$2,222.54	$222.25	1.67	0.03%
DESVENLAFAXINE TAB 100MG ER	6	4	$1,319.44	$219.91	1.5	0.02%
SUBTOTAL	**16**	**10**	**$3,541.98**	**$221.37**	**1.6**	**0.05%**
SELEGILINE PRODUCTS						
EMSAM 12MG/24H	4	1	$5,858.74	$1,464.69	4	0.09%
SUBTOTAL	**4**	**1**	**$5,858.74**	**$1,464.69**	**4**	**0.09%**
TIER-3 SUBTOTAL	**2,623**	**466***	**$916,940.91**	**$349.58**	**5.63**	**14.24%**
SPECIAL PRIOR AUTHORIZATION (PA) MEDICATIONS						
FLUOXETINE PRODUCTS						
FLUOXETINE TAB 10MG	354	111	$7,011.11	$19.81	3.19	0.11%
FLUOXETINE TAB 20MG	114	23	$3,200.18	$28.07	4.96	0.05%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
FLUOXETINE CAP 90MG DR	22	3	$2,869.50	$130.43	7.33	0.04%
FLUOXETINE TAB 60MG	14	4	$1,650.74	$117.91	3.5	0.03%
FLUOXETINE 20MG/5ML	1	1	$23.52	$23.52	1	0.00%
SUBTOTAL	**505**	**142**	**$14,755.05**	**$29.22**	**3.56**	**0.23%**
PAROXETINE PRODUCTS						
PAROXETINE TAB 37.5MG ER	129	17	$9,494.86	$73.60	7.59	0.15%
PAROXETINE TAB 25MG ER	121	16	$9,351.62	$77.29	7.56	0.15%
PAROXETINE TAB 12.5MG ER	21	3	$1,202.82	$57.28	7	0.02%
SUBTOTAL	**271**	**36**	**$20,049.30**	**$73.98**	**7.53**	**0.32%**
FLUVOXAMINE PRODUCTS						
FLUVOXAMINE CAP 150MG ER	62	7	$17,618.16	$284.16	8.86	0.27%
FLUVOXAMINE CAP 100MG ER	36	4	$9,942.33	$276.18	9	0.15%
SUBTOTAL	**98**	**11**	**$27,560.49**	**$281.23**	**8.91**	**0.42%**
VENLAFAXINE PRODUCTS						
VENLAFAXINE TAB 225MG ER	63	9	$18,159.36	$288.24	7	0.28%
VENLAFAXINE TAB 150MG ER2	2	2	$247.85	$123.93	1	0.00%
SUBTOTAL	**65**	**11**	**$18,407.21**	**$283.19**	**5.91**	**0.28%**
ESKETAMINE PRODUCTS						
SPRAVATO 84MG DOSE	21	6	$82,506.63	$3,928.89	3.5	1.28%
SPRAVATO 56MG DOSE	6	6	$3,707.15	$617.86	1	0.06%
SUBTOTAL	**27**	**12**	**$86,213.78**	**$3,193.10**	**2.25**	**1.34%**
DULOXETINE PRODUCTS						
DULOXETINE CAP 40MG	24	5	$3,040.12	$126.67	4.8	0.05%
DRIZALMA CAP 30MG DR	2	1	$373.82	$186.91	2	0.01%
SUBTOTAL	**26**	**6**	**$3,413.94**	**$131.31**	**4.33**	**0.06%**
BUPROPION PRODUCTS						
BUPROPION TAB 450MG XL	3	1	$960.00	$320.00	3	0.01%
SUBTOTAL	**3**	**1**	**$960.00**	**$320.00**	**3**	**0.01%**
SPECIAL PA SUBTOTAL	**995**	**203***	**$171,359.77**	**$172.22**	**4.9**	**2.66%**
TOTAL	**390,909**	**69,534***	**$6,436,380.02**	**$16.47**	**5.62**	**100.00%**

TAB = tablet; CAP = capsule; XL = extended-release; SR = sustained-release; ODT= orally disintegrating tablet;
ER = extended-release; DR = delayed-release
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020

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Appendix I

Fiscal Year 2020 Annual Review of Targeted Immunomodulator Agents And 30-Day Notice To Prior Authorize Abrilada™ (Adalimumab-afzb), Avsola™ (Infliximab-axxq), Hulio® (Adalimumab-fkjp)

Oklahoma Health Care Authority
December 2020

Current Prior Authorization Criteria

The current Tier chart and specific prior authorization criteria for the Targeted Immunomodulator Agents can be found in the *Recommendations* section at the end of this report.

Utilization of Targeted Immunomodulator Agents: Fiscal Year 2020

Comparison of Fiscal Years: Pharmacy Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	954	5,966	$35,809,181.49	$6,002.21	$199.96	32,851	179,078
2020	1,045	6,848	$42,716,509.96	$6,237.81	$210.97	39,919	202,477
% Change	**9.50%**	**14.80%**	**19.30%**	**3.90%**	**5.50%**	**21.50%**	**13.10%**
Change	**91**	**882**	**$6,907,328.47**	**$235.60**	**$11.01**	**7,068**	**23,399**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2019 = 07/01/2018 to 06/30/2019; Fiscal Year 2020 = 07/01/2019 to 06/30/2020

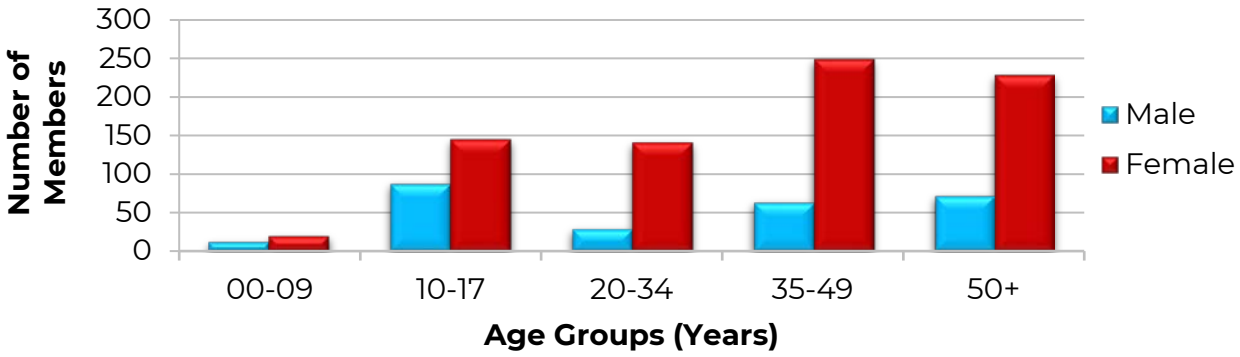
- The increase in cost can be accounted for by price increases for some medications in this class, in addition to increased utilization. However, the consumer price index (CPI) penalty of the federal rebate is designed to keep Medicaid net cost relatively flat despite manufacturer price increases. Additionally, the majority of pharmacy utilization was seen in Tier-2 medications which are supplementally rebated medications. The costs included in this report do not reflect rebated prices or net costs.

Comparison of Fiscal Years: Medical Claims

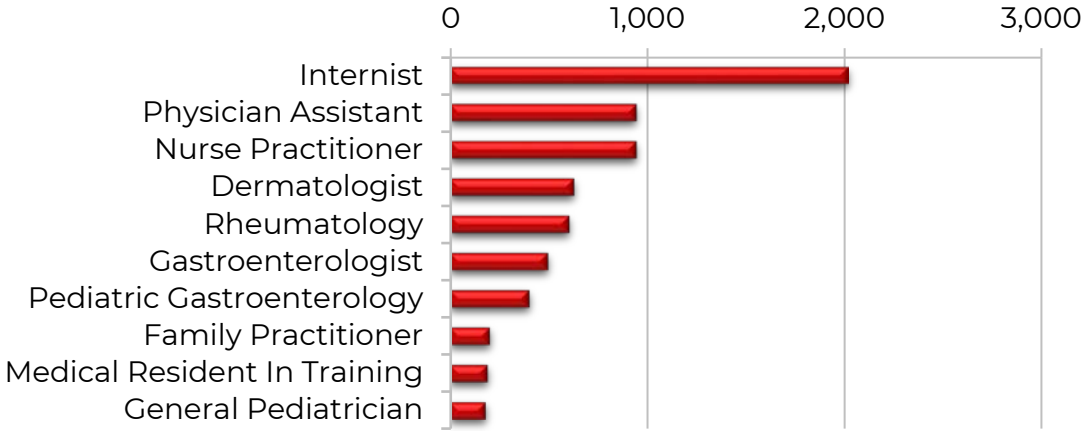
Fiscal Year	*Total Members	†Total Claims	Total Cost	Cost/ Claim	Total Units
2019	206	677	$3,011,845.39	$4,448.81	91,557
2020	249	873	$4,117,116.38	$4,716.06	128,861
% Change	**20.87%**	**28.95%**	**36.70%**	**6.01%**	**40.74%**
Change	**43**	**196**	**$1,105,270.99**	**$267.25**	**37,304**

*Total number of unduplicated members. †Total number of unduplicated claims.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2019 = 07/01/2018 to 06/30/2019; Fiscal Year 2020 = 07/01/2019 to 06/30/2020

Demographics of Members Utilizing Targeted Immunomodulator Agents: Pharmacy Claims



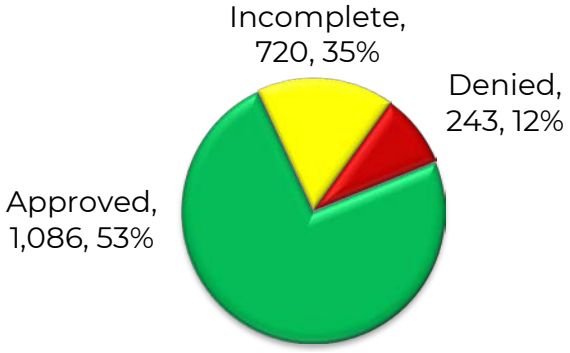
Top Prescriber Specialties of Targeted Immunomodulator Agents by Number of Claims: Pharmacy Claims



Prior Authorization of Targeted Immunomodulator Agents

There were 2,049 prior authorization requests submitted for targeted immunomodulatory agents during fiscal year 2020. 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 2020.

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) Biosimilar Approval(s):

- **November 2019:** The FDA approved Abrilada™ (adalimumab-afzb), as the fifth biosimilar to Humira® (adalimumab), for the treatment of patients with rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), Crohn's disease (CD), ulcerative colitis (UC), and plaque psoriasis (PsO). The FDA approval was based on the review of a comprehensive data package, which demonstrated biosimilarity of Abrilada™ to the reference product. This includes results from the REFLECTIONS B538-02 clinical comparative trial, which evaluated the efficacy, safety, and immunogenicity of Abrilada™. No clinically meaningful differences in efficacy, safety, or immunogenicity were found compared to the reference product, each used in combination with methotrexate in patients with moderate-to-severe RA. Pfizer is working to make Abrilada™ available in the United States based on the terms of an agreement with AbbVie and plans to launch Abrilada™ in 2023.
- **December 2019:** The FDA approved Avsola™ (infliximab-axxq) for all approved indications of the reference product, Remicade® (infliximab), which includes moderate-to-severe RA, moderate-to-severe CD, moderate-to-severe UC, chronic severe PsO, PsA, and AS. Avsola™, an anti-tumor necrosis factor alpha (anti-TNF) monoclonal antibody, was proven to be highly similar to Remicade® with no clinically meaningful differences based on a totality of evidence which included comparative analytical, nonclinical, and clinical data. The data package was composed of results from a pharmacokinetic (PK) similarity trial conducted in healthy subjects, and a comparative clinical trial conducted in patients with moderate-to-severe RA. The randomized, double-blind comparative clinical trial evaluated the efficacy and safety of Avsola™ compared to Remicade® in patients with moderate-to-severe RA. There were 558 patients enrolled and randomized (1:1) to receive either Avsola™ or Remicade® at a dose of 3mg/kg administered as an intravenous (IV) infusion on day 1, at weeks 2 and 6, and every 8 weeks thereafter. The primary endpoint was the response difference (RD) of 20% improvement in American College of Rheumatology (ACR) core set measurements at week 22. The trial also incorporated the evaluation of a single transition in 119 subjects from Remicade® to Avsola™ at week 22, which demonstrated similar safety and immunogenicity in patients who were previously on Remicade®.
- **July 2020:** The FDA approved Hulio® (adalimumab-fkjp), a biosimilar of Humira® (adalimumab), to treat chronic inflammatory disorders including RA, JIA, PsA, AS, CD, UC, and PsO. However, Hulio® will not be available in the United States until July 2023 due to a patent

agreement with AbbVie, the company that markets Humira®. Hulio® will be available as both pre-filled syringes and auto-injectors. The FDA's decision was based on positive results from the ARABESC Phase 3 clinical trial in patients with RA. Results showed no clinically meaningful differences compared to Humira® in terms of safety, efficacy, and immunogenicity.

New U.S. FDA Approved Indication(s)/Formulation(s):

- **December 2019:** The FDA approved Xeljanz® XR [tofacitinib extended-release (ER)] 11mg and 22mg tablets for the once-daily treatment of adult patients with moderately-to-severely active UC, after an inadequate response or intolerance to TNF inhibitors. Xeljanz® was FDA approved for the treatment of UC in May 2018. Use of Xeljanz® or Xeljanz® XR in combination with other biological therapies for UC or with potent immunosuppressants, such as azathioprine and cyclosporine, is not recommended. Xeljanz® 10mg twice daily or Xeljanz® XR 22mg once daily may be given for 8 weeks or up to a maximum of 16 weeks as induction therapy. Following induction therapy, Xeljanz® 5mg twice daily or Xeljanz® XR 11mg once daily may be given as maintenance treatment. For patients with loss of response during maintenance treatment, Xeljanz® 10mg twice daily or Xeljanz® XR 22mg once daily may be considered. Therapy should be limited to the lowest effective dose and shortest duration, with careful consideration of benefits and risks to the individual patient. Dosage adjustment is needed in patients with moderate or severe renal impairment or moderate hepatic impairment. Xeljanz® is approved in the United States for adult patients for 3 indications including moderately-to-severely active RA after methotrexate failure, active PsA after disease modifying antirheumatic drug (DMARD) failure, and moderately-to-severely active UC after TNF-inhibitor failure.
- **January 2020:** The FDA approved a label update for Cosentyx® (secukinumab), allowing the option for a higher 300mg dose among adults with active AS based on clinical response. The FDA based its approval on data from the MEASURE 3 trial, which demonstrated a 300mg dose of secukinumab sustained improvements in the signs and symptoms of active AS over 3 years without increasing the incidence of adverse events compared with a 150mg dose. Additionally, the MEASURE 3 trial showed response rates with more stringent clinical endpoints, including Assessment of Spondyloarthritis International Society 40 (ASAS40), were greater in the 300mg dose group, particularly among patients with previous anti-TNF exposure. ASAS40 measures disease signs and symptoms such as pain, inflammation, and function. By the end of the trial, 56.5% of patients assigned to the

300mg dose achieved ASAS40 vs. 47.7% of patients assigned to the 150mg dose.

- **March 2020:** The FDA approved a supplemental Biologics License Application (sBLA) for Taltz® (ixekizumab) 80mg/mL injection for the treatment of pediatric patients 6 years of age to younger than 18 years of age with moderate-to-severe PsO who are candidates for systemic therapy or phototherapy. The safety, tolerability, and efficacy of Taltz® in patients 6 years of age to younger than 18 years of age were demonstrated in a randomized, double-blind, placebo-controlled Phase 3 trial that included 171 patients with moderate-to-severe PsO. The co-primary endpoints of the trial were the proportion of patients achieving a 75% improvement from baseline on their Psoriasis Area and Severity Index score (PASI 75) and a static Physician's Global Assessment of clear or almost clear skin (sPGA 0 or 1) at week 12. Patients were randomized to receive Taltz® (20mg for <25kg, 40mg for 25-50kg, or 80mg for >50kg through week 12, with 40mg, 80mg, or 160mg starting doses, respectively) or placebo. At 12 weeks, the proportion of patients achieving the co-primary endpoints was superior to placebo with statistically significant differences (P<0.001): 89% of patients treated with Taltz® achieved PASI 75 compared to 25% of patients treated with placebo, and 81% of patients treated with Taltz® achieved sPGA 0 or 1 compared to 11% of patients treated with placebo. Taltz® also met all major secondary endpoints in the trial (P<0.001), which included the proportion of patients achieving PASI 90, sPGA 0, and PASI 100 at week 12, and at least a 4-point improvement in Itch Numeric Rating Scale (Itch NRS ≥4) among patients with baseline Itch NRS ≥4 at week 12, as well as PASI 75 and sPGA 0 or 1 at week 4. Overall, the safety profile observed in pediatric patients with PsO treated with Taltz® every 4 weeks is consistent with the safety profile in adult patients with PsO, with the exception of the frequencies of conjunctivitis (3%), influenza (2%), and urticaria (2%). In this clinical trial, CD occurred at a greater frequency in the Taltz® group (0.9%) than the placebo group (0%) during the 12-week, placebo-controlled period. CD occurred in a total of 4 Taltz®-treated patients (2%) in the clinical trial. The *Prescribing Information* for Taltz® includes a warning for the potential increased risk of inflammatory bowel disease, including CD and UC. Taltz® is also FDA approved for the treatment of moderate-to-severe PsO in adult patients who are candidates for systemic therapy or phototherapy, adult patients with active PsA, and adult patients with active AS.
- **June 2020:** The FDA approved a sBLA for Taltz® (ixekizumab) 80mg/mL injection for the treatment of active non-radiographic axial spondyloarthritis (nr-axSpA) in patients with objective signs of inflammation. Another first-in-class milestone for the treatment of nr-axSpA, the FDA approval makes Taltz® the first interleukin (IL)-17A

antagonist to be approved by the FDA for nr-axSpA. Axial spondyloarthritis (axSpA), which includes both AS and nr-axSpA, is a disease predominantly affecting the sacroiliac joints and the spine, resulting in chronic inflammatory back pain and fatigue. It is estimated that 2.3 million people in the United States have axSpA, with approximately half of those having nr-axSpA. For patients with AS, the disease is characterized by the presence of structural damage of the sacroiliac joints that appears on an X-ray, while patients with nr-axSpA do not have clearly detectable structural damage radiographically. These 2 patient subsets share a similar burden of disease and similar clinical features, but FDA-approved biologic treatment options for patients with nr-axSpA are much more limited and these patients are often underdiagnosed. This approval is based on the results from the Phase 3 COAST-X trial, which evaluated improvement in signs and symptoms of nr-axSpA as measured by the proportion of patients who achieved ASAS40 response criteria compared to placebo. In COAST-X, the safety and efficacy of Taltz® was demonstrated in a Phase 3, multicenter, randomized, double-blind, placebo-controlled 52-week trial of adult patients with active nr-axSpA with objective signs of inflammation. The primary endpoint of the trial was the proportion of patients achieving ASAS40 at week 52. The proportion of Taltz®-treated patients (N=96) achieving the primary endpoint was superior to placebo-treated (N=105), with 30% of patients treated with Taltz® 80mg every 4 weeks achieving ASAS40 response compared to 13% of patients treated with placebo at week 52 (P=0.0045). A major secondary endpoint was ASAS40 response at week 16, of which 35% of Taltz®-treated patients compared to 19% of placebo-treated patients achieved (P<0.01).

- **June 2020:** The FDA approved Cosentyx® (secukinumab) for the treatment of active nr-axSpA, confirming secukinumab's efficacy in addressing the axSpA disease spectrum. The approval of Cosentyx® for nr-axSpA is based on efficacy and safety outcomes from the PREVENT Phase 3 trial, which included 555 adults with active nr-axSpA who were biologic treatment naïve or who had an inadequate response or were intolerant to anti-TNFs. Cosentyx® met the primary endpoints achieving statistically significant improvements versus placebo in the signs and symptoms of nr-axSpA, as measured by the ASAS40 response criteria in biologic-naïve patients at week 52. Cosentyx®-treated patients showed improvement in both loading dose and non-loading dose arms compared to placebo-treated patients at week 16 in health-related quality of life as measured by the Ankylosing Spondylitis Quality of Life (ASQoL) questionnaire (least squares mean change at week 16: -3.5 and -3.6 vs. 1.8, respectively). General health status and quality of life were assessed by the 36-Item Short Form Health Survey (SF-36) Physical

Component Summary (PCS) score. At week 16, Cosentyx®-treated patients showed greater improvement from baseline in the SF-36-PCS score and in the Mental Component Summary (MCS) score. The safety profile of Cosentyx® in the PREVENT trial was shown to be consistent with previous clinical trials, and no new safety signals were detected.

- **June 2020:** The FDA approved Ilaris® (canakinumab) injection for the treatment of active Still's disease, including adult-onset Still's disease (AOSD). Ilaris® was previously FDA approved for systemic JIA (SJIA) in patients 2 years of age and older. AOSD is a rare and serious autoinflammatory disease of unknown origin. Characteristics of AOSD have considerable overlap with SJIA, and include fever, arthritis, rash, and elevated markers for inflammation. The overlapping features of AOSD and SJIA suggest this is a disease continuum, rather than 2 separate diseases. The role of IL-1, a type of cytokine important in regulating the body's immune system, is well-established in AOSD and SJIA. Ilaris® works by blocking the effects of IL-1 and suppressing inflammation in patients with this autoinflammatory disorder. The safety and efficacy of Ilaris® for the treatment of patients with AOSD was established using comparable PK exposure and extrapolation of established efficacy of canakinumab in patients with SJIA, as well as the safety of canakinumab in patients with AOSD and other diseases. The efficacy and safety data in AOSD were generally consistent with the results of a pooled analysis of SJIA patients. Ilaris® was granted Priority Review designation.
- **July 2020:** The FDA approved Tremfya® (guselkumab) as the second IL–23 inhibitor to be approved by the FDA for the treatment of adults with active PsA. The FDA's approval marks the second indication for Tremfya®, which was first approved for adults with PsO in 2017. The FDA based its approval on 2 pivotal Phase 3 clinical trials, DISCOVER-1 and DISCOVER-2, which tested 1,120 adults with active PsA who were naïve to biologics (both trials) or had an inadequate response or intolerance to 1 or 2 TNF inhibitors (about 30% of patients in DISCOVER-1). Part of the pretrial standard treatment could include at least 4 months of Otezla® (apremilast), at least 3 months of non-biologic DMARDs, or at least 4 weeks of nonsteroidal anti-inflammatory drugs (NSAIDs). In both trials, about 58% of patients took methotrexate. Tremfya®-treated patients achieved 20% improvement in ACR response criteria at week 24 at rates of 52% in DISCOVER-1 and 64% in DISCOVER-2, whereas placebo-treated patients had rates of 22% and 33%, respectively. Tremfya® improved patients' other symptoms, including skin manifestations of psoriasis, physical functioning, enthesitis, dactylitis, and fatigue. Tremfya®, a fully human monoclonal antibody that selectively binds to the p19 subunit of IL-23, is administered as a 100mg subcutaneous (sub-Q) injection every 8

weeks, following 2 starter doses at weeks 0 and 4, and can be used alone or in combination with a conventional DMARD. In Tremfya® clinical trials of patients with PsA, a minority of patients had bronchitis or a decreased neutrophil count, but the safety profile was otherwise generally consistent with what has been seen in patients with PsO. Other common adverse effects that occurred in ≥1% of patients included upper respiratory infections, headache, injection site reactions, arthralgia, diarrhea, gastroenteritis, tinea infections, and herpes simplex infections.

- **September 2020:** The FDA approved Xeljanz® (tofacitinib) for the treatment of children and adolescents 2 years of age and older with active polyarticular course JIA (pcJIA). Two formulations were approved, a tablet and an oral solution, and the recommended dosing for pcJIA is weight-based. This approval makes Xeljanz® the first and only Janus kinase (JAK) inhibitor approved in the United States for the treatment of pcJIA. This approval was based on data from a Phase 3 trial including 2 phases: an 18-week open-label, run-in phase (including 225 patients), followed by a 26-week double-blind, placebo-controlled, randomized, withdrawal phase (including 173 patients) for a total duration of 44 weeks. The trial evaluated the efficacy and safety of Xeljanz® taken as either a 5mg tablet or as an 1mg/mL oral solution twice daily based on the patient's body weight (<40kg for the oral solution) and/or patient preference. The trial met its primary endpoint showing the occurrence of disease flare in patients treated with Xeljanz® (31%; 27/88 patients) was statistically significantly (P=0.0007) lower than patients treated with placebo (55%; 47/85 patients) at week 44. In this trial, disease flare was defined as a 30% or more worsening in at least 3 of the 6 variables of the JIA ACR core set, with no more than 1 of the remaining JIA core response variables improving by ≥30% after randomization. In general, the types of adverse drug reactions in patients with pcJIA were consistent with those seen in adult RA patients. Xeljanz® oral solution is anticipated to be available by the end of quarter 1 (Q1) 2021. Xeljanz® 5mg tablets are currently available.

News:

- **April 2018:** The American College of Gastroenterology (ACG) Clinical Guideline of the Management of Crohn's Disease in Adults was most recently published 2 years ago (2018) in the *American Journal of Gastroenterology*. An important update from this treatment guideline was that the use of oral mesalamine has not consistently been demonstrated to be effective compared with placebo for induction of remission and achieving mucosal healing in patients with active CD and should not be used to treat patients with active CD (*strong recommendation, moderate level of evidence*).

- **January 2020:** A new guideline from the American Gastroenterological Association (AGA) on the management of moderate-to-severe UC was published in *Gastroenterology*, the official journal of the AGA Institute. The guideline focused on immunomodulators, biologics, and small molecules to induce and maintain remission for patients with moderate-to-severe UC and to decrease the risk of colectomy. Some important guideline recommendations according to the AGA are as follows:
    - In adult outpatients with moderate-to-severe UC, AGA recommends using infliximab, adalimumab, golimumab, vedolizumab, tofacitinib, or ustekinumab over no treatment (*strong recommendation; moderate quality evidence*).
    - In adult outpatients with moderate-to-severe UC who are new to biologics, AGA suggests using infliximab or vedolizumab rather than adalimumab for induction of remission (*conditional recommendation; moderate quality evidence*).
        - AGA Comment: Patients, particularly those with less severe disease, who place higher value on the convenience of self-administered sub-Q injection and lower value on the relative efficacy of medications, may reasonably chose adalimumab as an alternative.
    - In adult outpatients with moderate-to-severe UC who have been exposed to infliximab, particularly those who were not responsive, AGA suggests using ustekinumab or tofacitinib, rather than vedolizumab or adalimumab, for induction of remission (*conditional recommendation; low quality evidence*).
        - AGA Comment: Patients, particularly those with less severe disease who place higher value on the potential safety of medications and lower value on the relative efficacy of medications, may reasonably chose vedolizumab as an alternative.
    - In adult outpatients with moderate-to-severe UC, AGA suggests early use of biologics with or without immunomodulator therapy, rather than gradual step up after failure of 5-aminosalicylates (5-ASA) (*conditional recommendation; very low quality evidence*).
        - AGA Comment: Patients, particularly those with less severe disease, who place higher value on the safety of 5-ASA therapy and lower value on the efficacy of biologic agents, may reasonably choose gradual step therapy with 5-ASA therapy.
    - In hospitalized adult patients with acute severe UC refractory to IV corticosteroids, AGA suggests using infliximab or cyclosporine (*conditional recommendation; low quality evidence*).

- **June 2020:** In an observational cohort study, published in *ACR Open Rheumatology*, pharmaceutical epidemiologists searched to identify diabetes mellitus (DM) risk in RA patients receiving specific biologic DMARDs (bDMARDs), specifically Orencia® (abatacept). Abatacept has been shown to slow the reduction in beta cell functioning and is speculated to improve insulin sensitivity and reduce glycated hemoglobin. In this study, patients with RA were obtained from 2 health care databases: 50,505 from Truven Health Analytics and 17,251 from Medicare. Patients with a diagnosis of RA without DM were followed prospectively after receiving either abatacept, infliximab, or adalimumab to identify the development of DM. DM was determined based on new-onset hypoglycemic treatment and diagnosis code with a 96.5% positive predictive value. Patients with RA were identified based on diagnosis code with an 87% positive predictive value. RA patients with prevalent use of any study medication of interest or prior diagnosis of DM compared to index date were excluded. The authors also utilized an as-treated follow-up model that included patients with changes in medication, disenrollment, or administrative endpoint. Incidence measurements for certolizumab, golimumab, tocilizumab, and tofacitinib were deemed to be imprecise because of small sample size. The incidence of DM was 6.8 in Truven and 6.6 in Medicare per 1,000 person-years. Anti-TNF agents were the most commonly used bDMARD in both cohorts and the pooled hazard ratio (HR) was found to be higher in the anti-TNF group (HR 2.00 for adalimumab, 2.34 for infliximab) compared with the abatacept group. Patients receiving abatacept were older on average, with a higher prevalence of cardiovascular (CV) comorbidities, compared with the anti-TNF group. There was also an overall lower incidence of DM in the abatacept group. Although the study overall was able to show a decreased incidence of DM in patients with RA undergoing new treatment with bDMARDs, it is ultimately impossible to show cause and effect. This is secondary to the lack of a randomized controlled trial design. This study may help support the practice of early and aggressive treatment of RA to reduce CV risk factors, which include DM risk.
- **July 2020:** A large Swedish study found that patients with RA who were treated with Actemra® (tocilizumab) had twice the risk of gastrointestinal (GI) perforations, a rare but potentially deadly event, than those on TNF inhibitors. Compared with patients receiving TNF inhibitors, the fully adjusted HR for GI perforation among tocilizumab users was 2.20 [95% confidence interval (CI): 1.28-3.79, P=0.0045]. This represented 1 additional GI perforation event for each 451 patient-years of treatment with tocilizumab instead of a TNF inhibitor, the researchers reported online in *RMD Open: Rheumatic & Musculoskeletal Diseases*. Data from the Swedish Biologics Register

and the National Patient Register from 2009 to 2017, matching RA biologic-treated patients according to age, sex, and geographical location with general population controls were analyzed. Also included were patients considered biologic-naïve who had been diagnosed with RA but had not yet started a biologic treatment. Specific agents included in the analysis were the TNF inhibitors etanercept (Enbrel®), infliximab (Remicade®), adalimumab (Humira®), certolizumab pegol (Cimzia®), and golimumab (Simponi®), as well as rituximab (Rituxan®), abatacept (Orencia®), and tocilizumab (Actemra®). The analysis adjusted for multiple covariates including comorbidities, history of GI disorders, CV disease, and infections, as well as disease activity and severity, using inverse probability of treatment weighting. Further adjustments were made for glucocorticoid and NSAIDs exposure. Each treatment initiation was considered separately, with the TNF inhibitors being 1 group, so patients could have multiple initiations if they switched treatments. The study included 76,304 general population controls, 62,532 patients with RA who were biologic-naïve, 17,594 treatment initiations with TNF inhibitors, 2,527 initiations of abatacept, 3,552 initiations of rituximab, and 2,377 initiations of tocilizumab. Follow-up times were 5 years for the biologic-naïve group, 1.2 years for the TNF inhibitor group, 1.3 years for the abatacept group, 2.2 years for the rituximab group, 1.4 years for the tocilizumab group, and 4.4 years for controls. The age-and-sex standardized incidence rate of lower GI tract perforation in the general population was 1.1 per 1,000 person-years (95% CI: 1, 1.3). Rates were higher among all RA groups: 1.6 per 1,000 for biologic-naïve patients (95% CI: 1.5, 1.7), 1.8 for patients who received TNF inhibitors (95% CI: 1.4, 3.6), 2.0 for those who received rituximab (95% CI: 1.3, 5.7), 3.3 for those who received abatacept (95% CI: 1.7, 16.6), and 4.5 for those who received tocilizumab (95% CI: 2.7, 10.4). After full adjustment with inverse probability treatment weighting, neither abatacept nor rituximab had a significantly higher risk compared with the TNF inhibitors, with HRs of 1.07 (95% CI: 0.55, 2.10; P=0.8341) and 0.89 (95% CI: 0.50, 1.58; P=0.6980), respectively, leaving only tocilizumab with a statistically higher risk of 2.2. “The absolute rates remained low, but considering the seriousness of GI perforations, even a slightly increased risk warrants caution when using tocilizumab," the team concluded. The *Prescribing Information* for tocilizumab states that it should be used with caution in patients at an increased risk of GI perforation.

- **July 2020:** A cohort study was published in *Arthritis Care & Research* that sheds new light on the impact of comorbidities on the physical function of patients with AS and PsA. The study had a fairly large cohort of 1,459 Spanish patients. In particular, it was noted that the comorbidity burden specifically impacted the physical function of patients with PsA. The study also noted that traditional risk factors for

CV disease, such as high body mass index (BMI) and hypercholesterolemia, were more prevalent in patients with PsA vs. AS. These findings emphasized the importance of a collaborative approach with primary care in managing these patients to decrease such risk factors. Obesity was found to decrease the chance of achieving minimal disease activity even when patients were on traditional or biologic DMARD therapy. The study suggested a higher education level also appeared to impact physical function in a positive way. When patients were better equipped to describe and manage their disease, they appeared do better overall. For patients with AS, smoking can lead to worse outcomes, making tobacco cessation counseling an important joint effort among all doctors of a patient's care team. Another clinically applicable consideration was patients who are eventually diagnosed with PsA and AS may already have significant disease or damage affecting the patient's physical function by the time a diagnosis is reached. An integral approach with clinicians on the patient's care team gives the patient a better chance at early diagnosis and function restoration.

Pipeline:

- **Bimekizumab:** In September 2020, UCB announced the FDA accepted the BLA for bimekizumab for the treatment of adults with moderate-to-severe PsO. The BLA submission is based on data from a global Phase 3 clinical development program in patients with PsO. All Phase 3 trials met their primary endpoints, demonstrating bimekizumab-treated patients achieved superior skin clearance at week 16, compared to those who received placebo or Humira® (adalimumab) as measured by the PASI 90 and an Investigators Global Assessment (IGA) response of clear or almost clear skin (IGA 0 or 1). All the Phase 3 trials met their ranked secondary endpoints. Two trials demonstrated superior total skin clearance at week 16, as measured by PASI 100, confirming the superiority of bimekizumab over existing biologic treatments Stelara® (ustekinumab) and adalimumab. Furthermore, bimekizumab was superior to placebo, ustekinumab, and adalimumab in achieving rapid response, defined as PASI 75 at week 4. Clinical responses were maintained up to 1 year in all trials. The safety profile of bimekizumab continues to be consistent with earlier clinical trials with no new safety signals identified. Bimekizumab is also being evaluated in Phase 3 trials for potential indications in PsA, AS, nr-axSpA, and hidradenitis suppurativa.
- **Roflumilast:** Roflumilast, a phosphodiesterase type 4 (PDE-4) inhibitor, is being investigated as a cream (ARQ-151) for the topical treatment of PsO and AD and as a foam (ARQ-154) for seborrheic dermatitis. A Phase 2b trial of roflumilast cream showed greater reductions in PsO signs

and symptoms than placebo vehicle cream at week 6. A Phase 2 proof-of-concept trial of roflumilast cream for AD demonstrated consistent evidence of symptomatic improvement across endpoints and favorable tolerability, and a Phase 3 clinical program of roflumilast is currently underway. Topical roflumilast cream development is being advanced into Phase 3 in AD in Q4 2020 or Q1 2021. A Phase 2 trial of roflumilast foam for the treatment of seborrheic dermatitis demonstrated statistically significant improvement over vehicle foam on the trial's primary and secondary endpoints. At week 8, roflumilast 0.3% foam achieved an IGA scale success rate of 73.8% compared to a vehicle rate of 40.9% (P<0.0001). Roflumilast tablets have been approved by the FDA for systemic treatment to reduce the risk of exacerbations of chronic obstructive pulmonary disease (COPD) since 2011 under the trade name Daliresp®.

Recommendations

The College of Pharmacy recommends the removal of the trial requirement of a mesalamine product for a diagnosis of CD or UC for the Tier-2 Targeted Immunomodulator Agents and Entyvio® (vedolizumab) approval criteria to be consistent with current guideline recommendations (changes noted in red):

Targeted Immunomodulator Agents Tier-2 Approval Criteria:

1. An FDA approved diagnosis; and
2. A trial of at least 1 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 1 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 Agents Tier-3 Approval Criteria:

1. An FDA approved diagnosis; and
2. Recent trials of 1 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 medications.

Entyvio® (Vedolizumab) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of moderate-to-severely active Crohn's disease (CD) or moderate-to-severely active ulcerative colitis (UC); and
3. ~~History of failure of a mesalamine medication (does not have to be within the last 90 days) and a trial of 1 Tier-1 in the last 90 days that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; and~~
4. A minimum of a 4 week trial of a Tier-2 tumor necrosis factor (TNF) blocker indicated for the treatment of CD or UC that did not yield adequate relief of symptoms or resulted in intolerable adverse effects. Current Tier-2 medications include the following:
   a. UC: Humira® (adalimumab); or
   b. CD: Humira® (adalimumab); or
5. Prior stabilization on the medication documented within the last 100 days; and
6. A quantity limit of 300mg every 8 weeks will apply. Approvals will be granted for titration quantities required for initial dosing; and
7. Initial approvals will be for the duration of 14 weeks as Entyvio® should be discontinued in patients who do not show evidence of therapeutic benefit by week 14.

Additionally, the College of Pharmacy recommends updating the prior authorization criteria for Benlysta® (belimumab) to add hydroxychloroquine and chloroquine as acceptable trials based on the standard of care for the treatment of systemic lupus erythematosus (SLE). The following criteria will apply (changes and additions noted in red):

Benlysta® (Belimumab) Approval Criteria:

1. The intravenous (IV) formulation will be covered as a medical only benefit while the subcutaneous (sub-Q) formulation will be covered as a pharmacy only benefit; and
2. An FDA approved indication for the treatment of members 5 years of age and older with active, autoantibody-positive, systemic lupus erythematosus (SLE) already receiving standard therapy; and
3. Documented inadequate response to at least 2 of the following medications:
   a. High-dose oral corticosteroids; or
   b. Methotrexate; or
   c. Azathioprine; or
   d. Mycophenolate; or
   e. Cyclophosphamide; or
   f. Hydroxychloroquine/chloroquine; and

4. Member must not have severe active lupus nephritis or severe active central nervous system lupus; and
5. Benlysta® will not be approved for combination use with biologic therapies or IV cyclophosphamide.

The College of Pharmacy also recommends updating the prior authorization criteria for Ilaris® (canakinumab) based on the newly FDA approved indication for the treatment of AOSD. The following criteria will apply (changes and additions noted in red):

Ilaris® (Canakinumab) Approval Criteria [Active Systemic Juvenile Idiopathic Arthritis (SJIA) or Adult-Onset Still's Disease (AOSD) Diagnosis]:

1. An FDA approved indication of SJIA or AOSD; and
2. The member should not be using a tumor necrosis factor (TNF) blocking agent (e.g., adalimumab, etanercept, infliximab) or anakinra; and
3. Ilaris® should not be initiated in members with active or chronic infection including hepatitis B, hepatitis C, human immunodeficiency virus, or tuberculosis; and
4. Dosing should not be more often than once every 4 weeks; and
    a. Weight-based dosing in members 2 years of age and older (the member's recent weight must be provided):
        i. Body weight ≥7.5kg: 4mg/kg subcutaneous injection every 4 weeks (maximum 300mg/dose); and
5. Recent trials of 1 Tier-1 medication and all appropriate Tier-2 medications that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or
6. Prior stabilization on the Tier-3 medication documented within the last 100 days; and
7. Approvals will be for the duration of 1 year.

Lastly, the College of Pharmacy recommends the placement of Abrilada™ (adalimumab-afzb), Avsola™ (infliximab-axxq), and Hulio® (adalimumab-fkjp) into Tier-3 of the Targeted Immunomodulator Agents Product Based Prior Authorization (PBPA) category. Current Tier-3 approval criteria for this category will apply (changes and additions noted in red):

Abrilada™ (Adalimumab-afzb), Amjevita™ (Adalimumab-atto), Cyltezo™ (Adalimumab-adbm), Hadlima™ (Adalimumab-bwwd), Hulio® (Adalimumab-fkjp), and Hyrimoz™ (Adalimumab-adaz), Approval Criteria:

1. Member must meet Tier-3 trial requirements; and
2. A patient-specific, clinically significant reason why the member cannot use Humira® (adalimumab) must be provided.

Avsola™ (Infliximab-axxq), Inflectra™ (Infliximab-dyyb), and Renflexis™ (Infliximab-abda) Approval Criteria:

1. Member must meet Tier-3 trial requirements; and
2. A patient-specific, clinically significant reason why the member cannot use Remicade® (infliximab) must be provided.

Targeted Immunomodulator Agents*±		
Tier-1 (DMARDs appropriate to disease state)	**Tier-2***	**Tier-3**
6-mercaptopurine	adalimumab (Humira®)+	abatacept (Orencia®, Orencia® ClickJect™)≠
azathioprine	etanercept (Enbrel®)	**adalimumab-afzb (Abrilada™)±**
hydroxychloroquine		adalimumab-atto (Amjevita™)±
leflunomide		adalimumab-adbm (Cyltezo™)±
mesalamine		adalimumab-bwwd (Hadlima™)±
methotrexate		**adalimumab-fkjp (Hulio®)±**
minocycline		adalimumab-adaz (Hyrimoz™)±
NSAIDs		anakinra (Kineret®)
oral corticosteroids		apremilast (Otezla®)ß
sulfasalazine		baricitinib (Olumiant®)
		brodalumab (Siliq™)**
		canakinumab (Ilaris®)¥
		certolizumab pegol (Cimzia®)
		etanercept-szzs (Erelzi®)±
		etanercept-ykro (Eticovo™)±
		golimumab (Simponi®, Simponi® Aria™)
		guselkumab (Tremfya™)
		infliximab (Remicade®)
		infliximab-axxq (Avsola™)±
		infliximab-dyyb (Inflectra™)±
		infliximab-abda (Renflexis™)±
		ixekizumab (Taltz®)
		risankizumab-rzza (Skyrizi™)
		rituximab (Rituxan®)~
		sarilumab (Kevzara®)
		secukinumab (Cosentyx®) Ω
		tildrakizumab-asmn (Ilumya™)
		tocilizumab (Actemra®)π
		tofacitinib (Xeljanz®, Xeljanz® XR)**
		upadacitinib (Rinvoq™)
		ustekinumab (Stelara®)
		vedolizumab (Entyvio®)**

DMARDs = disease modifying anti-rheumatic 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.
ß Unique criteria applies for a diagnosis of Behçet's disease (BD).
¥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), Familial Mediterranean Fever (FMF), Systemic Juvenile Idiopathic Arthritis (SJIA), or Adult-Onset Still's Disease (AOSD).
~Unique criteria applies for a diagnosis of pemphigus vulgaris (PV). Unique criteria applies for a diagnosis of granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA).
ΩFor Cosentyx® (secukinumab), only a trial of Humira® from the available Tier-2 medications will be required (based on supplemental rebate participation).
ᵀUnique criteria applies for a diagnosis of giant cell arteritis (GCA) and chimeric antigen receptor (CAR) T-cell-induced cytokine release syndrome (CRS).
≠Orencia® ClickJect™ requires a patient-specific, clinically significant reason why the member cannot use the typical pre-filled syringe formulation.
** Unique criteria applies to this medication for approval.

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.

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

1. An FDA approved diagnosis of 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 corticosteroids for a minimum of 4 weeks or a reason why this is not appropriate must be provided; and
5. Actemra® must be taken in combination with tapering course of a corticosteroids 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 members 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(s).

Erelzi® (Etanercept-szza) and Eticovo™ (Etanercept-ykro) Approval Criteria:

1. Member must meet Tier-3 trial requirements; and
2. A patient-specific, clinically significant reason why the member cannot use Enbrel® (etanercept) must be provided.

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. Member must have at least 3 abscesses or inflammatory nodules; and
4. Previous failure of at least 2 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 members 2 years of age and older; and
2. A failed trial with a corticosteroid injection or systemic corticosteroid 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 must be provided.

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

1. An FDA approved indication of CAPS verified by genetic testing [which includes Familial Cold Auto-Inflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS)] in adults and children 4 years of age and older; and
2. Member must not be using a tumor necrosis factor (TNF) blocking agent (e.g., adalimumab, etanercept, infliximab) or anakinra; and
3. Ilaris® should not be initiated in members 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. Weight-based dosing (the member's recent weight must be provided):
        i. Body weight >40kg: 150mg; or
        ii. Body weight 15kg to 40kg: 2mg/kg. If inadequate response, dose may be increased to 3mg/kg; and
5. Approvals will be for the duration of 1 year.

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 6 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.

Orencia® ClickJect™ (Abatacept) Approval Criteria:

1. Member must meet Tier-3 trial requirements; and
2. A patient-specific, clinically significant reason why the member cannot use the typical pre-filled syringe formulation must be provided.

Otezla® (Apremilast) Approval Criteria [Behçet's Disease (BD) Diagnosis]:

1. An FDA approved indication for the treatment of oral ulcers associated with BD; and
2. Member must have had oral ulcers at least 3 times in the last 12 month period; and
3. Member must have had a 2 week trial of the following that resulted in inadequate efficacy or intolerable adverse effects (or be contraindicated for the member):
    a. Topical corticosteroids (applied topically to the mouth); and
    b. Colchicine; and
4. Quantity limits according to package labeling will apply.

Rituxan® (Rituximab) Approval Criteria [Granulomatosis with Polyangiitis (GPA, Wegener's Granulomatosis) and Microscopic Polyangiitis (MPA) Diagnosis]:

1. An FDA approved diagnosis of GPA or MPA in adult and pediatric members 2 years of age and older; and
2. Rituxan® must be used in combination with corticosteroids; and
3. Approval quantity will be based on Rituxan® *Prescribing Information* and FDA approved dosing regimen(s).

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 corticosteroids; and
3. Initial approvals will be for (2) 1,000mg intravenous (IV) infusions separated by 2 weeks and a 500mg IV infusion at month 12. Subsequent approvals may be authorized based on 6 month evaluations or upon relapse no sooner than 16 weeks after the previous infusion.

Siliq® (Brodalumab) Approval Criteria:

1. Member must meet Tier-3 approval criteria; and
2. Members must also be enrolled in the Siliq® REMS Program for approval; and
3. Members with a concomitant diagnosis of Crohn's disease will not be approved; and
4. Initial authorizations of Siliq® (brodalumab) will be for the duration of 12 weeks at which time the prescriber must verify the member is responding to treatment. If an adequate response has not been achieved after 12 to 16 weeks of treatment with brodalumab, consideration should be given to discontinuing therapy.

Xeljanz® (Tofacitinib) Approval Criteria:

1. Member must meet Tier-3 approval criteria; and
2. Member must have a negative tuberculosis test, successful treatment of active tuberculosis, or close evaluation and appropriate treatment of latent tuberculosis; and
3. Severe hepatic impairment has been ruled out; and
4. Approval will be for 12 weeks, after which time, prescriber must confirm performance of the following tests (and verification that the results are acceptable to prescriber) for further approval:
    a. Lymphocytes; and
    b. Neutrophils; and
    c. Hemoglobin; and
    d. Liver enzymes; and
    e. Lipid panel; and
5. Subsequent approvals will be for the duration of 1 year. Yearly approvals require performance of repeat tuberculosis test.

Xeljanz® XR [Tofacitinib Extended-Release (ER)] Approval Criteria:

1. Member must meet Tier-3 approval criteria and all Xeljanz® approval criteria; and
2. A patient-specific, clinically significant reason why the member cannot take the twice daily formulation of Xeljanz® must be provided.

Utilization Details of Targeted Immunomodulator Agents: Fiscal Year 2020

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
TIER-2 PRODUCTS					
ADALIMUMAB PRODUCTS					
HUMIRA PEN 40MG/0.4ML	2,025	364	$12,758,828.04	5.56	$6,300.66
HUMIRA PEN 40MG/0.8ML	589	104	$3,805,715.81	5.66	$6,461.32
HUMIRA INJ 40MG/0.4ML	450	85	$2,474,166.46	5.29	$5,498.15
HUMIRA KIT 40MG/0.8ML	163	38	$978,438.06	4.29	$6,002.69

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
HUMIRA INJ 20MG/0.2ML	149	21	$785,778.73	7.1	$5,273.68
HUMIRA PEN KIT 80MG/0.8ML CD/UC/HS	67	64	$1,054,022.85	1.05	$15,731.68
HUMIRA PEN KIT 80MG/0.8ML & 40MG/0.4ML PS/UV	47	47	$508,209.55	1	$10,812.97
HUMIRA INJ 10MG/0.1ML	8	1	$42,631.02	8	$5,328.88
HUMIRA PEN INJ 40MG/0.8ML PS/UV	7	7	$71,965.68	1	$10,280.81
HUMIRA PED INJ 80MG/0.8ML & 40MG/0.4ML CD	7	7	$56,705.27	1	$8,100.75
HUMIRA KIT 20MG/0.4ML	6	1	$36,285.47	6	$6,047.58
HUMIRA PEN INJ KIT 40MG/0.8ML CD/UC/HS	5	2	$78,813.94	2.5	$15,762.79
SUBTOTAL	**3,523**	**741**	**$22,651,560.88**	**4.75**	**$6,429.62**
ETANERCEPT PRODUCTS					
ENBREL PEN INJ 50MG/ML	1,008	180	$5,497,513.77	5.6	$5,453.88
ENBREL INJ SYG 50MG/ML	214	46	$1,138,075.83	4.65	$5,318.11
ENBREL INJ 25MG	81	15	$220,830.35	5.4	$2,726.30
ENBREL MINI INJ 50MG/ML	78	15	$385,974.72	5.2	$4,948.39
ENBREL INJ SYG 25MG/0.5ML	76	12	$245,024.53	6.33	$3,224.01
SUBTOTAL	**1,457**	**268**	**$7,487,419.20**	**5.44**	**$5,138.93**
TIER-2 SUBTOTAL	**4,980**	**1,009**	**$30,138,980.08**	**4.94**	**$6,052.00**
TIER-3 PRODUCTS					
INFLIXIMAB PRODUCTS					
REMICADE INJ 100MG	179	38	$1,293,601.06	4.71	$7,226.82
SUBTOTAL	**179**	**38**	**$1,293,601.06**	**4.71**	**$7,226.82**
SECUKINUMAB PRODUCTS					
COSENTYX PEN INJ 300MG	226	37	$1,366,553.14	6.11	$6,046.70
COSENTYX PEN 150MG/ML	50	11	$270,068.07	4.55	$5,401.36
COSENTYX INJ 300MG DOSE	30	7	$179,996.50	4.29	$5,999.88
COSENTYX INJ 150MG/ML	10	5	$83,333.02	2	$8,333.30
SUBTOTAL	**316**	**60**	**$1,899,950.73**	**5.27**	**$6,012.50**
ABATACEPT PRODUCTS					
ORENCIA INJ 125MG/ML	153	29	$666,347.15	5.28	$4,355.21
ORENCIA PEN INJ 125MG/ML	63	12	$253,458.51	5.25	$4,023.15
ORENCIA INJ 250MG	21	5	$60,193.68	4.20	$2,866.37
ORENCIA INJ 87.5MG/0.7ML	18	3	$59,086.42	6.00	$3,282.58
ORENCIA INJ 50MG/0.4ML	3	1	$3,334.53	3.00	$1,111.51
SUBTOTAL	**258**	**50**	**$1,042,420.29**	**5.16**	**$4,040.39**
TOFACITINIB PRODUCTS					
XELJANZ TAB 5MG	170	45	$748,615.03	3.78	$4,403.62
XELJANZ XR TAB 11MG	46	9	$206,057.01	5.11	$4,479.50
XELJANZ TAB 10MG	14	3	$52,925.84	4.67	$3,780.42
SUBTOTAL	**230**	**57**	**$1,007,597.88**	**4.04**	**$4,380.86**
USTEKINUMAB PRODUCTS					
STELARA INJ SYG 90MG/ML	100	19	$2,188,571.80	5.26	$21,885.72
STELARA INJ SYG 45MG/0.5ML	39	15	$426,089.27	2.60	$10,925.37
STELARA INJ 45MG/0.5ML	11	4	$126,002.37	2.75	$11,454.76
STELARA INJ 5MG/ML	3	2	$15,534.00	1.50	$5,178.00
SUBTOTAL	**153**	**40**	**$2,756,197.44**	**3.83**	**$18,014.36**
TOCILIZUMAB PRODUCTS					
ACTEMRA INJ 162MG/0.9ML	85	12	$315,859.36	7.08	$3,715.99

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
ACTEMRA INJ 400MG/20ML	32	6	$79,923.33	5.33	$2,497.60
ACTEMRA PEN 162MG/0.9ML	13	5	$53,821.99	2.60	$4,140.15
ACTEMRA INJ 80MG/4ML	10	2	$9,175.06	5.00	$917.51
ACTEMRA INJ 200MG/10ML	7	3	$11,608.87	2.33	$1,658.41
SUBTOTAL	**147**	**28**	**$470,388.61**	**5.25**	**$3,199.92**
APREMILAST PRODUCTS					
OTEZLA TAB 30MG	122	23	$395,826.31	5.30	$3,244.48
OTEZLA TAB 10/20/30MG	12	12	$41,464.37	1.00	$3,455.36
SUBTOTAL	**134**	**35**	**$437,290.68**	**3.83**	**$3,263.36**
CANAKINUMAB PRODUCTS					
ILARIS INJ 150MG/ML	60	10	$1,246,831.60	6.00	$20,780.53
SUBTOTAL	**60**	**10**	**$1,246,831.60**	**6.00**	**$20,780.53**
CERTOLIZUMAB PRODUCTS					
CIMZIA PREFL KIT 200MG/ML	73	16	$366,204.25	4.56	$5,016.50
CIMZIA KIT STARTER 200MG/ML	7	7	$94,582.36	1.00	$13,511.77
SUBTOTAL	**80**	**23**	**$460,786.61**	**3.48**	**$5,759.83**
GOLIMUMAB PRODUCTS					
SIMPONI INJ 50MG/0.5ML	40	6	$190,413.43	6.67	$4,760.34
SIMPONI INJ 100MG/ML	8	1	$45,328.84	8.00	$5,666.11
SUBTOTAL	**48**	**7**	**$235,742.27**	**6.86**	**$4,911.30**
IXEKIZUMAB PRODUCTS					
TALTZ INJ 80MG/ML	111	17	$741,542.37	6.53	$6,680.56
TALTZ INJ 80MG/ML	7	1	$44,955.87	7.00	$6,422.27
SUBTOTAL	**118**	**18**	**$786,498.24**	**6.56**	**$6,665.24**
SARILUMAB PRODUCTS					
KEVZARA PEN 200MG/1.14ML	25	4	$86,234.07	6.25	$3,449.36
KEVZARA INJ 200MG/1.14ML	8	1	$26,956.20	8.00	$3,369.53
SUBTOTAL	**33**	**5**	**$113,190.27**	**6.60**	**$3,430.01**
GUSELKUMAB PRODUCTS					
TREMFYA INJ 100MG/ML	25	5	$278,071.29	5.00	$11,122.85
TREMFYA PEN INJ 100MG/ML	6	1	$66,799.47	6.00	$11,133.25
SUBTOTAL	**31**	**6**	**$344,870.76**	**5.17**	**$11,124.86**
VEDOLIZUMAB PRODUCTS					
ENTYVIO INJ 300MG	55	10	$315,539.34	5.50	$5,737.08
SUBTOTAL	**55**	**10**	**$315,539.34**	**5.50**	**$5,737.08**
ANAKINRA PRODUCTS					
KINERET INJ 100MG/0.67ML	13	2	$55,013.31	6.50	$2,037.53
SUBTOTAL	**13**	**2**	**$55,013.31**	**6.50**	**$2,037.53**
BARICITINIB PRODUCTS					
OLUMIANT TAB 2MG	9	2	$19,814.65	4.50	$2,201.63
SUBTOTAL	**9**	**2**	**$19,814.65**	**4.50**	**$2,201.63**
RISANKIZUMAB PRODUCTS					
SKYRIZI INJ 150MG	4	2	$91,796.14	2.00	$22,949.04
SUBTOTAL	**4**	**2**	**$91,796.14**	**2.00**	**$22,949.04**
TIER-3 SUBTOTAL	**1,868**	**393**	**$12,577,529.88**	**4.75**	**$6,733.15**
TOTAL	**6,848**	**1,045***	**$42,716,509.96**	**6.55**	**$6,237.81**

INJ = injection; CD = Crohn's disease; UC = ulcerative colitis; HS = hidradenitis suppurativa; PS = psoriasis; UV = uveitis; PED = pediatric; TAB = tablet; SYG = syringe; PREFL = prefilled

*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

Fiscal Year 2020 = 07/01/2019 to 06/30/2020

Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
RITUXAN INJ J9310	351	118	$1,714,314.71	$4,884.09	2.97
REMICADE INJ J1745	268	64	$781,847.20	$2,917.34	4.19
ACTEMRA INJ J3262	130	15	$238,923.14	$1,837.87	8.67
SIMPONI ARIA INJ	60	19	$248,568.39	$4,142.81	3.16
ORENCIA INJ J0129	86	21	$404,524.22	$4,703.77	4.1
ENTYVIO INJ J3380	97	21	$562,963.32	$5,803.75	4.62
STELARA INJ J3357	9	3	$153,552.60	$17,061.40	3
INFLECTRA INJ Q5103	4	3	$12,422.80	$3,105.70	1.33
TOTAL	**873⁺**	**249***	**$4,117,116.38**	**$4,716.06**	**3.51**

INJ = injection
⁺Total number of unduplicated claims.
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020

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Appendix J

Fiscal Year 2020 Annual Review of Soliris® (Eculizumab) and Ultomiris® (Ravulizumab-cwvz) and 30-Day Notice to Prior Authorize Enspryng™ (Satralizumab-mwge) and Uplizna™ (Inebilizumab-cdon)

Oklahoma Health Care Authority
December 2020

Introduction[1,2,3,4]

Atypical Hemolytic Uremic Syndrome (aHUS) is a rare and severe form of thrombotic microangiopathy (TMA) caused by defects in the regulation of the complement system. These defects are inherited and/or acquired and can lead to uncontrolled activation of the complement system. The renal vasculature is predominantly affected, and many of these patients can sustain permanent renal damage leading to end stage renal disease or death.

Neuromyelitis Optica Spectrum Disorder (NMOSD) is a rare autoimmune disease that involves chronic inflammation of the optic nerve and spinal cord. The hallmark symptoms of this disease include eye pain, vision loss, bladder dysfunction, and mild-to-moderate paralysis. Anti-aquaporin-4 (AQP4) antibody has a direct role in the pathogenesis of NMOSD and is a specific biomarker for this disease. Acute attacks of NMOSD are generally treated with corticosteroids. The prevalence of NMOSD ranges from 0.5 to 10 per 100,000 individuals and affects more women than men.

Paroxysmal Nocturnal Hemoglobinuria (PNH) is an acquired hematopoietic stem cell disorder that causes the production of defective red blood cells (RBCs). These defective RBCs are prematurely destroyed by the body's complement system. Patients with PNH often present with signs and symptoms of RBC hemolysis which include unexplained hemolytic anemia, fatigue, dyspnea, and hemoglobinuria. The incidence of PNH ranges from 1 to 10 cases per 1,000,000 individuals and affects males and females equally. The leading cause of death in these patients is thrombosis.

Current Prior Authorization Criteria

Soliris® (Eculizumab) Approval Criteria [Generalized Myasthenia Gravis (gMG) Diagnosis]:

1. An FDA approved diagnosis of gMG; and
2. Positive serologic test for anti-AChR antibodies; and
3. Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II to IV; and

4. MG-Activities of Daily Living (MG-ADL) total score ≥6; and
5. Member must meet 1 of the following:
    a. Failed treatment over 1 year or more with 2 or more immunosuppressive therapies (ISTs) either in combination or as monotherapy; or
    b. Failed at least 1 IST and required chronic plasmapheresis or plasma exchange (PE) or intravenous immunoglobulin (IVIG); and
6. Initial approvals will be for the duration of 6 months at which time an updated MG-ADL score must be provided. Continued authorization requires improvement in the MG-ADL score from baseline. Subsequent approvals will be for the duration of 1 year.

Soliris® (Eculizumab) Approval Criteria [Neuromyelitis Optica Spectrum Disorder (NMOSD) Diagnosis]:

1. An FDA approved diagnosis of NMOSD; and
2. Member is anti-aquaporin-4 (AQP4) antibody positive; and
3. Member must be 18 years of age or older.

Soliris® (Eculizumab) Approval Criteria [Paroxysmal Nocturnal Hemoglobinuria (PNH) or Atypical Hemolytic Uremic Syndrome (aHUS) Diagnosis]:

1. Member must have an established diagnosis of PNH or aHUS via international classification of disease (ICD) coding in member's medical claims history; and
2. An age restriction of 18 years and older will apply; and
3. For members younger than 18 years of age, approval can be granted with a documented diagnosis of aHUS.

Ultomiris® (Ravulizumab-cwvz) Approval Criteria [Atypical Hemolytic Uremic Syndrome (aHUS) Diagnosis]:

1. Member must have a documented diagnosis of aHUS.

Ultomiris® (Ravulizumab-cwvz) Approval Criteria [Paroxysmal Nocturnal Hemoglobinuria Diagnosis (PNH) Diagnosis]:

1. Member must have an established diagnosis of PNH via international classification of disease (ICD) coding in member's medical claims history; and
2. An age restriction of 18 years and older will apply.

Utilization of Soliris® (Eculizumab) and Ultomiris® (Ravulizumab-cwvz): Fiscal Year 2020

Comparison of Fiscal Years: Pharmacy Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	6	89	$1,807,970.51	$20,314.28	$1,829.93	19,110	988
2020	7	107	$2,432,880.77	$22,737.20	$1,649.41	24,160	1,475
% Change	**16.7%**	**20.2%**	**34.6%**	**11.9%**	**-9.9%**	**26.4%**	**49.3%**
Change	**1**	**18**	**$624,910.26**	**$2,422.92**	**-$180.52**	**5,050**	**487**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2019 = 07/01/2018 to 06/30/2019; Fiscal Year 2020 = 07/01/2019 to 06/30/2020

Comparison of Fiscal Years: Medical Claims

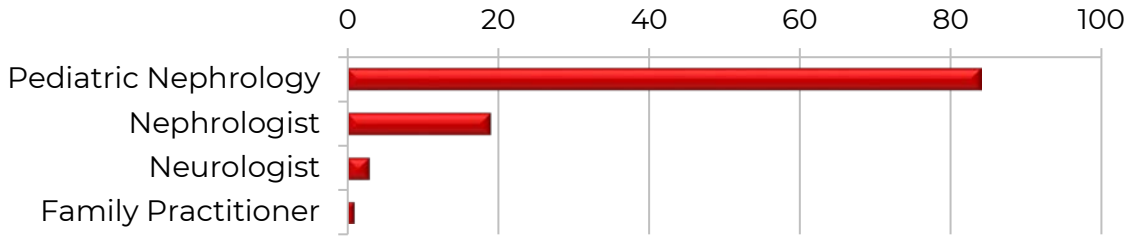
Fiscal Year	*Total Members	†Total Claims	Total Cost	Cost/ Claim	Total Units
2019	4	32	$1,500,424.80	$46,888.28	6,510
2020	5	17	$780,254.40	$45,897.32	3,660
% Change	**25.0%**	**-46.9%**	**-48.0%**	**-2.1%**	**-43.8%**
Change	**1**	**-17**	**-$720,170.40**	**-$990.96**	**-2,850**

*Total number of unduplicated members.
†Total number of unduplicated claims
Costs do not reflect rebated prices or net costs.
Fiscal Year 2019 = 07/01/2018 to 06/30/2019; Fiscal Year 2020 = 07/01/2019 to 06/30/2020

Demographics of Members Utilizing Soliris® (Eculizumab) and Ultomiris® (Ravulizumab-cwvz): Pharmacy Claims

- Due to the limited number of members utilizing Soliris® (eculizumab) and Ultomiris® (ravulizumab-cwvz) during fiscal year 2020, detailed demographic information could not be provided.

Top Prescriber Specialties of Soliris® (Eculizumab) and Ultomiris® (Ravulizumab-cwvz) by Number of Claims: Pharmacy Claims

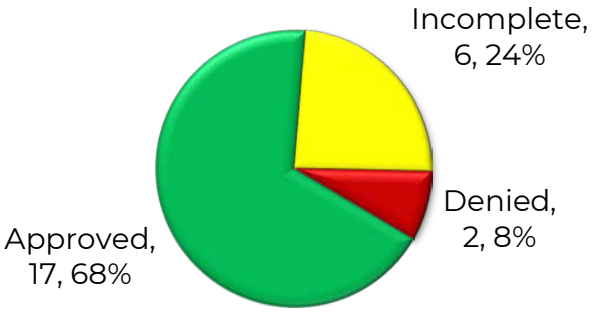


Prior Authorization of Soliris® (Eculizumab) and Ultomiris® (Ravulizumab-cwvz)

There were 25 prior authorization requests submitted for 11 unique members for Soliris® (eculizumab) and Ultomiris® (ravulizumab-cwvz) during fiscal year

2020. The following chart shows the status of the submitted petitions for fiscal year 2020.

Status of Petitions



Market News and Updates[5,6,7,8,9,10,11,12]

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

- **June 2020:** The FDA approved Uplizna™ (inebilizumab-cdon), the first and only B-cell depleter approved for AQP4 seropositive NMOSD. The safety and efficacy of inebilizumab was evaluated in a Phase 2/3, randomized (3:1), double-blind, placebo-controlled trial, known as the N-Momentum trial. In this trial, 89% of patients in the AQP4 seropositive treatment arm remained relapse-free during the 6 month period post treatment, compared to 58% in the placebo group.
- **August 2020:** The FDA approved Enspryng™ (satralizumab-mwge), the first and only self-administered treatment for AQP4 seropositive NMOSD. The safety and efficacy of satralizumab was demonstrated in 2 Phase 3 clinical trials, SAkuraStar and SAkuraSky. In the SAkuraStar monotherapy trial, 76.5% of satralizumab patients in the AQP4 seropositive treatment arm were relapse-free at 96 weeks, compared to 41.1% in the placebo group. In the SAkuraSky trial, the safety and efficacy of satralizumab used concurrently with baseline immunosuppressant treatment (IST) was evaluated. In the AQP4 seropositive treatment arm, 91.1% of the patients taking satralizumab plus IST were relapse-free at 96 weeks, compared to 56.8% in the placebo plus IST group.
- **October 2020:** The FDA approved a new 100mg/mL formulation of Ultomiris® (ravulizumab-cwvz) for the treatment of PNH in adult patients and for the treatment of aHUS in adult and pediatric patients. This new formulation will reduce the average annual infusion time by approximately 60% when compared to the previous 10mg/mL formulation. Alexion Pharmaceuticals will continue to supply the 10mg/mL formulation until mid-2021.

Pipeline:

- **ALXN2050:** In December 2019, Alexion initiated a Phase 2 clinical trial of ALXN2050 for the treatment of PNH. ALXN2050 is an oral factor D inhibitor that inhibits complement activation in the alternative pathway.
- **Danicopan:** Alexion plans to initiate a Phase 3 clinical trial of danicopan (ALXN2040) at the end of 2020 as an add-on therapy for patients with PNH with extravascular hemolysis (EVH). Danicopan is an oral factor D inhibitor that prevents uncontrolled complement activation on affected RBCs.
- **Iptacopan:** In August 2020, Novartis announced promising Phase 2 data on iptacopan (LNP023), an investigational oral treatment for PNH. Iptacopan is a selective factor B inhibitor of the complement system's alternative pathway and is currently being studied as add-on therapy with eculizumab. Initial results show significant improvements in hemoglobin (Hgb) levels and a significant reduction in lactate dehydrogenase level, a biomarker of intravascular hemolysis. Iptacopan is also currently being studied in a separate Phase 2 clinical trial in patients with aHUS.
- **Narsoplimab:** In July 2019, the FDA granted Omeros Corporation Fast Track designation for narsoplimab (OMS721) for the treatment of patients with aHUS and granted Orphan Drug designation for the prevention of complement-mediated thrombotic microangiopathy, which includes aHUS. Narsoplimab is a fully human monoclonal antibody (MAB) targeting mannan-binding lectin-associated serine protease (MASP)-2, the effector enzyme of the lectin pathway of the complement system. Phase 2 trial results were positive, and a Phase 3 trial is currently underway.
- **OMS906:** In August 2020, the FDA approved Omeros Corporation's Investigational New Drug (IND) Application to begin clinical trials with OMS906 for the treatment of PNH. OMS906 is an investigational human MAB targeting MASP-3. MASP-3 is a key activator of the body's complement system and is responsible for the conversion of pro-factor D to factor D.
- **Pegcetacoplan:** In November 2020, Apellis released new information about their Phase 3 head-to-head trial with eculizumab in patients with PNH. Pegcetacoplan is a targeted C3 therapy designed to regulate excessive activation of the complement cascade, which leads to the progression of PNH. Results from the trial demonstrated greater treatment response and quality of life improvements in patients with PNH when compared to eculizumab. The primary endpoint of this trial was the change from baseline in Hgb levels at week 16.

Enspryng™ (Satralizumab-mwge) Product Summary[13]

Indication(s): Enspryng™ (satralizumab-mwge) is an interleukin-6 (IL-6) receptor antagonist indicated for the treatment of NMOSD in adult patients who are AQP4 antibody positive.

Dosing:

- Enspryng™ is available as a 120mg/mL single-dose prefilled syringe (PFS) with a needle safety device.
- The recommended loading dose of Enspryng™ is 120mg subcutaneously (sub-Q) at weeks 0, 2, and 4, followed by a maintenance dosage of 120mg every 4 weeks.
- Enspryng™ PFS should be stored refrigerated at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light. Prior to administration, if unopened, Enspryng™ can be removed from and returned to the refrigerator if necessary; however, the total combined time out of refrigeration should not exceed 8 days at a temperature that does not exceed 30°C (86°F).

Mechanism of Action: The exact mechanism of how satralizumab exerts its effects in NMOSD is not fully understood. It is presumed that satralizumab is involved in the inhibition of IL-6-mediated signaling through binding to soluble and membrane-bound IL-6 receptors.

Contraindication(s):

- Active hepatitis B virus (HBV) infection
- Active or untreated latent tuberculosis (TB)

Warnings and Precautions:

- Infections: An increased risk of infection has been observed with IL-6 antagonists. The most common infections reported in the randomized clinical trial in patients who were on satralizumab and not on other chronic immunosuppressants were nasopharyngitis (12%) and cellulitis (10%). In patients on satralizumab and also a concurrent immunosuppressant, the most common infections reported in the trial were nasopharyngitis (31%), upper respiratory infection (19%), and pharyngitis (12%). Satralizumab should be delayed in patients with an active infection and initiated when the infection is resolved.
    - HBV Reactivation: Risk of HBV reactivation has been observed with other immunosuppressant therapies. Patients with chronic HBV infection were excluded from the satralizumab clinical trial.
    - TB: Patients should be evaluated for TB risk factors and tested for latent infection prior to initiating satralizumab. Anti-TB therapy should be considered prior to initiation of Enspryng™ in patients with a history of latent or active TB in whom an adequate course of treatment cannot be confirmed and for patients with a negative

test for latent TB but who have risk factors for a TB infection. Infectious disease experts should be consulted regarding whether initiating anti-TB therapy is appropriate before starting treatment. Patients should be monitored for the development of signs and symptoms of TB with Enspryng™, even if initial TB testing is negative.

- Vaccinations: Live or live-attenuated vaccines are not recommended during treatment with satralizumab. All live or live-attenuated vaccines should be given 4 weeks prior to initiating therapy with satralizumab. Non-live vaccines should be given 2 weeks prior to initiating therapy.

- Elevated Liver Enzymes: Mild to moderate elevations of liver enzymes were observed in patients treated with satralizumab while in Phase 3 clinical trials. ALT and AST levels should be monitored every 4 weeks for the first 3 months of therapy, followed by every 3 months for 1 year, and thereafter, as clinically indicated.
- Decreased Neutrophil Counts: Decreases in neutrophil count were observed at a higher incidence than placebo in patients treated with satralizumab. Neutrophil counts should be monitored 4 to 8 weeks after initiation of therapy, and thereafter at regular, clinically determined intervals.
- Hypersensitivity Reactions: Rash, urticaria, and fatal anaphylaxis have occurred with other IL-6 receptor antagonists.

Efficacy: The safety and efficacy of satralizumab were established in 2 clinical trials. SAkuraStar was a Phase 3, randomized (2:1), double blind, placebo-controlled trial in 95 patients not on IST in which 64 patients were AQP4 seropositive and 31 patients were AQP4 seronegative. In this study, 41 AQP4 seropositive patients were randomized to receive satralizumab 120mg and 23 AQP4 seropositive patients received placebo. The double-blind treatment period was 1.5 years after the random assignment of the last enrolled patient. The second trial, SAkuraSky, was a Phase 3, randomized (1:1), double blind, placebo-controlled-trial in 76 adult patients with concurrent IST in which 52 patients were AQP4 seropositive and 24 were AQP4 seronegative. In this trial, 26 AQP4 seropositive patients were randomized to receive satralizumab 120mg plus baseline IST and 26 AQP4 seropositive patients received placebo plus baseline IST. Baseline IST included azathioprine, mycophenolate mofetil, or oral corticosteroids. The double-blind treatment period ended when the total number of protocol defined relapse (PDR) reached 26. In both trials, patients were given satralizumab 120mg or placebo via sub-Q injection at weeks 0, 2, 4, and every 4 weeks thereafter.

- SAkuraStar Trial:
  - Inclusion Criteria: Eligible patients were 18-74 years of age with AQP4 seropositive or seronegative NMOSD. Each patient was

required to have a documented history of ≥1 attack requiring rescue therapy in the prior year, and an Expanded Disability Status Scale (EDSS) score of ≤6.5 at randomization. Members on concomitant IST were excluded from the trial.
    - Primary Endpoint: The primary endpoint was the time to the first PDR. PDR was defined as new or worsening neurological symptoms attributable to NMOSD.
    - Results: The time to the first PDR was significantly longer in AQP4 seropositive patients treated with satralizumab when compared to placebo-treated AQP4 seropositive patients [relative risk reduction (RR): 74%; hazard ratio (HR): 0.26; P=0.0014]. There was no evidence of benefit in AQP4 seronegative patients.
- SAkuraSky Trial:
    - Inclusion Criteria: Eligible patients included adults 18-74 years of age and adolescents 12-17 years of age with AQP4 seropositive or seronegative NMOSD. Each patient was required to have a documented history of ≥2 relapses in the 2 years prior to screening, with ≥1 in the previous 12 months, and an EDSS score of ≤6.5 at randomization. Patients must be receiving baseline IST at a stable dose for 8 weeks prior to baseline.
    - Primary Endpoint: The primary endpoint was the time to the first PDR. PDR was defined as new or worsening neurological symptoms attributable to NMOSD.
    - Results: The time to the first PDR was significantly longer in AQP4 seropositive patients treated with satralizumab plus IST when compared to AQP4 seropositive patients taking placebo plus IST (RR: 78%; HR: 0.22; P=0.0143). There was no evidence of benefit in AQP4 seronegative patients.

Uplizna™ (Inebilizumab-cdon) Product Summary[14]

Indication(s): Uplizna™ (inebilizumab-cdon) is a CD19-directed cytolytic antibody indicated for the treatment of NMOSD in adult patients who are AQP4 antibody positive.

Dosing:
- Uplizna™ is supplied as a carton containing (3) 100mg/10mL single-dose vials (SDVs) for intravenous (IV) infusion.
- The recommended initial dosing of Uplizna™ is 300mg via IV infusion, followed by a second 300mg dose 2 weeks later.
- Subsequent doses (starting 6 months from the first infusion) are 300mg via IV infusion every 6 months.

Mechanism of Action: The exact mechanism of how inebilizumab exerts its effects in NMOSD is not fully understood. It is presumed inebilizumab is

involved in the binding of CD19, a cell surface antigen present on pre-B and mature B lymphocytes leading to antibody-dependent cellular cytolysis.

Contraindication(s):

- Active HBV infection
- Active or untreated latent TB

Warnings and Precautions:

- Infusion Reactions: During the randomized clinical trial period, 9.3% of NMOSD patients had an infusion reaction that included headache, nausea, somnolence, dyspnea, fever, myalgia, or rash.
- Infections: An increased risk of infection has been observed with B-cell depleting therapies. The most common infections seen with inebilizumab during the randomized and open-label clinical trial periods include urinary tract infection (20%), nasopharyngitis (13%), upper respiratory tract infection (8%), and influenza (7%). Therapy with inebilizumab should be held in patients with an active infection.
    - Possible Increased Risk of Immunosuppressant Effects with Other Immunosuppressants: Inebilizumab has not been studied with other immunosuppressants. The potential for increased immunosuppressive effects may occur when combining inebilizumab with another immunosuppressive medication.
    - HBV Reactivation: Risk of HBV reactivation has been observed with other B-cell-depleting therapies. There have been no cases of HBV reactivation in patients treated with inebilizumab, but these patients were excluded from the inebilizumab clinical trials. All patients should have HBV screening performed before initiation of Uplizna™.
    - Progressive Multifocal Leukoencephalopathy (PML): PML is an opportunistic viral infection caused by the John Cunningham (JC) virus that typically occurs in immunocompromised patients. There were no confirmed cases of PML in the inebilizumab clinical trial, but 1 person died following the development of new brain lesions for which a definitive diagnosis could not be established. Uplizna™ should be withheld at the first sign or symptom suggestive of PML, and the appropriate diagnostic evaluation should be conducted. Typical symptoms associated with PML are diverse, progress over days to weeks, and include progressive weakness on 1 side of the body or clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes.
    - TB: Patients should be evaluated for TB risk factors and tested for latent TB infection prior to initiating inebilizumab. Anti-TB therapy should be considered prior to initiation of treatment with Uplizna™

in patients with a history of latent active TB for whom an adequate course of treatment cannot be confirmed and for patients with a negative test for latent TB but who have risk factors for a TB infection. Infectious disease experts should be consulted regarding whether initiating anti-TB therapy is appropriate before starting treatment.

- Vaccinations: The safety of immunization with live or live-attenuated vaccines following inebilizumab therapy has not been studied and is not recommended. Live or live-attenuated vaccinations should be completed at least 4 weeks prior to initiating inebilizumab.

- Reduction in Immunoglobulins: There may be a progressive and prolonged decline in the levels of total and individual immunoglobulins such as immunoglobulins G and M (IgG and IgM) with continued inebilizumab treatment. Monitoring the levels of quantitative serum immunoglobulins should be done during treatment and until B-cell repletion after therapy is discontinued.
- Fetal Risk: Inebilizumab has shown fetal harm in animal studies. Females of reproductive potential should use effective contraception while on therapy and for at least 6 months after the last dose.

Efficacy: The safety and efficacy of inebilizumab were assessed in the N-Momentum trial, a Phase 2/3, randomized (3:1), double-blind, placebo-controlled trial in 230 patients with NMOSD in which 213 patients were AQP4 seropositive and 17 were AQP4 seronegative. Of the 213 patients that were AQP4 seropositive, 161 were randomized to receive treatment with inebilizumab and 52 were randomized to receive placebo. Doses were administered via IV infusion on days 1 and 15 of a 28-week randomized controlled period (RCP). If the patient had an attack or completed the RCP without an attack, they had an option to enroll in the open-label extension. These patients were then randomized to receive inebilizumab on day 1 and placebo on day 15 or inebilizumab on both days 1 and 15. A single dose of 300mg inebilizumab was then administered via IV infusion every 26 weeks for at least 52 weeks. At the beginning of the trial, all patients received corticosteroids between days 1 and 14 (tapered to day 21) to minimize the risk of an attack immediately following the first dose of inebilizumab.

- Inclusion Criteria: Eligible patients were 18 years of age and older with AQP4 seropositive or seronegative NMOSD. Each patient was required to have a documented history of either ≥1 attack requiring rescue therapy in the prior year or ≥2 attacks requiring rescue therapy in the previous 2 years, and an EDSS score of ≤7.5 at randomization. Patients with an EDSS score of 8 were considered acceptable if they were deemed capable of participating.

- Primary Endpoint: The primary endpoint was the time (in days) from day 1 to the onset of an NMOSD attack, on or before day 197.
- Results: The time to the first NMOSD attack was significantly longer in patients treated with inebilizumab when compared to placebo in the AQP4 seropositive population (RR: 77%; HR: 0.227; P<0.0001). There was no evidence of benefit in patients who were AQP4 seronegative in this trial. During the RCP, 11% (18/161) of patients receiving inebilizumab had an attack compared with 42% (22/52) of patients receiving placebo.

Cost Comparison: NMOSD Therapies

Medication	Cost for First Year	Cost per Year for Maintenance
Enspryng™ (satralizumab-mwge)	$219,230.85	$190,000.07
Uplizna™ (inebilizumab-cdon)	$393,000.30	$262,000.20
Soliris® (eculizumab)	$704,473.20	$678,381.60

Cost of therapy calculated based on wholesale acquisition cost (WAC).
Costs do not reflect rebated prices or net costs.

Recommendations

The College of Pharmacy recommends the prior authorization of Enspryng™ (satralizumab-mwge) and Uplizna™ (inebilizumab-cdon) with the following criteria in red:

Enspryng™ (Satralizumab-mwge) Approval Criteria:

1. An FDA approved indication of neuromyelitis optica spectrum disorder (NMOSD) in adult members who are anti-aquaporin-4 (AQP4) antibody positive; and
2. Member must be 18 years of age or older; and
3. Member must have experienced at least 1 acute NMOSD attack in the prior 12 months; and
4. Member must have an Expanded Disability Severity Scale (EDSS) score ≤6.5; and
5. Prescriber must verify hepatitis B virus (HBV) and tuberculosis (TB) screening are negative before the first dose; and
6. Approvals will not be granted for members with active HBV infection or active or untreated latent TB; and
7. Prescriber must verify liver function tests have been assessed prior to initiation of treatment with Enspryng™ and levels are acceptable to prescriber; and
8. Prescriber must agree to monitor that there are no clinically significant active infections prior to every infusion (infusion should be delayed until infection resolves); and

9. Prescriber must agree to monitor neutrophil counts 4 to 8 weeks after initiation of therapy and thereafter as clinically appropriate; and
10. Prescriber must verify member has not received any vaccinations within 4 weeks prior to initiation of therapy; and
11. Member and/or caregiver must be trained by a health care professional on subcutaneous administration and storage of Enspryng™; and
12. A quantity limit of 1 syringe per 14 days will apply for the titration dose for a duration of 4 weeks, and a quantity limit of 1 syringe per 28 days will apply for the maintenance dose, according to the package labeling; and
13. Initial approvals will be for the duration of 6 months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment.

Uplizna™ (Inebilizumab-cdon) Approval Criteria:

1. An FDA approved indication of neuromyelitis optica spectrum disorder (NMOSD) in adult members who are anti-aquaporin-4 (AQP4) antibody positive; and
2. Member must be 18 years of age or older; and
3. Member must have experienced at least 1 acute NMOSD attack in the prior 12 months, or at least 2 attacks in the prior 24 months, requiring rescue therapy; and
4. Member must have an Expanded Disability Severity Scale (EDSS) score ≤8; and
5. Prescriber must verify hepatitis B virus (HBV) and tuberculosis (TB) screening are negative before the first dose; and
6. Approvals will not be granted for members with active HBV infection or active or untreated latent TB; and
7. Prescriber must agree to monitor that there are no clinically significant active infections prior to every infusion (infusion should be delayed until infection resolves); and
8. Prescriber must verify testing for quantitative serum immunoglobulins has been performed before the first dose and levels are acceptable to prescriber; and
9. Prescriber must agree to monitor the level of serum immunoglobulins during and after discontinuation of treatment with Uplizna™ until B-cell repletion; and
10. The infusion must be administered under the supervision of a health care professional with access to appropriate medical support to manage potential severe reactions, and the patient must be observed for at least 1 hour after the completion of each infusion; and
11. Female members of reproductive potential must not be pregnant and must have a negative pregnancy test prior to initiation of treatment; and

12. Female members of reproductive potential must use contraception while receiving Uplizna™ and for 6 months after the last infusion; and
13. Prescriber must verify member has not received any vaccinations within 4 weeks prior to initiation of therapy; and
14. A patient-specific, clinically significant reason why the member cannot use Enspryng™ must be provided; and
15. A quantity limit of 60mL per 14 days will apply for the titration dose, and a quantity limit of 30mL per 180 days will apply for the maintenance dose; and
16. Initial approvals will be for the duration of 6 months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment.

Additionally, the College of Pharmacy recommends the following changes shown in red to the current Soliris® (eculizumab) approval criteria for NMOSD:

Soliris® (Eculizumab) Approval Criteria [Neuromyelitis Optica Spectrum Disorder (NMOSD) Diagnosis]:

~~1. An FDA approved diagnosis of NMOSD; and~~
~~2. Member is anti-aquaporin-4 (AQP4) antibody positive; and~~
~~3. Member must be 18 years of age or older.~~
1. An FDA approved indication of NMOSD in adult members who are anti-aquaporin-4 (AQP4) antibody positive; and
2. Member must be 18 years of age or older; and
3. Member must have a history of at least 2 NMOSD attacks in last 12 months or 3 attacks in the last 24 months, with at least 1 attack in the past 12 months; and
4. Member must have an Expanded Disability Severity Scale (EDSS) score ≤7; and
5. A patient-specific, clinically significant reason why the member cannot use Enspryng™ or Uplizna™ must be provided; and
6. Initial approvals will be for the duration of 6 months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment.

Utilization Details of Soliris® (Eculizumab) and Ultomiris® (Ravulizumab-cwvz): Fiscal Year 2020

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	*TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
SOLIRIS INJ 10MG/ML	105	7	$2,349,605.95	$22,377.20	15.00
ULTOMIRIS INJ 300/30ML	2	1	$83,274.82	$41,637.41	2.00
TOTAL	**107**	**7**	**$2,432,880.77**	**$22,737.20**	**15.29**

INJ = Injection
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020

Medical Claims

PRODUCT UTILIZED	†TOTAL CLAIMS	*TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
SOLIRIS INJ 10MG/ML	17	5	$780,254.40	$45,897.32	3.4
TOTAL	**17**	**5**	**$780,254.40**	**$45,897.32**	**3.4**

INJ = Injection
†Total number of unduplicated claims
*Total number of unduplicated members
Costs do not reflect rebated prices or net costs.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020

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Appendix K

Fiscal Year 2020 Annual Review of Ulcerative Colitis (UC) and Crohn's Disease (CD) Medications and 30-Day Notice to Prior Authorize Ortikos™ [Budesonide Extended-Release (ER) Capsule]

Oklahoma Health Care Authority
December 2020

Current Prior Authorization Criteria

Apriso® (Mesalamine Extended-Release Capsules) Quantity Limit Approval Criteria:

1. A quantity limit of 120 capsules per 30 days will apply.

Asacol® HD (Mesalamine Delayed-Release Tablets) Approval Criteria:

1. An FDA approved indication for the treatment of moderately active ulcerative colitis (UC); and
2. A patient-specific, clinically significant reason the member cannot use other available mesalamine products that do not require prior authorization must be provided; and
3. Approvals will be for the duration of 6 weeks in accordance with manufacturer recommended duration of therapy; and
4. A quantity limit of 180 tablets per 30 days will apply.

Canasa® (Mesalamine Suppositories) Quantity Limit Approval Criteria:

1. A quantity limit of 30 suppositories per 30 days will apply.
2. The first 6 weeks of treatment do not require prior authorization.
3. After 6 weeks of treatment:
    a. Provider must document a patient-specific, clinically significant reason member needs longer duration of treatment.

Colazal® (Balsalazide Capsules) Quantity Limit Approval Criteria:

2. A quantity limit of 270 capsules per 30 days will apply.
3. The first 12 weeks of treatment do not require prior authorization.
4. After 12 weeks of treatment:
    a. Provider must document a patient-specific, clinically significant reason member needs a longer duration of treatment.
5. An age restriction of 5 years and older will apply.

Delzicol® (Mesalamine Delayed-Release Capsules) Quantity Limit Approval Criteria:

1. A quantity limit of 180 capsules per 30 days will apply.

Dipentum® (Olsalazine Capsules) Quantity Limit Approval Criteria:

1. A quantity limit of 120 capsules per 30 days will apply.

Giazo® (Balsalazide) Approval Criteria:

1. An FDA approved indication of mildly-to-moderately active ulcerative colitis (UC); and
2. Member must be 18 years of age or older; and
3. Member must be male (effectiveness of Giazo® was not demonstrated in female patients in clinical trials); and
4. A patient-specific, clinically significant reason why the member cannot use generic balsalazide 750mg capsules or other products available without prior authorization* must be provided; and
5. Approvals will be for the duration of 8 weeks. After 8 weeks of treatment the prescriber must document a patient-specific, clinically significant reason the member needs a longer duration of treatment.

Lialda® (Mesalamine Delayed-Release Capsules) Quantity Limit Approval Criteria:

1. A quantity limit of 60 capsules per 30 days will apply.
2. For quantity limit requests for >2 capsules per day:
    a. An FDA approved indication for the induction of remission in members with active, mild-to-moderate ulcerative colitis (UC); and
    b. A patient-specific, clinically significant reason the member cannot use other available mesalamine products that are indicated to induce remission that do not require prior authorization must be provided; and
    c. Approvals will be for the duration of 8 weeks in accordance with manufacturer recommended duration of therapy; and
    d. A maximum approval of 120 capsules per 30 days will apply.

Pentasa® (Mesalamine 250mg Controlled-Release Capsules) Quantity Limit Approval Criteria:

1. A quantity limit of 480 capsules per 30 days will apply.
2. The first 8 weeks of treatment do not require prior authorization.
3. After 8 weeks of treatment:
    a. Provider must document a patient-specific, clinically significant reason member needs longer duration of treatment.

Pentasa® (Mesalamine 500mg Controlled-Release Capsules) Approval Criteria:

1. An FDA approved indication for the induction of remission or for the treatment of patients with mildly-to-moderately active ulcerative colitis (UC); and
2. A patient-specific, clinically significant reason the member cannot use Pentasa® 250mg controlled-release capsules or other available

mesalamine products that do not require prior authorization must be provided; and
3. Approvals will be for the duration of 8 weeks in accordance with manufacturer recommended duration of therapy; and
4. A quantity limit of 240 capsules per 30 days will apply.

Rowasa® (Mesalamine Rectal Suspension Enema) Approval Criteria:

1. The first 3 weeks of treatment do not require prior authorization.
2. An FDA approved indication for the treatment of active, mild-to-moderate, distal ulcerative colitis (UC), proctosigmoiditis, or proctitis; and
3. A patient-specific, clinically significant reason the member cannot use Canasa® (mesalamine suppositories) which do not require prior authorization must be provided; and
4. Provider documentation that member is still having active symptoms after 3 weeks of treatment; and
5. Approvals will be for the duration of 6 weeks in accordance with manufacturer recommended duration of therapy; and
6. A quantity limit of 30 enemas (1,800mL) per 30 days will apply.

Uceris® (Budesonide Extended-Release Tablets) Approval Criteria:

2. An FDA approved indication of induction of remission in members with active, mild-to-moderate ulcerative colitis (UC); and
3. Previous failure of at least 2 of the following:
    a. Oral aminosalicylates; or
    b. Topical mesalamine; or
    c. Topical corticosteroids; or
    d. A contraindication to all preferred medications; and
4. A patient-specific, clinically significant reason why the member cannot use other oral corticosteroids available without prior authorization must be provided; and
5. Approvals will be for the duration of 8 weeks in accordance with manufacturer maximum recommended duration of therapy; and
6. A quantity limit of 30 tablets per 30 days will apply.

Uceris® (Budesonide Rectal Foam) Approval Criteria:

1. An FDA approved indication of induction of remission in members with active, mild-to-moderate, distal ulcerative colitis (UC) extending up to 40cm from the anal verge; and
2. A patient-specific, clinically significant reason why the member cannot use oral aminosalicylates, topical mesalamine, or other topical (rectally administered) corticosteroids available without prior authorization must be provided; and
3. Approvals will be for the duration of 6 weeks in accordance with manufacturer recommended duration of therapy; and

4. A quantity limit of 133.6 grams per 42 days will apply.

***The following medications do not require prior authorization:** sulfasalazine 500mg tablets, sulfasalazine delayed-release 500mg tablets, Rowasa® (mesalamine) rectal suspension enemas, Lialda® (mesalamine) delayed-release capsules, Colazal® (balsalazide) capsules, Dipentum® (olsalazine) capsules, Pentasa® (mesalamine) 250mg controlled-release capsules, Canasa® (mesalamine) suppositories, Apriso® (mesalamine) extended-release capsules, Delzicol® (mesalamine) delayed-release capsules, and hydrocortisone enemas.

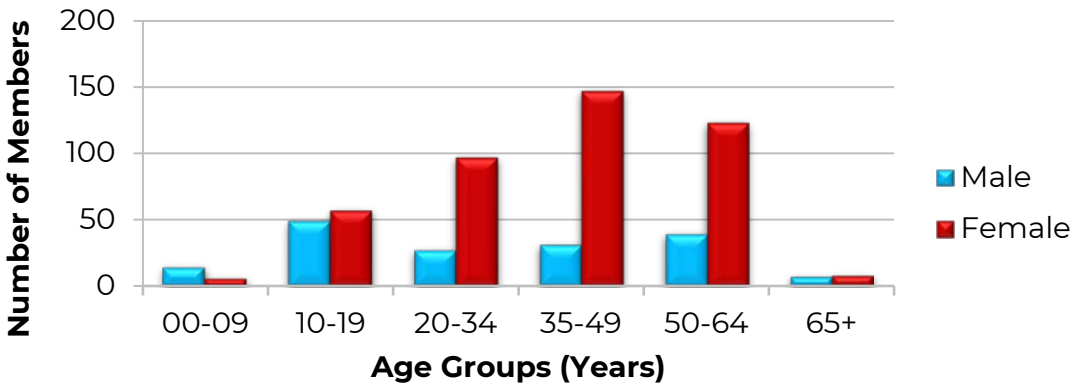
Utilization of UC and CD Medications: Fiscal Year 2020

Comparison of Fiscal Years

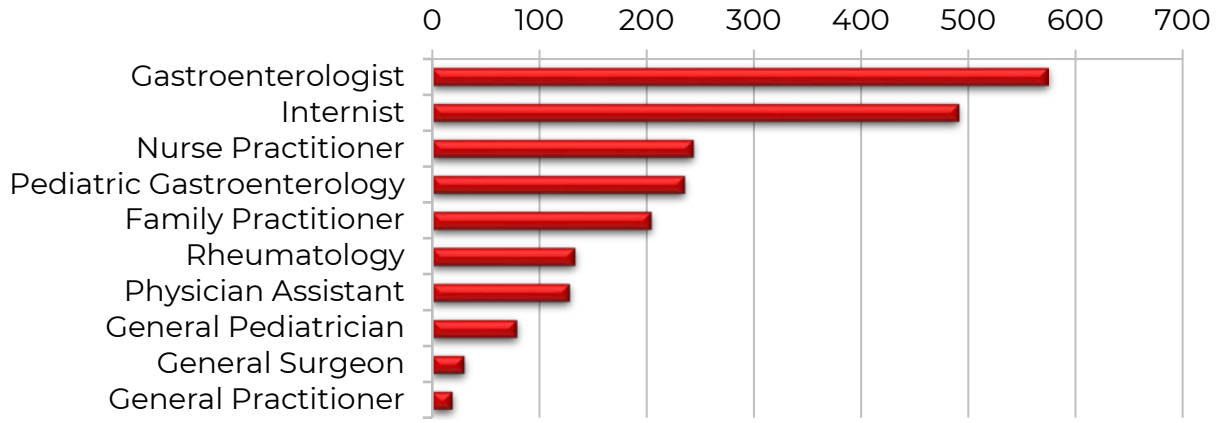
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	530	1,923	$441,169.38	$229.42	$7.66	236,547	57,613
2020	605	2,215	$412,227.51	$186.11	$6.19	263,640	66,552
% Change	**14.20%**	**15.20%**	**-6.60%**	**-18.90%**	**-19.20%**	**11.50%**	**15.50%**
Change	**75**	**292**	**-$28,941.87**	**-$43.31**	**-$1.47**	**27,093**	**8,939**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2019 = 07/01/2018 to 06/30/2019; Fiscal Year 2020 = 07/01/2019 to 06/30/2020

Demographics of Members Utilizing UC and CD Medications



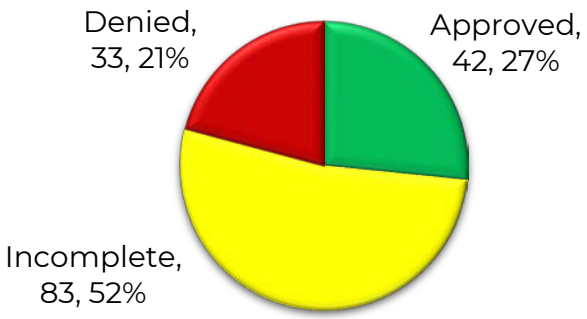
Top Prescriber Specialties of UC and CD Medications by Number of Claims



Prior Authorization of UC and CD Medications

There were 158 prior authorization requests submitted for UC and CD medications during fiscal year 2020. The following chart shows the status of the submitted petitions for fiscal year 2020.

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]

Anticipated Patent Expiration(s):

- Asacol® HD [mesalamine delayed-release (DR) tablets]: November 2021
- Colazal® (balsalazide capsules): February 2027
- Canasa® (mesalamine suppositories): June 2028
- Apriso® [mesalamine extended-release (ER) tablets]: May 2030
- Giazo® (balsalazide tablets): June 2031; discontinued
- Uceris® (budesonide ER tablets): September 2031
- Ortikos™ (budesonide ER capsules): September 2036

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

- **June 2019:** Ortikos™ (budesonide ER capsule) was FDA approved in June 2019 for the treatment of mild-to-moderate active CD involving

the ileum and/or the ascending colon in patients 8 years of age and older and for maintenance of clinical remission of mild-to-moderate CD involving the ileum and/or the ascending colon for up to 3 months in adults. In July 2020, Ferring Pharmaceuticals announced the launch of Ortikos™ in the United States. Ortikos™ contains a controlled ileal-release anti-inflammatory corticosteroid and is available as 6mg and 9mg ER capsules for convenient single-pill, once-daily dosing.

Guideline Update(s):

- **April 2020:** The American Gastroenterological Association (AGA) published updated guidelines for the management of moderate-to-severe UC. Although the majority of patients with UC have mild-to-moderate disease, about 15% of patients with UC experience an aggressive course and about 20% of those patients require hospitalization for severe disease.
  - Moderate-to-severe UC is defined by the AGA as:
    - Dependence on or refractory to corticosteroids; or
    - Severe endoscopic disease activity (ulcers); or
    - High risk of colectomy; or
    - Mayo Clinic score of 6-12 with an endoscopic subscore of 2-3.
  - Key recommendations from the AGA 2020 guidelines include:
    - Infliximab, adalimumab, golimumab, vedolizumab, tofacitinib, and ustekinumab are all recommended for induction and maintenance of moderate-to-severe UC over no treatment.
    - Infliximab and vedolizumab are preferred for induction over adalimumab for patients who are naïve to biologic agents.
    - Early use of biologic agents with or without immunomodulator therapy is suggested for moderate-to-severe UC rather than gradual step-up after failure of aminosalicylate (5-ASA) agents.
    - 5-ASA agents are not recommended to be continued in patients who have achieved remission with the use of biologics or immunomodulators.

News:

- **November 2019:** Mylan launched the first generic formulation of Apriso® (mesalamine 375mg ER capsule). Apriso® is FDA approved for the maintenance of remission in UC patients 18 years of age and older.
- **Giazo® Product Discontinuation:** Giazo® (balsalazide 1.1g tablet) has been discontinued by the manufacturer. Giazo® was indicated for the treatment of mildly-to-moderately active UC in male patients 18 years of age and older. There are currently no generic formulations of Giazo®,

but balsalazide continues to be available as Colazal® 750mg capsules, and generic capsule formulations are available.

Pipeline:

- **Brazikumab:** AstraZeneca is currently conducting Phase 2 clinical studies evaluating the use of brazikumab for the treatment of UC and Phase 3 clinical studies for the treatment of CD. Brazikumab is a monoclonal antibody (MAB) that binds to the interleukin-23 (IL-23) receptor and blocks IL-23 signaling, which is thought to prevent intestinal inflammation. Previous Phase 2 studies showed a benefit of brazikumab at week 8 in tumor necrosis factor (TNF)-resistant patients with CD. The Phase 2b/3 INTREPID study is ongoing and will evaluate brazikumab compared with placebo or adalimumab for the treatment of CD. The Phase 2 EXPEDITION study is ongoing and will evaluate brazikumab compared with placebo or vedolizumab for the treatment of UC.
- **Deucravacitinib:** Bristol Myers Squibb is currently conducting Phase 2 studies of deucravacitinib for the treatment of UC and CD. Deucravacitinib is a novel, oral, selective tyrosine kinase 2 (TYK2) inhibitor which mediates multiple cytokines involved in inflammatory and immune processes. In addition to UC and CD, deucravacitinib is being evaluated for the treatment of several other diseases, including psoriasis, psoriatic arthritis, and lupus.
- **Etrasimod:** Arena Pharmaceuticals is currently conducting Phase 3 studies of etrasimod for the treatment of UC and Phase 2 studies for the treatment of CD. Etrasimod is an oral, once-daily, selective sphingosine 1-phosphate (S1P) receptor modulator. In September 2020, Arena announced the first patient had been dosed in the Phase 3 ELEVATE UC 12 study, a double-blind, placebo-controlled study that will assess the efficacy and safety of etrasimod 2mg once daily compared with placebo for the treatment of moderately-to-severely active UC. Etrasimod is also being evaluated for the treatment of atopic dermatitis and alopecia areata.
- **Etrolizumab:** Genentech is conducting Phase 3 studies of etrolizumab for the treatment of both UC and CD. Etrolizumab is a humanized IgG1 MAB which targets the β7 integrin subunit by binding to 2 integrins (α4β7 and αEβ7) which play an important role in lymphocyte trafficking and retention in inflammatory bowel diseases. Etrolizumab is given as a subcutaneous (sub-Q) injection once monthly. In August 2020, Genentech announced results from the Phase 3 clinical studies in patients with moderately-to-severely active UC, showing mixed efficacy results in these patients, with some of the studies failing to meet primary efficacy endpoints. Genentech plans to continue to analyze the

data from these studies and from ongoing Phase 3 studies in patients with CD.

- **Filgotinib:** Gilead is currently conducting Phase 3 studies of filgotinib for the treatment of both UC and CD. Filgotinib is an oral selective Janus kinase 1 (JAK1) inhibitor. In May 2020, Gilead announced positive topline results from the Phase 2b/3 SELECTION study in patients with moderately-to-severely active UC. The study assessed filgotinib for induction and maintenance of remission and included both biologic-naïve and biologic-experienced patients. Filgotinib is also being evaluated for the treatment of rheumatoid arthritis (RA), psoriatic arthritis, ankylosing spondylitis, and uveitis.
- **Guselkumab:** Janssen is currently conducting Phase 2b/3 studies of guselkumab for the treatment of CD. Guselkumab is a fully human MAB which binds IL-23, inhibiting its interaction with the IL-23 receptor. In October 2020, Janssen announced positive interim results from the Phase 2 GALAXI 1 study in adult patients with moderately-to-severely active CD. The interim results included data from the first 250 patients enrolled, approximately 50% of whom had previously failed another biologic. At week 12, a significantly greater reduction in the Crohn's Disease Activity Index (CDAI) was seen for patients receiving guselkumab at all doses (200mg, 600mg, or 1,200mg) compared with placebo. Guselkumab was previously FDA approved for the treatment of plaque psoriasis and psoriatic arthritis and is marketed under the brand name Tremfya®.
- **Mirikizumab:** Lilly is conducting Phase 2 studies of mirikizumab for the treatment of UC and CD. Mirikizumab is a humanized IgG4 MAB that binds to the P19 subunit of IL-23. In October 2020, Lilly announced 52-week efficacy and safety data from the Phase 2 SERENITY study in patients with moderately-to-severely active CD. The study included a 12-week induction period and 40-week continuation period, with patients randomized to 1 of 3 doses of mirikizumab (200mg, 600mg, or 1,000mg) given either intravenously (IV) or sub-Q. At week 52, 69.6% and 66.7% of patients receiving mirikizumab IV or sub-Q, respectively, continued to have an endoscopic response, defined as a ≥50% reduction from baseline in Simple Endoscopic Score for Crohn's Disease (SES-CD). Lilly is also evaluating mirikizumab for the treatment of psoriasis.
- **Ozanimod:** Bristol Myers Squibb is currently conducting Phase 3 studies of ozanimod for the treatment of UC and CD. Ozanimod is an oral, S1P receptor modulator that binds with high affinity to S1P receptors 1 and 5. Ozanimod is believed to work by reducing the migration of lymphocytes into inflamed intestinal mucosa. In May 2020, Bristol Myers Squibb announced positive results from the Phase 3 True North study evaluating ozanimod for induction and maintenance

therapy in adult patients with moderate-to-severe UC. Both primary endpoints for induction of clinical remission (at week 10) and maintenance of remission (at week 52) were met. Ozanimod was previously FDA approved for the treatment of adults with relapsing remitting multiple sclerosis (RRMS) and is marketed under the brand name Zeposia®.

- **Risankizumab:** AbbVie is currently conducting Phase 3 studies of risankizumab for the treatment of UC and CD. Risankizumab is an anti-IL-23 MAB which was previously FDA approved for the treatment of plaque psoriasis and marketed under the brand name Skyrizi®. Risankizumab is also being evaluated for the treatment of psoriatic arthritis (Phase 3) and atopic dermatitis (Phase 2).
- **Upadacitinib:** AbbVie is currently conducting Phase 3 studies of upadacitinib for the treatment of UC and CD. Upadacitinib is an oral, selective JAK1 inhibitor which was previously FDA approved for the treatment of moderate-to-severe RA and marketed under the brand name Rinvoq®. Upadacitinib is also being evaluated for the treatment of other conditions such as ankylosing spondylitis, atopic dermatitis, and giant cell arteritis.

Ortikos™ (Budesonide ER Capsule) Product Summary[22,23]

Indication(s): Ortikos™ (budesonide ER capsule) is an anti-inflammatory corticosteroid indicated for:

- Treatment of mild-to-moderate active CD involving the ileum and/or the ascending colon, in patients 8 years of age and older
- Maintenance of clinical remission of mild-to-moderate CD involving the ileum and/or the ascending colon for up to 3 months in adults

How Supplied: 6mg and 9mg ER capsules

Dosing:

- Mild-to-moderate active CD:
  - Adults: 9mg once daily for up to 8 weeks; repeat 8 week treatment courses for recurring episodes of active disease
  - Pediatric patients 8 to 17 years of age weighing >25kg: 9mg once daily for up to 8 weeks, followed by 6mg once daily for up to 2 weeks
- Maintenance of clinical remission of mild-to-moderate CD:
  - Adults: 6mg once daily for up to 3 months; taper to cessation after 3 months
  - Continued treatment for >3 months has not been shown to provide substantial clinical benefit

Contraindication(s):

- Hypersensitivity to budesonide or any of the ingredients in Ortikos™

Adverse Reactions: The most common adverse reactions (reported in ≥5% of patients treated with another oral budesonide product) include headache, respiratory infection, nausea, back pain, dyspepsia, dizziness, abdominal pain, flatulence, vomiting, fatigue, and pain.

Efficacy: The determination of efficacy and safety of Ortikos™ was based primarily on previous clinical studies of another oral budesonide product, Entocort® EC (budesonide DR capsule), which was first FDA approved in 2001. Prior to FDA approval of Ortikos™, a bioequivalence study was conducted to demonstrate bioequivalence of Ortikos™ 9mg to (3) Entocort® EC 3mg capsules. The study evaluated pharmacokinetic parameters in 48 healthy adult patients and showed systemic exposure was comparable between Ortikos™ 9mg capsule and (3) Entocort® EC 3mg capsules, meeting the FDA's bioequivalence criteria.

Cost Comparison:

Product	Cost Per Capsule	Cost Per 30 Days*
Ortikos™ (budesonide ER) 6mg capsule	**$40.00**	**$1,200.00**
Ortikos™ (budesonide ER) 9mg capsule	**$40.00**	**$1,200.00**
budesonide DR 3mg capsule	$0.96	$161.94

DR = delayed-release; ER = extended-release
Costs do not reflect rebated prices or net costs.
Costs based on Wholesale Acquisition Costs (WAC) for Ortikos™ and State Maximum Allowable Cost (SMAC) for budesonide DR.
*Cost per 30 days based on 1 capsule daily for Ortikos™ and 3 capsules daily for budesonide DR.

Recommendations

The College of Pharmacy recommends the prior authorization of Ortikos™ (budesonide ER capsule) with the following criteria:

Ortikos™ [Budesonide Extended-Release (ER) Capsule] Approval Criteria:

1. An FDA approved indication of 1 of the following:
    a. For the treatment of mild-to-moderate active Crohn's disease (CD) involving the ileum and/or the ascending colon, in members 8 years of age or older; or
    b. For the maintenance of clinical remission of mild-to-moderate Crohn's disease (CD) involving the ileum and/or the ascending colon for up to 3 months duration in adult members; and
2. Member must have previous failure of Entocort® EC (budesonide controlled ileal-release enteric coated capsules) within the last 3

months at recommended dosing and a reason for trial failure with Entocort® EC must be provided; or

3. A patient-specific, clinically significant reason (beyond convenience) why the member cannot use other oral corticosteroids, including Entocort® EC, that are available without prior authorization must be provided; and
4. Dosing regimen and duration of therapy must be in accordance with the Ortikos™ *Prescribing Information*; and
5. Approval length will be based on the manufacturer maximum recommended duration of therapy; and
6. A quantity limit of 30 capsules per 30 days will apply.

Utilization Details of UC and CD Medications: Fiscal Year 2020

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
SULFASALAZINE PRODUCTS						
SULFASALAZINE TAB 500MG	563	168	$14,566.45	$25.87	3.35	3.53%
SULFASALAZINE TAB 500MG DR	505	196	$15,850.64	$31.39	2.58	3.85%
AZULFIDINE TAB 500MG EN	1	1	$244.03	$244.03	1	0.06%
SUBTOTAL	**1,069**	**365**	**$30,661.12**	**$28.68**	**2.93**	**7.44%**
MESALAMINE PRODUCTS						
MESALAMINE TAB 1.2GM	371	90	$117,579.53	$316.93	4.12	28.52%
PENTASA CAP 250MG CR	105	27	$61,268.10	$583.51	3.89	14.86%
APRISO CAP 0.375GM	88	27	$40,395.42	$459.04	3.26	9.80%
MESALAMINE CAP 0.375GM	74	27	$25,849.22	$349.31	2.74	6.27%
MESALAMINE SUP 1000MG	66	39	$19,473.37	$295.05	1.69	4.72%
MESALAMINE CAP 400MG DR	49	10	$14,959.24	$305.29	4.9	3.63%
MESALAMINE TAB 800MG DR	43	20	$27,726.93	$644.81	2.15	6.73%
PENTASA CAP 500MG CR	29	17	$25,471.27	$878.32	1.71	6.18%
MESALAMINE ENE 4GM	16	11	$3,874.83	$242.18	1.45	0.94%
DELZICOL CAP 400MG	12	4	$5,362.56	$446.88	3	1.30%
LIALDA TAB 1.2GM	7	2	$7,061.93	$1,008.85	3.5	1.71%
CANASA SUP 1000MG	1	1	$1,126.21	$1,126.21	1	0.27%
SUBTOTAL	**861**	**275**	**$350,148.61**	**$406.68**	**3.13**	**84.94%**
BUDESONIDE PRODUCTS						
BUDESONIDE CAP 3MG DR	232	72	$24,316.52	$104.81	3.22	5.90%
BUDESONIDE CAP 3MG	10	5	$819.44	$81.94	2	0.20%
BUDESONIDE TAB ER 9MG	3	2	$3,423.87	$1,141.29	1.5	0.83%
SUBTOTAL	**245**	**79**	**$28,559.83**	**$116.57**	**3.10**	**6.93%**
BALSALAZIDE PRODUCTS						
BALSALAZIDE CAP 750MG	34	6	$2,195.03	$64.56	5.67	0.53%
SUBTOTAL	**34**	**6**	**$2,195.03**	**$64.56**	**5.67**	**0.53%**
HYDROCORTISONE PRODUCTS						
HYDROCORTISONE ENE 100MG	6	5	$662.92	$110.49	1.2	0.16%
SUBTOTAL	**6**	**5**	**$662.92**	**$110.49**	**1.2**	**0.16%**
TOTAL	**2,215**	**605***	**$412,227.51**	**$186.11**	**3.66**	**100.00%**

CAP = capsule; CR = controlled-release; DR = delayed release; EN = enteric; ENE = enema; ER = extended-release; SUP = suppository; TAB = tablet
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020

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Appendix L

Fiscal Year 2020 Annual Review of Constipation and Diarrhea Medications and 30-Day Notice to Prior Authorize Pizensy™ (Lactitol)

Oklahoma Health Care Authority
December 2020

Current Prior Authorization Criteria: Constipation Medications

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 3 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. 1 of the 3 trials must be polyethylene glycol 3350 (PEG-3350); and
    b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
5. Approvals will initially be for 12 weeks of therapy. Further approval may be granted if the prescriber documents member is responding well to treatment; and
6. A quantity limit of 60 capsules per 30 days 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 members 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 3 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. 1 of the 3 trials must be polyethylene glycol 3350 (PEG-3350); and
    b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
5. Approvals will initially be for 12 weeks of therapy. Further approval may be granted if the prescriber documents member is responding well to treatment; and
6. Amitiza® must be discontinued if treatment with the opioid pain medication is also discontinued; and
7. A quantity limit of 60 capsules per 30 days will apply.

Ibsrela® (Tenapanor) Approval Criteria:

1. An FDA approved diagnosis of 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 3 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. 1 of the 3 trials must be polyethylene glycol 3350 (PEG-3350); and
    b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
5. A patient-specific, clinically significant reason why the member cannot use Amitiza® (lubiprostone), Linzess® (linaclotide), or Trulance® (plecanatide) must be provided; and
6. Approvals will initially be for 12 weeks of therapy. Further approval may be granted if the prescriber documents the member is responding well to treatment; and
7. A quantity limit of 60 tablets per 30 days 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 3 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. 1 of the 3 trials must be polyethylene glycol 3350 (PEG-3350); and
    b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
5. Approvals will initially be for 12 weeks of therapy. Further approval may be granted if the prescriber documents the member is responding well to treatment; and
6. A quantity limit of 30 capsules per 30 days will apply.

Motegrity® (Prucalopride) 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 3 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. 1 of the 3 trials must be polyethylene glycol 3350 (PEG-3350); and
    b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
5. A patient-specific, clinically significant reason why the member cannot use Amitiza® (lubiprostone), Linzess® (linaclotide), or Trulance® (plecanatide) must be provided; and
6. Approvals will initially be for 12 weeks of therapy. Further approval may be granted if the prescriber documents the member is responding well to treatment; and
7. A quantity limit of 30 tablets per 30 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 members 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 3 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. 1 of the 3 trials must be polyethylene glycol 3350 (PEG-3350); and
    b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
6. Approvals 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 per 30 days 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 the 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 3 different 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. 1 of the 3 trials must be polyethylene glycol 3350 (PEG-3350); and
    b. Members with an oncology-related diagnosis are exempt from trial requirements; and
6. Member must not have known or suspected gastrointestinal obstruction; and
7. A patient-specific, clinically significant reason why the member cannot use Amitiza® (lubiprostone), Movantik® (naloxegol), or Symproic® (naldemedine) must be provided; and

8. A patient-specific, clinically significant reason why the 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; and
10. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment; and
11. Relistor® must be discontinued if treatment with the opioid pain medication is also discontinued; and
12. A quantity limit of 30 units per month will apply.

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

1. An FDA approved diagnosis of OIC in members with severe terminal disease who are receiving only palliative care (life expectancy <6 months); and
2. Member must have current use of opioid medications; and
3. Documented treatment attempts with a minimum of 3 alternative products, excluding bulk forming laxatives; and
    a. 1 of the 3 trials must be polyethylene glycol 3350 (PEG-3350); and
    b. Members with an oncology-related diagnosis are exempt from trial requirements; and
4. Mechanical gastrointestinal obstruction has been ruled out; 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 62 kg; and/or
    b. Caregiver unable to draw up dose from vial; and
6. A quantity limit of 30 units per month will apply; and
7. Approvals will be for the duration of 16 weeks of therapy. Use of Relistor® beyond 4 months has not been studied in patients with severe terminal disease.

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 members 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 the 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 3 different types of products that have 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. 1 of the 3 trials must be polyethylene glycol 3350 (PEG-3350); and
    b. Members with an oncology-related diagnosis are exempt from trial requirements; and
6. A patient-specific, clinically significant reason why the 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; and
8. Relistor® must be discontinued if treatment with the opioid pain medication is also discontinued; and
9. A quantity limit of 90 tablets per 30 days 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 paid who are currently on chronic opioid therapy, including members 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 3 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. 1 of the 3 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; and

8. Symproic® must be discontinued if treatment with the opioid pain medication is also discontinued; and
9. A quantity limit of 30 tablets per 30 days will apply.

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 3 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. 1 of the 3 trials must be polyethylene glycol 3350 (PEG-3350); and
    b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
5. Approvals will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment; and
6. A quantity limit of 30 tablets per 30 days will apply.

Zelnorm™ (Tegaserod) Approval Criteria:

1. An FDA approved diagnosis of irritable bowel syndrome with constipation (IBS-C) in female members 18 to 64 years of age; and
2. Member must be female for authorization of Zelnorm™ (the safety and efficacy of Zelnorm™ in men with IBS-C have not been established); and
3. Member must not have any of the contraindications for use of Zelnorm™ [i.e., history of myocardial infarction (MI), stroke, transient ischemic attack (TIA), or angina; history of ischemic colitis or other forms of intestinal ischemia; severe renal impairment (estimated glomerular filtration rate {eGFR} <15mL/min/1.73m^2) or end-stage renal disease (ESRD); moderate or severe hepatic impairment (Child-Pugh B or C); history of bowel obstruction, symptomatic gallbladder disease, suspected sphincter or Oddi dysfunction, or abdominal adhesions; hypersensitivity to tegaserod)]; and
4. Documentation that constipation-causing therapies for other disease states have been discontinued (excluding opioid pain medications for cancer patients); and

5. Documented and updated colon screening for members older than 50 years of age; and
6. Documentation of hydration attempts and trials of at least 3 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. 1 of the 3 trials must be for polyethylene glycol 3350 (PEG-3350); and
    b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
7. A patient-specific, clinically significant reason why the member cannot use Amitiza® (lubiprostone), Linzess® (linaclotide), or Trulance® (plecanatide) must be provided; and
8. Approval will initially be for 6 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment. Zelnorm™ should be discontinued in patients who have not had adequate control of symptoms after 4 to 6 weeks of treatment; and
9. A quantity limit of 60 tablets per 30 days will apply.

Current Prior Authorization Criteria: Diarrhea Medications

Aemcolo® (Rifamycin) Approval Criteria:

1. An FDA approved diagnosis of traveler's diarrhea; and
2. Member must be 18 years of age or older; and
3. Traveler's diarrhea must be due to non-invasive strains of *Escherichia coli*; and
4. A patient-specific, clinically significant reason why the member cannot use Xifaxan® (rifaximin) oral tablets must be provided; and
5. A quantity limit of 12 tablets per 3 days 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;
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.

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® (i.e., 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 2 of the following 3 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
5. Approval will initially be for 12 weeks of therapy. Further approval may be granted if the prescriber documents the member is responding well to treatment; and
6. A quantity limit of 60 tablets per 30 days 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 3 months and be inadequately controlled (4 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; and
6. A quantity limit of 90 tablets per 30 days will apply.

Xifaxan® (Rifaximin) 200mg Approval Criteria:

1. An FDA approved diagnosis of traveler's diarrhea; and
2. Member must be 12 years of age or older; and
3. Traveler's diarrhea must be due to noninvasive strains of *Escherichia coli*; and
4. A quantity limit of 9 tablets per 3 days will apply.

Xifaxan® (Rifaximin) 550mg Approval Criteria:

1. An FDA approved indication for the reduction in risk of overt hepatic encephalopathy (HE) recurrence; 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 2 of the following 3 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 if IBS-D: Member must be 18 years of age or older; and
3. A quantity limit of 60 tablets per 30 days will apply. Patients with the diagnosis of IBS-D needing 42 tablets for a 14-day treatment regimen (550mg 3 times daily for 14 days) will be approved for a quantity limit override upon meeting Xifaxan® approval criteria. Patients with IBS-D who experience a recurrence of symptoms can be retreated up to 2 times with the same 14-day treatment regimen (550mg 3 times daily for 14 days).

Utilization of Constipation and Diarrhea Medications: Fiscal Year 2020

Comparison of Fiscal Years: Constipation Medications

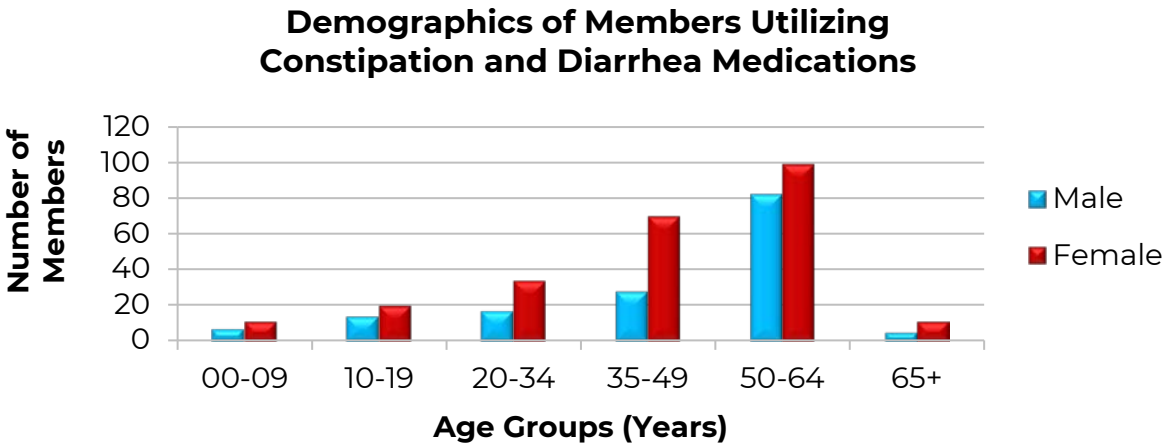
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	182	846	$316,294.95	$373.87	$12.62	13,548	25,064
2020	205	998	$395,461.58	$396.25	$13.38	38,294	29,552
% Change	**12.60%**	**18.00%**	**25.00%**	**6.00%**	**6.00%**	**21.40%**	**17.90%**
Change	**23**	**152**	**$79,166.63**	**$22.38**	**$0.76**	**6,746**	**4,488**

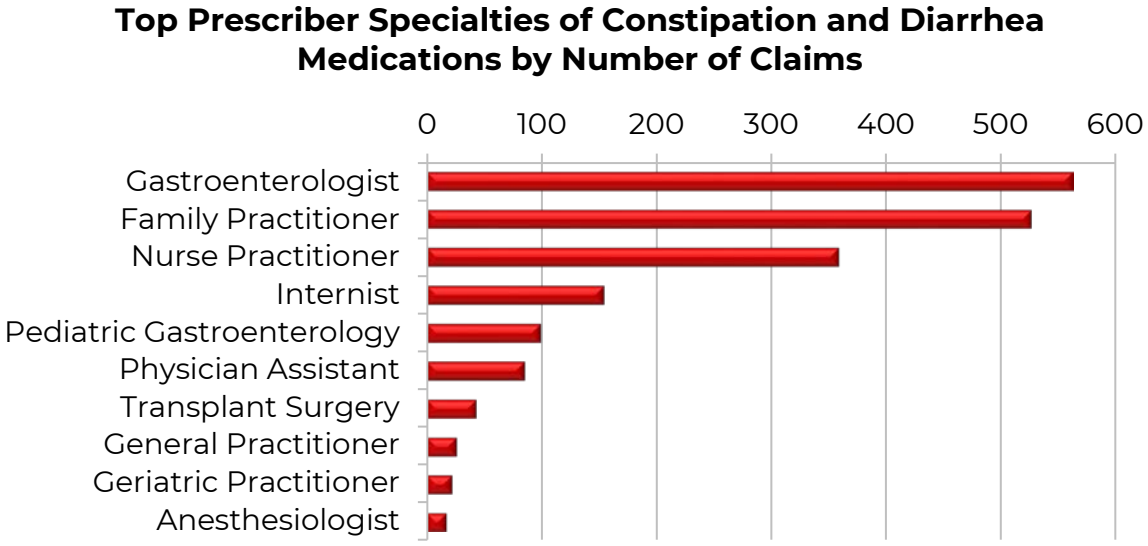
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2019 = 07/01/2018 to 06/30/2019; Fiscal Year 2020 = 07/01/2019 to 06/30/2020

Comparison of Fiscal Years: Diarrhea Medications

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	230	1,056	$2,087,378.29	$1,976.68	$70.35	59,249	29,671
2020	194	969	$2,105,369.64	$2,172.72	$76.78	54,566	27,422
% Change	**-15.70%**	**-8.20%**	**0.90%**	**9.90%**	**9.10%**	**-7.90%**	**-7.60%**
Change	**-36**	**-87**	**$17,991.35**	**$196.04**	**$6.43**	**-4,683**	**-2,249**

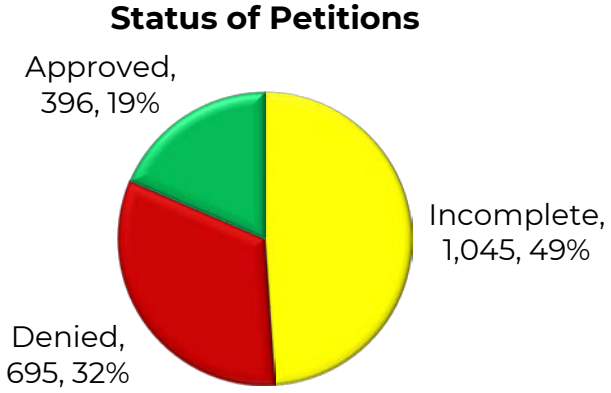
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs. The above table includes Xifaxan®, which was first FDA approved in 2004 and has a significant federal rebate. Please note, the majority of utilization of rifaximin was for the 550mg strength for the reduction in risk of overt hepatic encephalopathy (HE) recurrence.
Fiscal Year 2019 = 07/01/2018 to 06/30/2019; Fiscal Year 2020 = 07/01/2019 to 06/30/2020





Prior Authorization of Constipation and Diarrhea Medications

There were 2,136 prior authorization requests submitted for constipation and diarrhea medications during fiscal year 2020. The following chart shows the status of the submitted petitions for fiscal year 2020.



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

Anticipated Patent Expiration(s):

- Aemcolo® (rifamycin): May 2025
- Amitiza® (lubiprostone): October 2027
- Xifaxan® (rifaximin): October 2029
- Relistor® (methylnaltrexone injection): December 2030
- Xermelo® (telotristat): February 2031
- Relistor® (methylnaltrexone tablet): March 2031
- Symproic® (naldemedine): November 2031
- Movantik® (naloxegol): April 2032
- Viberzi® (eluxadoline): March 2033
- Linzess® (linaclotide): August 2033

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

- **January 2020:** The FDA approved a New Drug Application (NDA) for the macrolide antibacterial Dificid® (fidaxomicin) for oral suspension, and a supplemental NDA (sNDA) for fidaxomicin tablets for the treatment of *Clostridioides difficile*-associated diarrhea (CDAD) in children 6 months of age and older. The fidaxomicin pediatric trial was the first randomized controlled trial of CDAD treatment in children. The approval for the new formulation and new indication was based on the Phase 3 SUNSHINE trial, which demonstrated the safety and efficacy of fidaxomicin in pediatric patients 6 months to younger than 18 years of age. The trial included 148 patients with a confirmed *C. difficile* infection, of whom 142 received either fidaxomicin (suspension or tablets, twice daily) or vancomycin (suspension or tablets, 4 times daily). The clinical response against CDAD through 2 days after 10 days of treatment was similar between the fidaxomicin and vancomycin groups (77.6% vs. 70.5%, respectively).
- **February 2020:** The FDA approved Pizensy™ (lactitol) oral solution for the once-daily treatment of chronic idiopathic constipation (CIC) in adults. Pizensy™ is a simple monosaccharide sugar alcohol that exerts an osmotic effect, causing the influx of water into the small intestine leading to laxative effects. Pizensy™ is the only FDA approved product which the patient can self-titrate based on their own results for stool consistency.

Pipeline:

- **RHB-102 (Bekinda®):** RHB-102 is an oral, extended-release, once-daily tablet formulation of the antiemetic ondansetron. The drug molecule is in development for gastroenteritis and gastritis, as well as irritable bowel syndrome with diarrhea (IBS-D). RedHill announced positive results from a randomized, double-blind, placebo-controlled Phase 2

trial in the United States. The trial evaluated the efficacy and safety of RHB-102 12mg in patients with IBS-D, and the primary efficacy endpoint was stool consistency response. The trial found that when RHB-102 was given daily for 8 weeks there was an increase in stool consistency when compared to placebo (56.0% vs. 35.5%, respectively; P=0.036). In addition, there was a trend towards improvement of pain and the composite endpoint (meeting the stool consistency and pain response definitions for a given week for ≥50% of planned treatment weeks).

Pizensy™ (Lactitol) Product Summary[5,6,7]

Indication(s): Pizensy™ (lactitol) is an osmotic laxative indicated for the treatment of CIC in adults.

Dosing:

- The recommended adult dosage is 20 grams orally once daily, preferably with meals. The dose should be reduced to 10 grams once daily for persistent loose stools.
- Other oral medications should be administered at least 2 hours before or 2 hours after Pizensy™.
- The multi-dose bottles, 280 and 560 grams, are equipped with a measuring cap marked to contain 10 grams of powder. The unit-dose packets contain 10 grams of Pizensy™ each and are supplied in cartons of 28 unit-dose packets.
- The powder should be added to 4 to 8 ounces of water, juice, or other common beverage (e.g., coffee, tea, soda) and stirred to dissolve prior to administration.

Mechanism of Action: Lactitol exerts an osmotic effect, causing the influx of water into the small intestine leading to a laxative effect in the colon.

Contraindication(s):

- Known or suspected mechanical gastrointestinal obstruction
- Galactosemia

Adverse Reactions: In the clinical trials, the most common adverse reactions (incidence ≥3%) following administration of Pizensy™ were upper respiratory tract infection, flatulence, diarrhea, increased blood creatinine phosphokinase, abdominal distension, and increased blood pressure (BP).

Efficacy: The efficacy of Pizensy™ was established in 2 trials, a placebo-controlled trial (Study 1) and a 3-month active-controlled trial (Study 2).

- Study 1 was a double-blind, randomized, placebo-controlled, multicenter clinical trial in adult patients with symptoms of CIC. Pizensy™ 20 grams once daily was compared to placebo in a 6-month treatment period. Patients were allowed to dose reduce to 10 grams

daily if persistent diarrhea and loose stools developed. To be eligible for the trial, patients were required to meet the modified Rome II criteria for at least 12 weeks in the preceding 12 months. Rome II criteria requires patients to have <3 defecations per week, rarely having a loose stool without the use of laxatives, and not meeting criteria for irritable bowel syndrome with constipation (IBS-C). In addition, patients were required to report at least 1 of the following symptoms: straining during at least 25% of defecations, lumpy or hard stool in at least 25% of defecations, or sensation of incomplete evacuations for at least 25% of defecations. The primary efficacy endpoint of Pizensy™ was assessed using a responder analysis and was a change-from-baseline in complete spontaneous bowel movements (CSBMs). The primary efficacy endpoint was based on the first 12 weeks of the 6-month treatment period for 594 patients. A responder was defined as a patient who had at least 3 CSBMs in a given week and an increase of at least 1 CSBM from baseline in the same week for at least 9 weeks out of the first 12-week treatment period and at least 3 of the 4 final weeks (weeks 9-12). Roughly 25% of patients were responders in the Pizensy™ group versus 13% in the placebo group ($P<0.05$). A responder analysis based on weeks 13 to 24 of the treatment period showed similar results to the first 12 weeks. Improvements in the mean frequency of CSBMs/week were seen at week 1 with improvement generally maintained through week 12. The Pizensy™ group had a mean increase of 0.8 CSBM/week from baseline to week 12 over the placebo group. The most common adverse reactions leading to study drug discontinuation were elevated creatinine kinase, flatulence, diarrhea, and increased BP.

- Study 2 compared Pizensy™ to an active control (lubiprostone) in a Phase 3, double-blind, randomized, parallel assignment trial and investigated the safety and efficacy of Pizensy™ 20 grams versus lubiprostone 24mcg for the treatment of CIC. The trial enrolled 459 patients, 18 years of age and older, with a primary outcome of a CSBM response. The primary endpoint was based on the number of patients who were weekly responders for at least 9 out of 12 weeks, with at least 3 of these weeks occurring in the last 4 weeks of treatment. A responder was defined as having ≥3 CSBMs and an increase from baseline of >1 CSBM in that week. When compared to lubiprostone, Pizensy™ showed non-inferiority with 25.1% meeting the primary endpoint versus 28.1% with lubiprostone ($P=0.016$). The frequency of CSBMs per week for the Pizensy™ group was consistent with results from Study 1.

Cost Comparison: CIC Therapies

Medication	Recommended Dose	Cost Per Month
Amitiza® (lubiprostone) 24mcg cap	24mcg PO twice daily	$355.80
Linzess® (linaclotide) 145mcg cap	72mcg or 145mcg PO daily	$426.90
Motegrity® (prucalopride) 2mg tab	2mg PO daily	$419.70
Trulance® (plecanatide) 3mg tab	3mg PO daily	$418.80

PO = by mouth; cap = capsule; tab = tablet
Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Cost (WAC), if NADAC is unavailable.
Please note: Cost information is not yet available for Pizensy™.

Recommendations

The College of Pharmacy recommends the prior authorization of Pizensy™ (lactitol) with the following criteria:

Pizensy™ (Lactitol) Approval Criteria:

1. An FDA approved indication for treatment of chronic idiopathic constipation (CIC) in members 18 years of age or older; and
2. Member must not have a known contraindication to Pizensy™ (i.e., suspected gastrointestinal obstruction, galactosemia); and
3. Documentation that constipation-causing therapies for other disease states have been discontinued (excluding opioid pain medications for cancer patients); 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 3 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. 1 of the 3 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 the member cannot use Linzess® (linaclotide), Amitiza® (lubiprostone), or Trulance® (plecanatide) must be provided; and
7. Use of the unit-dose packets will require a patient-specific, clinically significant reason why the member cannot use the multi-dose bottle; and
8. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment; and
9. A quantity limit of 560 grams per 28 days will apply.

Utilization Details of Constipation Medications: Fiscal Year 2020

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
LINACLOTIDE PRODUCTS						
LINZESS CAP 290MCG	294	51	$122,208.27	$415.67	5.76	30.90%
LINZESS CAP 145MCG	197	43	$83,708.72	$424.92	4.58	21.17%
LINZESS CAP 72MCG	83	23	$34,433.44	$414.86	3.61	8.71%
SUBTOTAL	**574**	**117**	**$240,350.43**	**$418.73**	**4.91**	**60.78%**
LUBIPROSTONE PRODUCTS						
AMITIZA CAP 24MCG	171	44	$61,436.70	$359.28	3.89	15.54%
AMITIZA CAP 8MCG	113	34	$42,828.18	$379.01	3.32	10.83%
SUBTOTAL	**284**	**78**	**$104,264.88**	**$367.13**	**3.64**	**26.37%**
NALOXEGOL PRODUCTS						
MOVANTIK TAB 25MG	87	22	$26,050.21	$299.43	3.95	6.59%
MOVANTIK TAB 12.5MG	5	2	$1,741.60	$348.32	2.5	0.44%
SUBTOTAL	**92**	**24**	**$27,791.81**	**$302.08**	**3.83**	**7.03%**
PLECANATIDE PRODUCTS						
TRULANCE TAB 3MG	38	13	$15,849.11	$417.08	2.92	4.01%
SUBTOTAL	**38**	**13**	**$15,849.11**	**$417.08**	**2.92**	**4.01%**
PRUCALOPRIDE PRODUCTS						
MOTEGRITY TAB 2MG	4	2	$1,091.26	$272.82	2	0.28%
SUBTOTAL	**4**	**2**	**$1,091.26**	**$272.82**	**2**	**0.28%**
NALDEMEDINE PRODUCTS						
SYMPROIC TAB 0.2MG	3	2	$1,073.27	$357.76	1.5	0.27%
SUBTOTAL	**3**	**2**	**$1,073.27**	**$357.76**	**1.5**	**0.27%**
METHYLNALTREXONE PRODUCTS						
RELISTOR INJ 12MG/0.6ML	2	1	$3,242.26	$1,621.13	2	0.82%
RELISTOR TAB 150MG	1	1	$1,798.56	$1,798.56	1	0.45%
SUBTOTAL	**3**	**2**	**$5,040.82**	**$1,680.27**	**1.5**	**1.27%**
TOTAL	**998**	**205***	**$395,461.58**	**$396.25**	**4.86**	**100%**

TAB = tablet; CAP = capsule; INJ = injection
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020

Utilization Details of Diarrhea Medications: Fiscal Year 2020

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
RIFAXIMIN PRODUCTS						
XIFAXAN TAB 550MG	905	176	$2,006,809.81	$2,217.47	5.14	95.32%
XIFAXAN TAB 200MG	37	14	$33,569.06	$907.27	2.64	1.59%
SUBTOTAL	**942**	**190**	**$2,040,378.87**	**$2,166.01**	**4.96**	**96.91%**
ELUXADOLINE PRODUCTS						
VIBERZI TAB 100MG	18	2	$22,226.31	$1,234.80	9.0	1.06%
VIBERZI TAB 75MG	3	1	$3,648.00	$1,216.00	3.0	0.17%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
SUBTOTAL	**21**	**3**	**$25,874.31**	**$1,232.11**	**7.0**	**1.23%**
TELOTRISTAT PRODUCTS						
XERMELO TAB 250MG	6	1	$39,116.46	$6,519.41	6.0	1.86%
SUBTOTAL	**6**	**1**	**$39,116.46**	**$6,519.41**	**6.0**	**1.86%**
TOTAL	**969**	**194***	**$2,105,369.64**	**$2,172.72**	**4.99**	**100%**

TAB = tablet
*Total number of unduplicated member
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.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020

[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 11/2020. Last accessed 11/09/2020.
[2] Sebela Pharmaceuticals. Sebela Pharmaceuticals Announces FDA Approval of Pizensy™ for Oral Solution for the Treatment of Chronic Idiopathic Constipation in Adults. *BioSpace*. Available online at: https://www.biospace.com/article/sebela-pharmaceuticals-announces-fda-approval-of-pizensy-for-oral-solution-for-the-treatment-of-chronic-idiopathic-constipation-in-adults/. Issued 03/02/2020. Last accessed 11/09/2020.
[3] Brooks M. FDA OKs Fidaxomicin (Dificid®) for *C. difficile* Infection in Children as Young as 6 Months. *Medscape*. Available online at: https://www.medscape.com/viewarticle/924273. Issued 01/27/2020. Last accessed 11/09/2020.
[4] RedHill Biopharma. Randomized, Double-Blind, Placebo-Controlled, Phase 2 Trial of Ondansetron 12mg Bimodal Release Tablets for Diarrhea Predominant Irritable Bowel Syndrome. *RedHill Biopharma*. Available online at: https://www.redhillbio.com/RedHill//userdata/SendFile.asp?DBID=1&LNGID=1&GID=7073. Last accessed 11/09/2020.
[5] A Safety and Efficacy Evaluation of BLI400 Laxative in Constipated Adults. *ClinicalTrials.gov*. Available online at: https://clinicaltrials.gov/ct2/show/results/NCT02481947. Last revised 07/27/2020. Last accessed 11/12/2020.
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Appendix M

Fiscal Year 2020 Annual Review of Thrombocytopenia Medications

Oklahoma Health Care Authority
December 2020

Current Prior Authorization Criteria

Cablivi® (Caplacizumab-yhdp) Approval Criteria:

1. An FDA approved indication for acquired thrombotic thrombocytopenic purpura (aTTP); and
2. Member must be undergoing plasma exchange therapy; and
    a. Dates of initiation of plasma exchange therapy must be listed on the prior authorization request; and
    b. Authorizations will be for the duration of plasma exchange and for 30 days after discontinuation of plasma exchange; and
3. Member must be utilizing immunosuppressant therapy; and
4. Cablivi® must be prescribed by, or in consultation with, a hematologist; and
5. A quantity limit of 11mg per day will apply. Initial approvals will be for the duration of plasma exchange plus 30 days. Reauthorization, after completing 30 days post-plasma exchange, may be considered if the prescriber documents sign(s) of persistent underlying disease remain. Reauthorization will be for a maximum of 28 days.

Doptelet® (Avatrombopag) Approval Criteria [Chronic Immune Thrombocytopenia (ITP) Diagnosis]:

1. An FDA approved indication for the treatment of thrombocytopenia in adult patients with chronic ITP who have had an insufficient response to a previous treatment; and
2. Member must be 18 years of age or older; and
3. Previous insufficient response with at least 1 of the following treatments:
    a. Corticosteroids; or
    b. Immunoglobulins; or
    c. Splenectomy; and
4. A patient-specific, clinically significant reason why the member cannot use an alternative thrombopoietin (TPO) receptor agonist available without a prior authorization must be provided; and
5. Prescriber must verify the degree of thrombocytopenia and clinical condition increase the risk for bleeding; and

6. Prescriber must verify platelet counts will be assessed weekly until a stable platelet count >50 x 10^9/L has been achieved, and then obtained monthly thereafter; and
7. Must be prescribed by, or in consultation with, a hematologist or oncologist; and
8. Doptelet® must not be used in an attempt to normalize platelet counts; and
9. Female members must not be pregnant and much have a negative pregnancy test prior to therapy initiation; and
10. Prescriber must verify female member is not breastfeeding; and
11. A quantity limit of 60 tablets per 30 days will apply.

Doptelet® (Avatrombopag) Approval Criteria [Thrombocytopenia in Chronic Liver Disease (CLD) Diagnosis]:

1. An FDA approved indication for the treatment of thrombocytopenia in adult patients with CLD who are scheduled to undergo a procedure; and
2. Date of procedure must be listed on the prior authorization request; and
3. Prescriber must verify the member will have the procedure within 5 to 8 days after the member receives the last dose of Doptelet®; and
4. Member must have a baseline platelet count <50 x 10^9/L (recent baseline platelet count must be provided); and
5. Must be prescribed by, or in consultation with, a hematologist, gastroenterologist, or hepatologist; and
6. Doptelet® must not be used in an attempt to normalize platelet counts; and
7. Female members must not be pregnant and must have a negative pregnancy test prior to therapy initiation; and
8. Prescriber must verify female member is not breastfeeding; and
9. A quantity limit of 15 tablets per scheduled procedure will apply.

Mulpleta® (Lusutrombopag) Approval Criteria:

1. An FDA approved indication for the treatment of thrombocytopenia in adult patients with chronic liver disease (CLD) who are scheduled to undergo a procedure; and
2. Date of procedure must be listed on the prior authorization request; and
3. Prescriber must verify the member will have the procedure 2 to 8 days after the member receives the last dose of Mulpleta®; and
4. Member must have a baseline platelet count <50 x 10^9/L (recent baseline platelet count must be provided); and
5. Must be prescribed by, or in consultation with, a hematologist, gastroenterologist, or hepatologist; and

6. Mulpleta® must not be used in an attempt to normalize platelet counts; and
7. A quantity limit of 7 tablets per scheduled procedure will apply.

Tavalisse™ (Fostamatinib) Approval Criteria:

1. An FDA approved indication for the treatment of thrombocytopenia in adult members with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment; and
2. Member must be 18 years of age or older (Tavalisse™ is not recommended for use in patients younger than 18 years of age because adverse effects on actively growing bones were observed in nonclinical studies); and
3. Member must have a clinical diagnosis of persistent/chronic ITP for at least 3 months; and
4. Previous insufficient response with at least 2 of the following treatments:
    a. Corticosteroids; or
    b. Immunoglobulins; or
    c. Splenectomy; or
    d. Thrombopoietin (TPO) receptor agonists; and
5. Degree of thrombocytopenia and clinical condition increase the risk for bleeding; and
6. Must be prescribed by, or in consultation with, a hematologist or oncologist; and
7. Prescriber must verify the member's complete blood count (CBC), including platelet counts, will be monitored monthly until a stable platelet count (at least 50 x 10^9/L) is achieved and will be monitored regularly thereafter; and
8. Prescriber must verify liver function tests (LFTs) (e.g., ALT, AST, bilirubin) will be monitored monthly; and
9. Prescriber must verify member's blood pressure will be monitored every 2 weeks until establishment of a stable dose, then monthly thereafter; and
10. Female members must not be pregnant and must have a negative pregnancy test immediately prior to therapy initiation. Female members of reproductive potential must be willing to use effective contraception while on therapy and for at least 1 month after therapy completion; and
11. Prescriber must verify female member is not breastfeeding; and
12. Member must not be taking strong CYP3A4 inducers (e.g., rifampicin) concurrently with Tavalisse™; and
13. Initial approvals will be for the duration of 12 weeks; and
14. Discontinuation criteria:

a. Platelet count does not increase to a level sufficient to avoid clinically important bleeding after 12 weeks of therapy; and

15. A quantity limit of 2 tablets daily will apply.

Utilization of Thrombocytopenia Medication: Fiscal Year 2020

Comparison of Fiscal Years

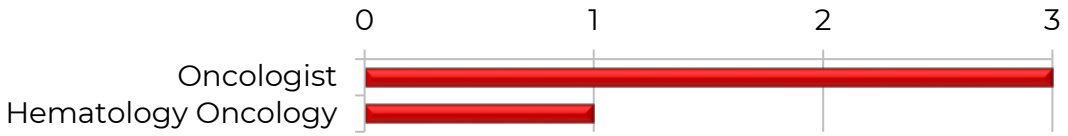
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2019	1	6	$58,631.22	$9,771.87	$325.73	360	180
2020	2	4	$38,006.14	$9,501.53	$316.72	150	120
% Change	**100.00%**	**-33.30%**	**-35.20%**	**-2.80%**	**-2.80%**	**-58.30%**	**-33.30%**
Change	**1**	**-2**	**-$20,625.08**	**-$270.34**	**-$9.01**	**-210**	**-60**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2019 = 07/01/2018 to 06/30/2019; Fiscal Year 2020 = 07/01/2019 to 06/30/2020

Demographics of Members Utilizing Thrombocytopenia Medications

- There was 1 unique member utilizing Doptelet® (avatrombopag) and 1 unique member utilizing Tavalisse™ (fostamatinib) during fiscal year 2020. Due to the limited number of members utilizing thrombocytopenia medications, detailed demographic information could not be provided.

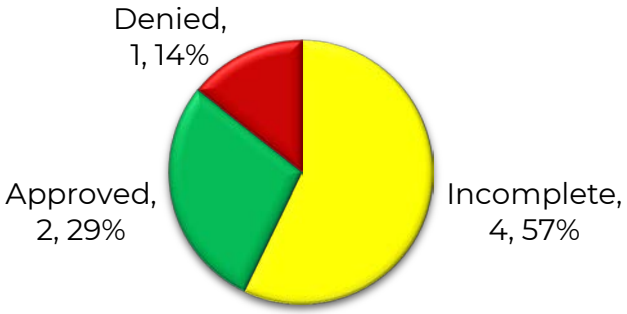
Top Prescriber Specialties of Thrombocytopenia Medications By Number of Claims



Prior Authorization of Thrombocytopenia Medications

There were 7 prior authorization requests submitted for thrombocytopenia medications during fiscal year 2020. The following chart shows the status of the submitted petitions.

Status of Petitions



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

Anticipated Patent Expiration(s):

- Nplate® (romiplostim): January 2022
- Doptelet® (avatrombopag): May 2025
- Promacta® (eltrombopag): January 2026
- Mulpleta® (lusutrombopag): September 2031
- Tavalisse™ (fostamatinib): July 2032

Pipeline:

- **Efgartigimod:** There are 2 Phase 3 studies currently recruiting to evaluate efgartigimod for the treatment of primary immune thrombocytopenia (ITP). The ADVANCE study is a multicenter, randomized, double-blind, placebo-controlled study that will evaluate the safety and efficacy of 10mg/kg intravenous (IV) efgartigimod versus placebo. The primary efficacy endpoint is a sustained platelet count response (platelets ≥50 x 10^9/L for at least 4 out of 6 weekly visits between weeks 19 and 24) in patients with chronic primary ITP. The ADVANCE+ is a multi-center, open-label, long-term study that will evaluate the safety and efficacy of efgartigimod 10mg/kg IV versus placebo in patients with primary ITP. The primary outcomes include frequency and severity of adverse events, vital signs, and laboratory assessments up to 56 weeks.
- **BT-595:** BT-595 is an IV administered novel polyvalent immunoglobulin (IVIG) designed to treat primary immune deficiencies, secondary antibody deficiency syndromes, and several autoimmune disorders. A Phase 3, open-label, prospective, randomized, multicenter study is investigating the clinical efficacy and safety of BT-595 in patients with chronic ITP and enrolled 34 patients. The primary outcome is rate of patients with response (defined as a platelet count of >30 x 10^9/L and at least a 2 fold increase of the baseline count, confirmed on at least 2 separate occasions at least 7 days apart) and the absence of bleeding. The study is currently completed, but results have yet to be released.
- **Rozanolixizumab:** Rozanolixizumab is a monoclonal FcRn antibody being investigated as a subcutaneous (sub-Q) treatment option for primary ITP. Results from a multi-center, open-label Phase 2 study demonstrated a generally tolerated safety profile across all reported dose groups, consistent with other rozanolixizumab studies. The most common adverse event was mild-to-moderate headache, with the highest occurrence in the 20mg/kg group. Other adverse events included diarrhea and vomiting. No patient discontinued the study due to side effects. The study also showed clinically relevant improvements in platelet count (reaching >50 x 10^9/L) and meaningful decreases in immunoglobulin G (IgG) levels across all dose groups. Platelet counts of >50 x 10^9/L were achieved by more patients following a single infusion

of 15 or 20mg/kg (66.7% and 54.5% patients, respectively) versus multiple infusions.

- **SKI-O-703:** Genosco is currently recruiting patients with persistent and chronic ITP who have failed to respond or relapsed after prior therapy, with a platelet count <30,000/mcL for a study that will evaluate the safety, efficacy, tolerability, pharmacokinetics, and pharmacodynamics of select doses (200mg twice daily and 400mg twice daily) of SKI-O-703, a spleen tyrosine kinase (SYK) inhibitor. The study duration will be 20 weeks per patient, consisting of up to 4 weeks of a screening period, 12 weeks of a treatment period, and 4 weeks of a follow-up period.
- **KZR-616:** A Phase 2 clinical study, MARINA, is currently underway assessing the selective immunoproteasome inhibitor as a treatment option for autoimmune hemolytic anemia and ITP. KZR-616 selectively inhibits LMP7 and LMP2 subunits of the immunoproteasome within 4 hours of dosing. KZR-616 has been shown to block the acute production of inflammatory cytokines, modulate T- and B-cell activation and differentiation *in vitro*, and was efficacious in animal models of autoimmunity. The study is evaluating activity at doses of 30 and 45mg of KZR-616 administered sub-Q weekly. While this study is still in progress, results from a study with systemic lupus erythematous (SLE) patients showed promising results with KZR-616.
- **PRN1008:** In October 2019, Principia Biopharma announced positive preliminary data from an ongoing Phase 1/2 study of PRN1008 for the highly treatment-resistant and refractory patient population (median of 5 prior therapies) with ITP. The study enrolled 26 adult patients with 2 platelet counts <30,000/mcL within 15 days prior to treatment. The starting doses were 200mg once daily, 400mg once daily, 300mg twice daily, and 400mg twice daily with intra-patient dose escalation allowed every 4 weeks. The study had a current treatment duration of 12.7 weeks. The primary endpoint was ≥2 consecutive platelet counts of ≥50,000/mcL, separated by at least 5 days, and increased by ≥20,000/mcL from baseline without requiring rescue medication. Of the 26 patients enrolled, 39% achieved the primary endpoint.

Recommendations

The College of Pharmacy does not recommend any changes to the current thrombocytopenia medications prior authorization criteria at this time.

Utilization Details of Thrombocytopenia Medications: Fiscal Year 2020

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
AVATROMBOPAG PRODUCTS						
DOPTELET TAB 20MG	3	1	$26,752.73	$8,917.58	3	70.39%
FOSTAMATINIB PRODUCTS						
TAVALISSE TAB 100MG	1	1	$11,253.41	$11,253.41	1	29.61%
TOTAL	**4**	**2***	**$38,006.14**	**$9,501.54**	**2**	**100%**

TAB = tablet
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Fiscal Year 2020 = 07/01/2019 to 06/30/2020

[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 09/2020. Last accessed 09/23/2020.
[2] A Study to Assess the Efficacy and Safety of Efgartigimod in Adult Patients with Primary Immune Thrombocytopenia (ITP) (ADVANCE). *ClinicalTrials.gov*. Available online at: https://www.clinicaltrials.gov/ct2/show/NCT04188379. Last revised 11/03/2020. Last accessed 11/05/2020.
[3] A Study to Assess the Efficacy and Safety of Efgartigimod in Adult Patients with Primary Immune Thrombocytopenia (ITP) (ADVANCE2). *ClinicalTrials.gov*. Available online at: https://www.clinicaltrials.gov/ct2/show/NCT04274452. Last revised 09/14/2020. Last accessed 11/05/2020.
[4] This Clinical Study is to Test Efficacy and Safety of BT595 in Chronic Primary Immune Thrombocytopenia (ITP). *ClinicalTrials.gov*. Available online at: https://clinicaltrials.gov/ct2/show/NCT02859909. Last revised 08/14/2019. Last accessed 11/05/2020.
[5] UCB Biopharma, Inc. Final Phase II Results for UCB's Rozanolixizumab in Primary Immune Thrombocytopenia (ITP) Published in Blood Advances. Available online at: https://www.ucb-usa.com/ITP%20Phase%20II%20Data. Issued 09/09/2020. Last accessed 11/05/2020.
[6] A Phase 2, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel Dose Study to Evaluate the Efficacy and Safety of Oral SKI-O-703, SYK Inhibitor, in Patients with Persistent and Chronic Immune Thrombocytopenia (ITP). *ClinicalTrials.gov*. Available online at: https://clinicaltrials.gov/ct2/show/NCT04056195. Last revised 09/18/2020. Last accessed 11/05/2020.
[7] European Hematology Association. Selective Immunoproteasome Inhibitor, KZR-616, A Novel Therapy for Autoimmune Hemolytic Anemia and Immune Thrombocytopenia: Biomarker Activity and Phase II Clinical Trial in Progress (MARINA). Available online at: https://library.ehaweb.org/eha/2020/eha25th/295137/julia.lawrence.selective.immunoproteasome.inhibitor.kzr-616.a.novel.therapy.html. Issued 06/12/2020. Last accessed 11/05/2020.
[8] Principia Biopharma, Inc. Principia Announces Positive Preliminary Data of PRN1008 for Immune Thrombocytopenia in Ongoing Phase 1/2 Trial. *GlobeNewswire*. Available online at: https://www.globenewswire.com/news-release/2019/10/15/1929580/0/en/Principia-Announces-Positive-Preliminary-Data-of-PRN1008-for-Immune-Thrombocytopenia-in-Ongoing-Phase-1-2-Trial.html. Issued 10/19/2019. Last accessed 11/05/2020.

Appendix N

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

FDA NEWS RELEASE

For Immediate Release: November 09, 2020

Coronavirus (COVID-19) Update: FDA Authorizes Monoclonal Antibody for Treatment of COVID-19

The FDA issued an emergency use authorization (EUA) for the investigational monoclonal antibody therapy bamlanivimab for the treatment of mild-to-moderate COVID-19 in adult and pediatric patients. Bamlanivimab is authorized for patients with positive results of direct SARS-CoV-2 viral testing who are 12 years of age and older weighing at least 40kg and who are at high risk for progressing to severe COVID-19 and/or hospitalization. This includes those who are 65 years of age or older or who have certain chronic medical conditions.

While the safety and effectiveness of this investigational therapy continues to be evaluated, bamlanivimab was shown in clinical trials to reduce COVID-19-related hospitalization or emergency room visits in patients at high risk for disease progression within 28 days after treatment when compared to placebo.

Bamlanivimab is not authorized for patients who are hospitalized due to COVID-19 or require oxygen therapy due to COVID-19. A benefit of bamlanivimab treatment has not been shown in patients hospitalized due to COVID-19. Monoclonal antibodies, such as bamlanivimab, may be associated with unfavorable clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.

“As illustrated by today’s action, the FDA remains committed to expediting the development and availability of potential COVID-19 treatments and providing sick patients timely access to new therapies where appropriate, while at the same time supporting research to further evaluate whether they are safe and effective,” said FDA Commissioner Stephen M. Hahn, M.D. “Through our Coronavirus Treatment Acceleration Program, the FDA continues to work around the clock and use every tool at our disposal toward these efforts.”

Monoclonal antibodies are laboratory-made proteins that mimic the immune system’s ability to fight off harmful antigens such as viruses. Bamlanivimab is a monoclonal antibody that is specifically directed against the spike protein of SARS-CoV-2, making it designed to block the virus’ attachment and entry into human cells.

“The FDA’s emergency authorization of bamlanivimab provides health care professionals on the frontline of this pandemic with another potential tool in treating COVID-19 patients,” said Patrizia Cavazzoni, M.D., acting director of the FDA’s Center for Drug Evaluation and Research. “We will continue to evaluate new data on the safety and efficacy of bamlanivimab as they become available.”

The issuance of an EUA is different than an FDA approval. In determining whether to issue an EUA, the FDA evaluates the available evidence and carefully balances any known or potential risks with any known or potential benefits of the product for use during an emergency. Based on the FDA’s review of the totality of the scientific evidence available, the agency determined that it is reasonable to believe that bamlanivimab may

be effective in treating non-hospitalized patients with mild-or-moderate COVID-19. When used to treat COVID-19 for the authorized population, the known and potential benefits outweigh the known and potential risks of the drug. There are no adequate, approved, and available alternative treatments to bamlanivimab for the authorized population. As part of the evaluation of the EUA, the FDA imposed several quality measures to protect patients. The drug company is required to implement these quality measures to manufacture this drug under the EUA.

The data supporting this EUA for bamlanivimab is based on an interim analysis from a Phase 2 randomized, double-blind, placebo-controlled clinical trial in 465 non-hospitalized adults with mild-to-moderate COVID-19 symptoms. Of these patients, 101 received a 700mg dose of bamlanivimab, 107 received a 2,800mg dose, 101 received a 7,000mg dose, and 156 received a placebo within 3 days of obtaining the clinical sample for the first positive SARS-CoV-2 viral test.

The pre-specified primary endpoint in the Phase 2 trial was the change in viral load from baseline to day 11 for bamlanivimab versus placebo. Most patients, including those receiving placebo, cleared the virus by day 11. However, the most important evidence that bamlanivimab may be effective came from the predefined secondary endpoint of COVID-19-related hospitalizations or emergency room (ER) visits within 28 days after treatment. For patients at high risk for disease progression, hospitalizations and ER visits occurred in 3% of bamlanivimab-treated patients on average compared to 10% in placebo-treated patients. The effects on viral load, reduction in hospitalizations and ER visits, and safety were similar in patients receiving any of the 3 bamlanivimab doses.

The EUA allows for bamlanivimab to be distributed and administered intravenously (IV) as a single dose by health care providers. The EUA requires fact sheets that provide important information about using bamlanivimab in treating COVID-19 be made available to health care providers and to patients and caregivers, including dosing instructions, potential side effects, and drug interactions. Possible side effects of bamlanivimab include anaphylaxis and infusion-related reactions, nausea, diarrhea, dizziness, headache, itching, and vomiting. The EUA was issued to Eli Lilly and Company.

FDA NEWS RELEASE

For Immediate Release: November 09, 2020

FDA Offers Guidance to Enhance Diversity in Clinical Trials, Encourage Inclusivity in Medical Product Development

To further promote and protect public health, it is important that people who are in clinical trials represent the populations most likely to use the potential medical product. In that spirit, the FDA issued final guidance with the agency's recommendations on designing and executing clinical trials of drugs and biologics that include people with different demographic characteristics (e.g., sex, race, ethnicity, age, location of residency) and non-demographic characteristics (e.g., patients with organ dysfunction, comorbid conditions, and disabilities; those at weight range extremes; populations with diseases or conditions with low prevalence).

The final guidance issued, "Enhancing the Diversity of Clinical Trial Populations--Eligibility Criteria, Enrollment Practices, and Trial Designs," was first issued as a draft in 2019, and provides the FDA's current thinking on steps to broaden eligibility criteria in clinical trials through inclusive trial practices, trial designs, and methodological approaches. The guidance aims to provide recommendations for how sponsors can increase enrollment of underrepresented populations in their clinical trials.

This guidance offers recommendations on how product sponsors can improve clinical trial diversity by accounting for logistical and other participant-related factors that could limit participation. For example, clinical trials requiring frequent visits to specific sites may place an added burden on participants. Sponsors are encouraged to think about reducing visit frequency, when appropriate, in addition to considering whether flexibility in visit windows is possible and whether electronic communications, such as phone, email, social media platforms, or other digital health technology tools can replace site visits and provide investigators with real-time data.

Additionally, this guidance provides recommendations on broadening clinical trial eligibility criteria for clinical trials of investigational drugs intended to treat rare diseases and recommendations on improving enrollment and retention of participants with rare diseases. The guidance notes that sponsors should consider early engagement with patient advocacy groups and patients to elicit suggestions for designing trials that participants would be willing to enroll in and support. The guidance also includes other high-level considerations about inclusion of other important groups, including but not limited to: women (including pregnant women), racial and ethnic minorities, children, and older adults.

FDA NEWS RELEASE

For Immediate Release: November 06, 2020

FDA Takes Efforts to Protect Patients from Potentially Harmful Compounded Drugs through Finalizing Insanitary Conditions Guidance

Protecting patients from exposure to poor quality compounded drugs is a fundamental part of the FDA's drug compounding program, and the FDA is committed to protecting patients. While compounded drugs can serve an important role for patients whose medical needs cannot be met by an FDA-approved drug product, these drugs have not been reviewed by the FDA for safety, effectiveness, or quality. The FDA, through its oversight of compounded drugs, strives to help improve the quality of compounded drugs and reduce risk to patients.

Under federal law, a drug is considered adulterated if it is prepared, packed, or held under insanitary conditions that could cause the drug to become contaminated or rendered injurious to health. While some compounders work hard to meet quality standards, too often FDA investigators continue to observe poor conditions at compounding facilities that impact drug quality and have the potential to harm patients who use the drugs. These insanitary conditions include dirt, mold, insects, trash, peeling paint, unclean exhaust vents, and dirty high-efficiency particulate air filters, among many other examples. Numerous compounders have voluntarily recalled drug products intended to be sterile, and also temporarily or permanently stopped sterile operations because of these inspectional observations. The FDA has also taken regulatory and enforcement actions when insanitary conditions were observed.

Because of these and other concerning examples that have been witnessed, the FDA is releasing a final guidance to further the efforts to help compounders identify and prevent insanitary conditions at their facilities. The final guidance provides recent examples of insanitary conditions observed at compounding facilities and details corrective actions that facilities should take when these conditions are identified.

Based on comments to the revised draft guidance, the FDA also added recommendations for compounders to use risk management tools to develop appropriate controls to prevent insanitary conditions at their facilities. Additionally, the guidance addresses the regulatory actions that the FDA may take in response to

insanitary conditions. The FDA will continue to take appropriate action to protect patients from poor quality drugs made in facilities that have insanitary conditions. The FDA's collaborative work with states and the Department of Justice remains ongoing.

Both traditional compounders and outsourcing facilities should take measures to avoid insanitary conditions. The FDA urges compounders to use this valuable resource to better understand insanitary conditions and take necessary actions to avoid such issues for the safety of the patients who receive their drugs.

FDA NEWS RELEASE

For Immediate Release: October 30, 2020

FDA, Homeland Security Agencies Take Additional Action to Prevent Import of Illegal and Harmful Medical Products through International Mail Facilities

Recently, leadership from the FDA, the U.S. Customs and Border Protection (CBP), and the U.S. Immigration and Customs Enforcement, Homeland Security Investigations (ICE-HSI) signed a Memorandum of Understanding (MOU) to stop harmful products that pose a threat to public health and attempt to enter the U.S. through International Mail Facilities (IMFs). The MOU will maximize inspection and detection capabilities in order to prevent this illegal activity.

As a core part of this collaborative effort, CBP and ICE-HSI will continue to partner with the FDA in joint operations at the IMFs to target illicit opioids (including fentanyl and other unapproved or unlawful drugs), medical devices, and dietary supplements regulated under the Federal Food, Drug, and Cosmetic Act. This partnership is also critical in our continuing efforts to intercept fraudulent, counterfeit, or illegitimate COVID-19 products that may pose risks to public health. Additionally, the agencies will work to coordinate ongoing activities through collaborative information sharing, shared facilities, and future coordinated operations.

"Americans must have confidence that the products they receive are reliable and fully comply with U.S. laws," said FDA Commissioner Stephen M. Hahn, M.D. "The collaborative efforts we've announced will enable more resourceful, effective, and efficient oversight to prevent illegal and potentially harmful products from entering the United States—thereby aiding our essential mission to protect the health and safety of the American people. We remain committed to using all tools and authorities available and leveraging our strong relationship with our federal partners to help stop the illegal flow of counterfeit and unapproved medical products into our country."

The FDA and CBP signed a letter of intent in April 2019, to maximize inspection and detection capabilities at the IMFs. As outlined in the letter of intent and in the recently signed MOU, the FDA, CBP, and ICE-HSI will expand the types of information and how that information is shared among the agencies to quickly and effectively identify trends in incoming violative packages. This collaboration involves sharing of both general and specific data points, which can be used to target impending product entries and to inform future enforcement strategies. An additional focus of this effort will be coordinating shared space as well as increased scientific presence at high-volume IMF locations, helping to facilitate and support real-time entry decisions and increased data sharing.

Since April 2016, when the FDA implemented its administrative destruction authority at all 9 IMFs, the agency has destroyed more than 12.9 million capsules/tablets/pieces – weighing over 41.2 tons. The destruction of almost 13 million violative drug units by the FDA represents a key component of the agency's public health mission, as these potentially dangerous drugs were destined for over 31,000 United States

consumers. New authorities and resources provided by Congress under the Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment (SUPPORT) for Patients and Communities Act have enabled the FDA to create a more efficient destruction process for violative drugs containing certain active pharmaceutical ingredients (APIs), and to expand its presence at IMF locations nationwide, which has resulted in more rapid, on-site scientific support, increased staffing and improved work facilities.

In fiscal year (FY) 2019, the FDA screened approximately 25,200 parcels containing more than 41,000 products at its IMF facilities. The agency subsequently refused to admit more than 35,000 of those products and nearly half (>17,000 products) were identified as violative drugs and destroyed using FDA's administrative destruction authority. So far in FY 2020, the FDA has screened approximately 27,500 mail parcels, containing almost 43,000 FDA-regulated products. Of these products, >34,000 were refused admission and >24,000 were violative drug products that have been destroyed.

FDA NEWS RELEASE

For Immediate Release: October 27, 2020

FDA Approves Lotion for Nonprescription Use to Treat Head Lice

The FDA approved a lotion to treat head lice for nonprescription, or over-the-counter (OTC), use through a process called the prescription (Rx)-to-OTC switch. The FDA initially approved Sklice (ivermectin) 0.5% lotion for the treatment of head lice infestation in patients 6 months of age and older as a prescription drug in February 2012.

"The Rx-to-OTC switch process aims to promote public health by increasing consumer access to drugs that would otherwise only be available by prescription," said Theresa Michele, M.D., acting director of the Office of Nonprescription Drugs in the FDA's Center for Drug Evaluation and Research. "Today's approval expands access to another effective topical treatment for the thousands of people with head lice."

Rx-to-OTC switches are generally initiated by the manufacturer of the Rx drug. For a drug to switch from Rx to OTC status, the data provided must demonstrate that the drug is safe and effective when used as directed in the proposed labeling. The manufacturer must show that consumers can understand how to use the drug safely and effectively without the supervision of a health care professional.

In the United States, it is estimated that between 6 and 12 million cases of head lice infestation occur each year in children 3 to 11 years of age, according to the U.S. Centers for Disease Control and Prevention (CDC). Head lice are most common among preschool children attending child care, elementary school children, and members of a household where children have lice.

Sklice contains the active ingredient ivermectin 0.5% for single-use topical treatment of head lice infestations in patients 6 months of age and older. Sklice is for external use only and should only be used on the scalp and dry hair in accordance with label directions. Sklice is not approved for any other use.

Sklice will be marketed in the United States as an OTC drug and will no longer be available as an Rx drug. Consumers should read and follow the Drug Facts label for the OTC product. Patients who currently use Rx versions of this product should talk to their health care professional.

Current Drug Shortages Index (as of November 18, 2020):

The information provided in this section is provided voluntarily to the FDA by manufacturers and is not specific to Oklahoma.

Amifostine Injection	***Currently in Shortage***
Aminophylline Injection, USP	***Currently in Shortage***
Amoxapine Tablets	***Currently in Shortage***
Amphetamine Aspartate; Amphetamine Sulfate; Dextroamphetamine Saccharate; Dextroamphetamine Sulfate Tablets	***Currently in Shortage***
Anagrelide Hydrochloride Capsules	***Currently in Shortage***
Asparaginase Erwinia Chrysanthemi (Erwinaze)	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Atropine Sulfate Ophthalmic Ointment	***Currently in Shortage***
Avycaz® (ceftazidime and avibactam) for Injection, 2 grams/0.5 grams	***Currently in Shortage***
Azithromycin Tablets	***Currently in Shortage***
Belatacept (Nulojix®) Lyophilized Powder for Injection	***Currently in Shortage***
Bumetanide Injection, USP	***Currently in Shortage***
Bupivacaine Hydrochloride and Epinephrine Injection, USP	***Currently in Shortage***
Bupivacaine Hydrochloride Injection, USP	***Currently in Shortage***
Calcitriol Injection USP 1MCG /ML	***Currently in Shortage***
Calcium Chloride Injection, USP	***Currently in Shortage***
Capreomycin Injection, USP	***Currently in Shortage***
Cefazolin Injection	***Currently in Shortage***
Cefepime Injection	***Currently in Shortage***
Cefotaxime Sodium Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***
Cefoxitin for Injection, USP	***Currently in Shortage***
Chlorothiazide (Diuril®) Oral Suspension	***Currently in Shortage***
Cisatracurium Besylate Injection	***Currently in Shortage***
Continuous Renal Replacement Therapy (CRRT) Solutions	***Currently in Shortage***
Cyclopentolate Ophthalmic Solution	***Currently in Shortage***
Cysteamine Hydrochloride Ophthalmic Solution	***Currently in Shortage***
Dexamethasone Sodium Phosphate Injection	***Currently in Shortage***
Dexmedetomidine Injection	***Currently in Shortage***
Dextrose 25% Injection	***Currently in Shortage***
Dextrose 50% Injection	***Currently in Shortage***
Dicyclomine Oral Tablets/Capsules	***Currently in Shortage***
Diltiazem Hydrochloride	***Currently in Shortage***
Dimercaprol (Bal in Oil) Injection USP	***Currently in Shortage***
Diphenhydramine Injection	***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***
Doxycycline Hyclate Injection	***Currently in Shortage***
Echothiophate Iodide (Phospholine Iodide®) Ophthalmic Solution	***Currently in Shortage***
Enalaprilat Injection, USP	***Currently in Shortage***
Epinephrine Injection, 0.1mg/mL	***Currently in Shortage***
Epinephrine Injection, Auto-Injector	***Currently in Shortage***
Erythromycin Lactobionate for Injection, USP	***Currently in Shortage***
Erythromycin Ophthalmic Ointment	***Currently in Shortage***
Etomidate Injection	***Currently in Shortage***
Famotidine Injection	***Currently in Shortage***
Famotidine Tablets	***Currently in Shortage***
Fentanyl Citrate (Sublimaze®) Injection	***Currently in Shortage***
Floxuridine for Injection, USP	***Currently in Shortage***
Fluorescein Injection	***Currently in Shortage***
Fluorescein Strips	***Currently in Shortage***
Flurazepam Hydrochloride Capsules	***Currently in Shortage***
Fluvoxamine ER Capsules	***Currently in Shortage***
Furosemide Injection, USP	***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***
Hydralazine Hydrochloride Injection, USP	***Currently in Shortage***
Hydrocortisone Tablets, USP	***Currently in Shortage***
Hydromorphone Hydrochloride Injection, USP	***Currently in Shortage***
Hydroxypropyl (Lacrisert®) Cellulose Ophthalmic Insert	***Currently in Shortage***
Hydroxyzine Pamoate Oral Capsules	***Currently in Shortage***
Imipenem and Cilastatin for Injection, USP	***Currently in Shortage***
Ketamine Injection	***Currently in Shortage***
Ketoprofen Capsules	***Currently in Shortage***
Ketorolac Tromethamine Injection	***Currently in Shortage***
Labetalol Hydrochloride Injection	***Currently in Shortage***
Letermovir (Prevymis®) Injection	***Currently in Shortage***
Leucovorin Calcium Lyophilized Powder for Injection	***Currently in Shortage***
Leuprolide Acetate Injection	***Currently in Shortage***
Levetiracetam Extended-Release Oral Tablets, USP	***Currently in Shortage***
Levetiracetam Immediate-Release Oral Tablets, USP	***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***
Lithium Oral Solution	***Currently in Shortage***
Lorazepam Injection, USP	***Currently in Shortage***
Loxapine Capsules	***Currently in Shortage***
Methadone Hydrochloride Injection	***Currently in Shortage***
Methyldopa Tablets	***Currently in Shortage***
Metoprolol Tartrate Injection, USP	***Currently in Shortage***
Metronidazole Injection, USP	***Currently in Shortage***
Midazolam Injection, USP	***Currently in Shortage***
Morphine Sulfate Injection, USP	***Currently in Shortage***
Multi-Vitamin Infusion (Adult and Pediatric)	***Currently in Shortage***
Nalbuphine Hydrochloride Injection	***Currently in Shortage***
Nefazodone Hydrochloride Tablets	***Currently in Shortage***
Nizatidine Capsules	***Currently in Shortage***
Ondansetron Hydrochloride Injection	***Currently in Shortage***
Oxytocin Injection, USP Synthetic	***Currently in Shortage***
Pantoprazole Sodium for Injection	***Currently in Shortage***
Parathyroid Hormone (Natpara®) Injection	***Currently in Shortage***
Physostigmine Salicylate Injection, USP	***Currently in Shortage***
Pindolol Tablets	***Currently in Shortage***
Potassium Acetate Injection, USP	***Currently in Shortage***
Procainamide Hydrochloride Injection, USP	***Currently in Shortage***
Promethazine (Phenergan®) Injection	***Currently in Shortage***
Propofol Injectable Emulsion	***Currently in Shortage***
Rifapentine Tablets	***Currently in Shortage***
Ropivacaine Hydrochloride Injection	***Currently in Shortage***
Sclerosol Intrapleural Aerosol	***Currently in Shortage***
Sertraline Hydrochloride Oral Solution, USP	***Currently in Shortage***
Sertraline Hydrochloride Tablets	***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 23.4% Injection	***Currently in Shortage***
Sodium Chloride Injection USP, 0.9% Vials and Syringes	***Currently in Shortage***
Sulfasalazine Tablets	***Currently in Shortage***
Tacrolimus Capsules	***Currently in Shortage***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***

Thiothixene Capsules	***Currently in Shortage***
Timolol Maleate Ophthalmic Gel Forming Solution	***Currently in Shortage***
Timolol Maleate Ophthalmic Solution	***Currently in Shortage***
Timolol Maleate Tablets	***Currently in Shortage***
Tobramycin Lyophilized Powder for Injection	***Currently in Shortage***
Triamcinolone Acetonide (Triesence®) Injection, Suspension	***Currently in Shortage***
Trifluridine Ophthalmic Solution	***Currently in Shortage***
Vecuronium Bromide for Injection	***Currently in Shortage***