Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
March 11, 2020
4:00pm

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

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

MEMORANDUM

TO: Drug Utilization Review (DUR) Board Members

FROM: Michyla Adams, Pharm.D.

SUBJECT: Packet Contents for DUR Board Meeting – March 11, 2020

DATE: February 24, 2020

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

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

Call to Order

Public Comment Forum

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

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

Action Item – Vote to Prior Authorize Xcopri® (Cenobamate) – Appendix C

Action Item – Vote to Prior Authorize Tosymra™ (Sumatriptan Nasal Spray), Reyvow™ (Lasmiditan), and Ubrelvy™ (Ubrogepant) – Appendix D

Action Item – Vote to Prior Authorize Esperoct® [Antihemophilic Factor (Recombinant), Glycopegylated-exei] – Appendix E

Action Item – Vote to Prior Authorize ProAir® Digihaler™ (Albuterol Sulfate Inhalation Powder) – Appendix F

Action Item – Vote to Prior Authorize Evenity® (Romosozumab-aqqg) – Appendix G

Action Item – Vote to Prior Authorize Asparlas™ (Calaspargase Pegol-mknl), Daurismo™ (Glasdegib), Idhifa® (Enasidenib), Lumoxiti® (Moxetumomab Pasudotox-tdfk), Tibsovo® (Ivosidenib), and Xospata® (Gilteritinib) – Appendix H

Action Item – Vote to Prior Authorize Azedra® (Iobenguane I-131) – Appendix I

Annual Review of Lymphoma Medications and 30-Day Notice to Prior Authorize Aliqopa™ (Copanlisib), Brukinsa™ (Zanubrutinib), Polivy™ (Polatuzumab Vedotin-piiq), and Ruxience™ (Rituximab-pvvr) – Appendix J

Annual Review of Lutathera® (Lutetium Lu-177 Dotatate) and Vitrakvi® (Larotrectinib) – Appendix K

Annual Review of Multiple Sclerosis (MS) Medications and 30-Day Notice to Prior Authorize Mayzent® (Siponimod), Mavenclad® (Cladribine), and Vumerity™ (Diroximel Fumarate) – Appendix L

30-Day Notice to Prior Authorize Tepezza™ (Teprotumumab-trbw) – Appendix M

Annual Review of Anti-Emetic Medications – Appendix N

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

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – March 11, 2020 @ 4:00pm

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

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

1. Call to Order

A. Roll Call – Dr. Skrepnek

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. February 12, 2020 DUR Minutes – Vote
B. February 12, 2020 DUR Recommendations Memorandum

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

4. Update on Medication Coverage Authorization Unit/SoonerPsych Program Update – See Appendix B

A. Pharmacy Helpdesk Activity for February 2020
B. Medication Coverage Activity for February 2020
C. SoonerPsych Program Update

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

5. Action Item – Vote to Prior Authorize Xcopri® (Cenobamate) – See Appendix C

A. Introduction
B. College of Pharmacy Recommendations

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

6. Action Item – Vote to Prior Authorize Tosymra™ (Sumatriptan Nasal Spray), Reyvow™ (Lasmiditan), and Ubrelvy™ (Ubrogepant) – See Appendix D

A. Introduction
B. College of Pharmacy Recommendations

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

7. Action Item – Vote to Prior Authorize Esperoct® [Antihemophilic Factor (Recombinant), Glycopegylated-exei] – See Appendix E

A. Introduction
B. Recommendations

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

8. Action Item – Vote to Prior Authorize ProAir® Digihaler™ (Albuterol Sulfate Inhalation Powder) – See Appendix F

A. Introduction
B. College of Pharmacy Recommendations

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

9. Action Item – Vote to Prior Authorize Evenity® (Romosozumab-aqqg) – See Appendix G

A. Introduction
B. College of Pharmacy Recommendations

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

10. Action Item – Vote to Prior Authorize Asparlas™ (Calaspargase Pegol-mknl), Daurismo™ (Glasdegib), Idhifa® (Enasidenib), Lumoxiti® (Moxetumomab Pasudotox-tdfk), Tibsovo® (Ivosidenib), and Xospata® (Gilteritinib) – See Appendix H

A. Introduction
B. Product Summaries
C. Recommendations

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

11. Action Item – Vote to Prior Authorize Azedra® (Iobenguane I-131) – See Appendix I

A. Introduction
B. Azedra® (Iobenguane I-131) Product Summary
C. Recommendations

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

12. Annual Review of Lymphoma Medications and 30-Day Notice to Prior Authorize Aliqopa™ (Copanlisib), Brukinsa™ (Zanubrutinib), Polivy™ (Polatuzumab Vedotin-piiq), and Ruxience™ (Rituximab-pvvr) – See Appendix J

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

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

13. Annual Review of Lutathera® (Lutetium Lu-177 Dotatate) and Vitrakvi® (Larotrectinib) – See Appendix K

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Lutathera® (Lutetium Lu-177 Dotatate) and Vitrakvi® (Larotrectinib)
D. Prior Authorization of Lutathera® (Lutetium Lu-177 Dotatate) and Vitrakvi® (Larotrectinib)
E. Market News and Updates
F. Recommendations

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

14. Annual Review of Multiple Sclerosis (MS) Medications and 30-Day Notice to Prior Authorize Mayzent® (Siponimod), Mavenclad® (Cladribine), and Vumerity™ (Diroximel Fumarate) – See Appendix L

A. Current Prior Authorization Criteria
B. Utilization of MS Medications
C. Prior Authorization of MS Medications
D. Market News and Updates
E. Mayzent® (Siponimod) Product Summary
F. Mavenclad® (Cladribine) Product Summary
G. Vumerity™ (Diroximel Fumarate) Product Summary
H. College of Pharmacy Recommendations
I. Utilization Details of MS Medications

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

15. 30-Day Notice to Prior Authorize Tepezza™ (Teprotumumab-trbw) – See Appendix M

A. Introduction
B. Market News and Updates
C. Tepezza™ (Teprotumumab-trbw) Product Summary
D. College of Pharmacy Recommendations

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

16. Annual Review of Anti-Emetic Medications – See Appendix N

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

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

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

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

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

A. Annual Review of Pharmacy Benefit
B. Anti-Diabetic Medications
C. Antihypertensive Medications
D. Lung Cancer Medications

**Future business subject to change.*

19. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF FEBRUARY 12, 2020

BOARD MEMBERS:	PRESENT	ABSENT
Stephen Anderson, Pharm.D.	x	
Markita Broyles, D.Ph.; MBA	x	
Darlla D. Duniphin, MHS; PA-C	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 Munoz, D.Ph.		x
James Osborne, Pharm.D.	x	

COLLEGE OF PHARMACY STAFF:	PRESENT	ABSENT
Michyla Adams, Pharm.D.; Clinical Pharmacist	x	
Wendi Chandler, Pharm.D.; Clinical Pharmacist	x	
Karen Egesdal, D.Ph.; SMAC-ProDUR Coordinator/OHCA Liaison	x	
Thomas Ha, Pharm.D.; Clinical Pharmacist		x
Bethany Holderread, Pharm.D.; Clinical Coordinator	x	
Amy Miller, Operations Coordinator	x	
Brandy Nawaz, Pharm.D.; Clinical Pharmacist	x	
Grant H. Skrepnek, Ph.D.; Associate Professor; Interim Director	x	
Regan Smith, Pharm.D.; Clinical Pharmacist		x
Ashley Teel, Pharm.D.; Clinical Pharmacist	x	
Jacquelyn Travers, Pharm.D.; Practice Facilitating Pharmacist	x	
Tri Van, Pharm.D.; Pharmacy Resident	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): Tyler Shannon	x	

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	
Michael Herndon, D.O.; Chief Medical Officer		x
Nancy Nesser, Pharm.D.; J.D.; Pharmacy Director		x
Jill Ratterman, D.Ph.; Clinical Pharmacist	x	
Nathan Valentine, M.D.; Medical Director		x
Kerri Wade, Pharmacy Operations Manager	x	

OTHERS PRESENT:		
Dave Poskey, UCB	Nima Nabavi, Amgen	Bobby White, Eisai
Doug Wood, ViiV	Jim Chapman, AbbVie	Doug McCann, Takeda
Amy Stanford, Pfizer	Kathy Gornatti, Greenwich	Audrey Rattan, Alkermes
Brian Maves, Pfizer		

PRESENT FOR PUBLIC COMMENT:
N/A

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

1A: ROLL CALL

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

ACTION: NONE REQUIRED

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

ACTION: NONE REQUIRED

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

3A: DECEMBER 11, 2019 DUR MINUTES – VOTE

3B: DECEMBER 11, 2019 DUR RECOMMENDATIONS MEMORANDUM

3C: JANUARY 8, 2020 DUR RECOMMENDATIONS MEMORANDUM

Materials included in agenda packet; presented by Dr. Muchmore

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: **NARROW THERAPEUTIC INDEX (NTI) DRUG LIST**

4A: NTI DRUG LIST

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: **UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/ADHD PRESCRIPTION USE IN REPRODUCTIVE-AGED WOMEN**

5A: PHARMACY HELPDESK ACTIVITY FOR JANUARY 2020

5B: MEDICATION COVERAGE ACTIVITY FOR JANUARY 2020

5C: ADHD PRESCRIPTION USE IN REPRODUCTIVE-AGED WOMEN

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE ULTOMIRIS® (RAVULIZUMAB-CWVZ)**

6A: INTRODUCTION

6B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Holderread

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: **VOTE TO PRIOR AUTHORIZE KORLYM® (MIFEPRISTONE)**

7A: INTRODUCTION

7B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Holderread

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: **VOTE TO PRIOR AUTHORIZE DUAKLIR® PRESSAIR® (ACLIDINIUM BROMIDE/FORMOTEROL FUMARATE) AND TO UPDATE THE PRIOR AUTHORIZATION CRITERIA FOR FASENRA® (BENRALIZUMAB) AND NUCALA® (MEPOLIZUMAB)**

8A: INTRODUCTION

8B: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Nawaz
Dr. Garton moved to approve; seconded by Dr. Broyles
ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: VOTE TO PRIOR AUTHORIZE ROCKLATAN® (NETARSUDIL/LATANOPROST 0.02%/0.005% OPHTHALMIC SOLUTION)
9A: INTRODUCTION
9B: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Nawaz
Dr. Anderson moved to approve; seconded by Dr. Garton
ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: VOTE TO PRIOR AUTHORIZE SCENESSE® (AFAMELANOTIDE) AND GIVLAARI™ (GIVOSIRAN)
10A: INTRODUCTION
10B: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Adams
Dr. Broyles moved to approve; seconded by Dr. Anderson
ACTION: MOTION CARRIED

AGENDA ITEM NO. 11: VOTE TO PRIOR AUTHORIZE RUZURGI® (AMIFAMPRIDINE)
11A: INTRODUCTION
11B: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Van
Dr. Mitchell moved to approve; seconded by Dr. Garton
ACTION: MOTION CARRIED

AGENDA ITEM NO. 12: ANNUAL REVIEW OF LEUKEMIA MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ASPARLAS™ (CALASPARGASE PEGOL-MKNL), DAURISMO™ (GLASDEGIB), IDHIFA® (ENASIDENIB), LUMOXITI™ (MOXETUMOMAB PASUDOTOX-TDFK), TIBSOVO® (IVOSIDENIB), AND XOSPATA® (GILTERITINIB)
12A: INTRODUCTION
12B: CURRENT PRIOR AUTHORIZATION CRITERIA
12C: UTILIZATION OF LEUKEMIA MEDICATIONS
12D: PRIOR AUTHORIZATION OF LEUKEMIA MEDICATIONS
12E: MARKET NEWS AND UPDATES
12F: PRODUCT SUMMARIES
12G: RECOMMENDATIONS
12H: UTILIZATION DETAILS OF LEUKEMIA MEDICATIONS
Materials included in agenda packet; presented by Dr. Schmidt
ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: 30-DAY NOTICE TO PRIOR AUTHORIZE AZEDRA® (IOBENGUANE I-131)
13A: INTRODUCTION
13B: MARKET NEWS AND UPDATES
13C: AZEDRA® (IOBENGUANE I-131) PRODUCT SUMMARY
13D: RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Schmidt
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: ANNUAL REVIEW OF FACTOR REPLACEMENT PRODUCTS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ESPEROCT® [ANTIHEMOPHILIC FACTOR (RECOMBINANT), GLYCOPEGYLATED-EXEI]
14A: CURRENT PRIOR AUTHORIZATION CRITERIA

14B: UTILIZATION OF FACTOR REPLACEMENT PRODUCTS
14C: PRIOR AUTHORIZATION OF FACTOR REPLACEMENT PRODUCTS
14D: MARKET NEWS AND UPDATES
14E: ESPEROCT® [ANTIHEMOPHILIC FACTOR (RECOMBINANT), GLYCOPEGYLATED-EXEI] PRODUCT SUMMARY
14F: RECOMMENDATIONS
14G: UTILIZATION DETAILS OF FACTOR REPLACEMENT PRODUCTS
Materials included in agenda packet; presented by Dr. Ratterman
ACTION: NONE REQUIRED

AGENDA ITEM NO. 15: ANNUAL REVIEW OF ANTI-MIGRAINE MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE TOSYMRA™ (SUMATRIPTAN NASAL SPRAY), REYVOW™ (LASMIDITAN), AND UBRELVY™ (UBROGEPANT)
15A: CURRENT PRIOR AUTHORIZATION CRITERIA
15B: UTILIZATION OF ANTI-MIGRAINE MEDICATIONS
15C: PRIOR AUTHORIZATION OF ANTI-MIGRAINE MEDICATIONS
15D: MARKET NEWS AND UPDATES
15E: TOSYMRA™ (SUMATRIPTAN NASAL SPRAY) PRODUCT SUMMARY
15F: REYVOW™ (LASMIDITAN TABLETS) PRODUCT SUMMARY
15G: UBRELVY™ (UBROGEPANT TABLETS) PRODUCT SUMMARY
15H: COLLEGE OF PHARMACY RECOMMENDATIONS
15I: UTILIZATION DETAILS OF ANTI-MIGRAINE MEDICATIONS
Materials included in agenda packet; presented by Dr. Holderread
ACTION: NONE REQUIRED

AGENDA ITEM NO. 16: ANNUAL REVIEW OF ANTICONVULSANTS AND 30-DAY NOTICE TO PRIOR AUTHORIZE XCOPRI® (CENOBAMATE)
16A: CURRENT PRIOR AUTHORIZATION CRITERIA
16B: UTILIZATION OF ANTICONVULSANTS
16C: PRIOR AUTHORIZATION OF ANTICONVULSANTS
16D: MARKET NEWS AND UPDATES
16E: XCOPRI® (CENOBAMATE) PRODUCT SUMMARY
16F: COLLEGE OF PHARMACY RECOMMENDATIONS
16G: UTILIZATION DETAILS OF ANTICONVULSANTS
Materials included in agenda packet; presented by Dr. Adams
ACTION: NONE REQUIRED

AGENDA ITEM NO. 17: ANNUAL REVIEW OF OSTEOPOROSIS MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE EVENITY® (ROMOSOZUMAB-AQQG)
17A: CURRENT PRIOR AUTHORIZATION CRITERIA
17B: UTILIZATION OF OSTEOPOROSIS MEDICATIONS
17C: PRIOR AUTHORIZATION OF OSTEOPOROSIS MEDICATIONS
17D: MARKET NEWS AND UPDATES
17E: EVENITY® (ROMOSOZUMAB-AQQG) PRODUCT SUMMARY
17F: COLLEGE OF PHARMACY RECOMMENDATIONS
17G: UTILIZATION DETAILS OF OSTEOPOROSIS MEDICATIONS
Materials included in agenda packet; presented by Dr. Van
ACTION: NONE REQUIRED

AGENDA ITEM NO. 18: ANNUAL REVIEW OF INHALED SHORT-ACTING BETA$_2$ AGONISTS AND 30-DAY NOTICE TO PRIOR AUTHORIZE PROAIR® DIGIHALER™ (ALBUTEROL SULFATE INHALATION POWDER)
18A: CURRENT PRIOR AUTHORIZATION CRITERIA
18B: UTILIZATION OF INHALED SHORT-ACTING BETA$_2$ AGONISTS

18C: PRIOR AUTHORIZATION OF INHALED SHORT-ACTING BETA$_2$ AGONISTS
18D: MARKET NEWS AND UPDATES
18E: PROAIR® DIGIHALER™ (ALBUTEROL SULFATE INHALATION POWDER) PRODUCT SUMMARY
18F: COLLEGE OF PHARMACY RECOMMENDATIONS
18G: UTILIZATION DETAILS OF INHALED SHORT-ACTING BETA$_2$ AGONISTS
Materials included in agenda packet; presented by Dr. Nawaz
ACTION: NONE REQUIRED

AGENDA ITEM NO. 19: U.S. FOOD AND DRUG ADMINISTRATION (FDA) AND DRUG ENFORCEMENT ADMINISTRATION (DEA) UPDATES
Materials included in agenda packet; presented by Dr. Holderread
ACTION: NONE REQUIRED

AGENDA ITEM NO. 20: FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)
20A: MULTIPLE SCLEROSIS (MS) MEDICATIONS
20B: LYMPHOMA MEDICATIONS
20C: ANTI-PARASITIC MEDICATIONS
20D: ANTI-EMETIC MEDICATIONS
**Future business subject to change.*
Materials included in agenda packet; Non-presentation; Questions only
ACTION: NONE REQUIRED

AGENDA ITEM NO. 21: ADJOURNMENT
The meeting was adjourned at 5:02pm.

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

Memorandum

Date: February 13, 2020

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

Terry Cothran, D.Ph.
Pharmacy Director
OHCA

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

Subject: Drug Utilization Review (DUR) Board Recommendations from Meeting of February 12, 2020

Recommendation 1: Narrow Therapeutic Index (NTI) Drug List

NO ACTION REQUIRED.

Recommendation 2: ADHD Prescription Use in Reproductive-Aged Women

NO ACTION REQUIRED.

Recommendation 3: Vote to Prior Authorize Ultomiris® (Ravulizumab-cwvz)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following criteria for Soliris® (eculizumab) for the treatment of neuromyelitis optica spectrum disorder:

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.

Additionally, the College of Pharmacy recommends the prior authorization of Ultomiris® (ravulizumab) with the following criteria:

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

1. Member must have an established diagnosis of paroxysmal nocturnal hemoglobinuria 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.

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

1. Member must have a documented diagnosis of aHUS.

Recommendation 4: Vote to Prior Authorize Korlym® (Mifepristone)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Korlym® (mifepristone) with the following criteria:

Korlym® (Mifepristone) Approval Criteria:

1. An FDA approved indication to control hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing's syndrome who have type 2 diabetes mellitus (T2DM) or glucose intolerance; and
2. Member must have failed surgery intended to correct the cause of endogenous Cushing's syndrome or not be a candidate for surgery that is expected to correct the cause of endogenous Cushing's syndrome; and
3. Member must be 18 years of age or older; and
4. Korlym® must be prescribed by, or in consultation with, an endocrinologist (or be an advanced care practitioner with a supervising physician who is an endocrinologist); and
5. Female members must not be pregnant and must have a negative pregnancy test prior to initiation of therapy; and
6. Female members of reproductive potential must use a non-hormonal, medically acceptable method of contraception (unless member has undergone surgical sterilization) during treatment with Korlym® and for at least 1 month after discontinuing treatment; and
7. Member must not have any contraindications to taking Korlym® including the following:
    a. Taking drugs metabolized by CYP3A such as simvastatin, lovastatin, and CYP3A substrates with narrow therapeutic ranges, such as cyclosporine, dihydroergotamine, ergotamine, fentanyl, pimozide, quinidine, sirolimus, and tacrolimus; and

b. Receiving systemic corticosteroids for lifesaving purposes (e.g., immunosuppression after organ transplantation); and
c. Female members must not have a history of unexplained vaginal bleeding or endometrial hyperplasia with atypia or endometrial carcinoma; and
d. Known hypersensitivity to mifepristone or to any of the product components; and

8. Authorizations will be for the duration of 12 months; and
9. Reauthorization may be granted if the prescriber documents the member is responding well to treatment.

Recommendation 5: Vote to Prior Authorize Duaklir® Pressair® (Aclidinium Bromide/Formoterol Fumarate) and to Update the Prior Authorization Criteria for Fasenra® (Benralizumab) and Nucala® (Mepolizumab)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Duaklir® Pressair® (aclidinium bromide/formoterol fumarate) with the following criteria (changes and additions noted in red):

Anoro® Ellipta® (Umeclidinium/Vilanterol), Bevespi Aerosphere® (Glycopyrrolate/Formoterol Fumarate), Duaklir® Pressair® (Aclidinium Bromide/Formoterol Fumarate), Stiolto® Respimat® (Tiotropium/Olodaterol), and Utibron® Neohaler® (Indacaterol/Glycopyrrolate) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of chronic obstructive pulmonary disease (COPD); and
3. A patient-specific, clinically significant reason why the member cannot use Tier-1 long-acting beta$_2$ agonist (LABA) and long-acting muscarinic antagonist (LAMA) individual components must be provided.

Additionally, the College of Pharmacy recommends updating the Fasenra® (benralizumab) and Nucala® (mepolizumab) prior authorization criteria with the following changes noted in red:

Fasenra® (Benralizumab Injection) Approval Criteria:

1. An FDA approved indication for add-on maintenance treatment of patients with severe eosinophilic phenotype asthma; and
2. Member must be 12 years of age or older; and
3. Member must have a blood eosinophil count of ≥150cells/mcL (can apply to either a recent level or in history prior to oral corticosteroid use); and
4. Member must have had at least 2 asthma exacerbations requiring systemic corticosteroids within the last 12 months or require daily systemic corticosteroids despite compliant use of medium-to-high dose inhaled corticosteroid (ICS) plus at least 1 additional controller medication; and
5. Member must have failed a medium-to-high dose ICS used compliantly for at least the past 12 months (for ICS/LABA combination products, the ICS component would meet criteria at an equivalent medium-to-high dose); and
6. Member must have failed at least 1 other asthma controller medication used in addition to the medium-to-high-dose ICS compliantly for at least the past 3 months; and

7. For authorization of Fasenra® prefilled syringe, prescriber must verify the injection will be administered in a health care setting by a health care professional prepared to manage anaphylaxis; or
8. For authorization of Fasenra® prefilled autoinjector pen, 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 Fasenra®; and
9. Fasenra® must be prescribed by an allergist, pulmonologist, or pulmonary specialist or the member must have been evaluated by an allergist, pulmonologist, or pulmonary specialist within the last 12 months (or be an advanced care practitioner with a supervising physician who is an allergist, pulmonologist, or pulmonary specialist); and
10. Initial approvals will be for the duration of 6 months after which time compliance will be evaluated for continued approval; and
11. A quantity limit of 1 prefilled syringe or prefilled autoinjector pen per 56 days will apply.

Nucala® (Mepolizumab Injection) Approval Criteria [Severe Eosinophilic Phenotype Asthma Diagnosis]:

1. An FDA approved indication for add-on maintenance treatment of patients with severe eosinophilic phenotype asthma; and
2. Member must be ~~12~~ 6 years of age or older; and
3. Member must have a blood eosinophil count of ≥150 cells/mcL (can apply to either a recent level or in history prior to oral corticosteroid use); and
4. Member must have had at least 2 asthma exacerbations requiring systemic corticosteroids within the last 12 months or require daily systemic corticosteroids despite compliant use of medium-to-high dose inhaled corticosteroid (ICS) plus at least 1 additional controller medication; and
5. Member must have failed a medium-to-high dose ICS used compliantly for at least the past 12 months (for ICS/LABA combination products, the ICS component would meet criteria at an equivalent medium-to-high dose); and
6. Member must have failed at least 1 other asthma controller medication used in addition to the medium-to-high-dose ICS compliantly for at least the past 3 months; and
7. 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
8. 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
9. Nucala® must be prescribed by an allergist, pulmonologist, or pulmonary specialist or the member must have been evaluated by an allergist, pulmonologist, or pulmonary specialist within the last 12 months (or be an advanced care practitioner with a supervising physician who is an allergist, pulmonologist, or pulmonary specialist); and
10. Initial approvals will be for the duration of 6 months after which time compliance will be evaluated for continued approval; and
11. A quantity limit of 1 vial, prefilled autoinjector, or prefilled syringe per 28 days will apply.

Nucala® (Mepolizumab Injection) Approval Criteria [Eosinophilic Granulomatosis with Polyangiitis (EGPA) Diagnosis]:

1. An FDA approved diagnosis of EGPA; and
2. Member meets 1 of the following:
    a. Member must have a past history of at least 1 confirmed EGPA relapse [requiring increase in oral corticosteroid (OCS) dose, initiation/increased dose of immunosuppressive therapy, or hospitalization] within the past 12 months; or
    b. Member must have refractory disease within the last 6 months following induction of a standard treatment regimen administered compliantly for at least 3 months; and
3. Diagnosis of granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) will not be approved; and
4. Failure to achieve remission despite corticosteroid therapy (oral prednisone equivalent ≥7.5mg/day) for a minimum of 4 weeks duration; and
5. Nucala® must be prescribed by an allergist, pulmonologist, pulmonary specialist, or rheumatologist or the member must have been evaluated by an allergist, pulmonologist, pulmonary specialist, or rheumatologist within the last 12 months (or be an advanced care practitioner with a supervising physician who is an allergist, pulmonologist, pulmonary specialist, or rheumatologist); and
6. 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
7. 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
8. A quantity limit of 3 vials, prefilled autoinjectors, or prefilled syringes per 28 days will apply; and
9. 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 a Birmingham Vasculitis Activity Score (BVAS) of 0 (zero), fewer EGPA relapses from baseline, or a decrease in daily OCS dosing from baseline.

Recommendation 6: Vote to Prior Authorize Rocklatan® (Netarsudil/Latanoprost 0.02%/0.005% Ophthalmic Solution)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the placement of Rocklatan® (netarsudil/latanoprost 0.02%/0.005% ophthalmic solution) into Tier-1 of the Glaucoma Medications Product Based Prior Authorization (PBPA) category based on manufacturer supplemental rebate participation. If the manufacturer chooses not to provide a supplemental rebate, Rocklatan® will be placed into the Special Prior Authorization (PA) Tier and current Special PA criteria would apply. Tier placement is shown in blue in the following chart to reflect current supplemental rebate status.

Glaucoma Medications Tier-2 Approval Criteria:

1. An FDA approved diagnosis; and
2. The member must have documented, recent (within the last 120 days) trials with at least 3 Tier-1 medications for a minimum of 4 weeks duration each. Tier-1 trials may be from any pharmacologic class; or
3. Approvals may be granted if there is a documented adverse effect, drug interaction, or contraindication to all Tier-1 medications; or
4. Approvals may be granted if there is a unique FDA approved indication not covered by all Tier-1 medications; and
5. The member must have had a comprehensive, dilated eye exam within the last 365-day period as recommended by the National Institutes of Health; and
6. Approvals will be for the duration of 1 year.

Glaucoma Medications Special Prior Authorization (PA) Approval Criteria:

1. An FDA approved diagnosis; and
2. A patient-specific, clinically significant reason why a special formulation is needed over a Tier-1 or Tier-2 medication must be provided; or
3. Approvals may be granted if there is a documented adverse effect, drug interaction, or contraindication to all Tier-1 and Tier-2 medications; or
4. Approvals may be granted if there is a unique FDA approved indication not covered by all Tier-1 and Tier-2 medications; and
5. The member must have had a comprehensive, dilated eye exam within the last 365-day period as recommended by the National Institutes of Health; and
6. Approvals will be for the duration of 1 year.

Glaucoma Medications*		
Tier-1	**Tier-2**	**Special PA**
Alpha-2 Adrenergic Agonists		
brimonidine (Alphagan® 0.2%)	apraclonidine (Iopidine® 0.5%, 1%)	brimonidine (Alphagan-P® 0.15%)
brimonidine (Alphagan-P® 0.1%)		
brimonidine/timolol (Combigan® 0.2%/0.5%)		
brinzolamide/brimonidine (Simbrinza® 0.2%/1%)		
Beta-Blockers		
brimonidine/timolol (Combigan® 0.2%/0.5%)	betaxolol (Betoptic® 0.5%, Betoptic-S® 0.25%)	dorzolamide/timolol (Cosopt® PF 2%/0.5%)
carteolol (Ocupress® 1%)		timolol maleate (Timoptic Ocudose® 0.25%, 0.5%; Timoptic-XE® 0.25%, 0.5%)
dorzolamide/timolol (Cosopt® 22.3/6.8mg/mL)		
levobunolol (Betagan® 0.25%, 0.5%)		
timolol maleate (Istalol® 0.5%, Timoptic® 0.25%, 0.5%)		

Glaucoma Medications*		
Tier-1	**Tier-2**	**Special PA**
Carbonic Anhydrase Inhibitors		
acetazolamide (Diamox® 500mg caps; 125mg, 250mg tabs)+		dorzolamide/timolol (Cosopt® PF 2%/0.5%)
brinzolamide (Azopt® 1%)		methazolamide (Neptazane® 25mg, 50mg tabs)+
brinzolamide/brimonidine (Simbrinza® 0.2%/1%)		
dorzolamide (Trusopt® 2%)		
dorzolamide/timolol (Cosopt® 22.3/6.8mg/mL)		
Cholinergic Agonists/Cholinesterase Inhibitors		
echothiophate iodide (Phospholine Iodide® 0.125%)	pilocarpine (Isopto® Carpine 1%, 2%, 4%)	
Prostaglandin Analogs		
latanoprost (Xalatan® 0.005%)	bimatoprost (Lumigan® 0.01%, 0.03%)	latanoprost (Xelpros® 0.005%)
netarsudil/latanoprost (Rocklatan® 0.02%/0.005%)	tafluprost (Zioptan® 0.0015%)	latanoprostene bunod (Vyzulta® 0.024%)
travoprost (Travatan-Z® 0.004%)		
Rho Kinase Inhibitors		
netarsudil (Rhopressa® 0.02%)		
netarsudil/latanoprost (Rocklatan® 0.02%/0.005%)		

*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
+Indicates available oral medications.
Please note: Combination products are included in both applicable pharmaceutical classes; therefore, combination products are listed twice in the tier chart.
caps = capsules; tabs = tablets; PA = prior authorization; PF = preservative free

Recommendation 7: Vote to Prior Authorize Scenesse® (Afamelanotide) and Givlaari™ (Givosiran)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Scenesse® (afamelanotide) and Givlaari™ (givosiran) with the following criteria:

Scenesse® (Afamelanotide) Approval Criteria:

1. An FDA approved indication to increase pain-free light exposure in adult patients with a history of phototoxic reactions from erythropoietic protoporphyria (EPP); and
   a. The diagnosis of EPP must be confirmed by genetic testing; and
2. Member must be 18 years of age or older; and
3. Scenesse® must be administered by a health care professional who is proficient in the subcutaneous (subQ) implantation procedure and has completed the training program provided by the manufacturer prior to administration of the Scenesse® implant; and

a. Scenesse® must be shipped via cold chain supply shipping and delivery to the health care setting where the member is scheduled to receive the implant administration; and
b. Scenesse® must be stored under refrigeration (36 to 46°F) and protected from light prior to implantation; and

4. The Scenesse® implant should be inserted using an SFM Implantation Cannula or other implantation device that has been determined by the manufacturer to be suitable for implantation of Scenesse®; and
5. The prescriber must agree that the member will be monitored by a health care provider for at least 30 minutes after the implant administration; and
6. The prescriber must agree that the member will have a full body skin examination performed at least twice yearly while the member is being treated with Scenesse® to monitor pre-existing and new skin pigmentary lesions; and
7. Documentation that member will maintain sun and light protection measures during treatment with Scenesse® to prevent phototoxic reactions related to EPP; and
8. A quantity limit of 1 implant per 60 days will apply. Initial approvals will be for 2 implants for the duration of 4 months. Further approval may be granted if the prescriber documents that the member is responding well to treatment as indicated by increased tolerance of sunlight (i.e., less phototoxic reactions).

Givlaari™ (Givosiran) Approval Criteria:

1. An FDA approved diagnosis of acute hepatic porphyria (AHP) confirmed by:
   a. Genetic testing; or
   b. Elevated urinary porphobilinogen (PBG) and signs/symptoms of AHP; and
2. Member must be 18 years of age or older; and
3. Givlaari™ must be administered in a health care setting by a health care professional prepared to manage anaphylaxis; and
   a. Givlaari™ must be shipped to the health care setting where the member is scheduled to receive treatment; and
4. The prescriber must agree to monitor liver function tests prior to initiating treatment with Givlaari™, every month during the first 6 months of treatment, and as clinically indicated thereafter; and
5. The prescriber must agree to monitor renal function during treatment with Givlaari™ as clinically indicated; and
6. Member must not be taking sensitive CYP1A2 or CYP2D6 substrates (e.g., caffeine, dextromethorphan, duloxetine, amitriptyline, olanzapine, fluoxetine, paroxetine, hydrocodone, tramadol) concomitantly with Givlaari™; and
7. 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; and
8. Initial approvals will be for the duration of 6 months. Further approval may be granted if the prescriber documents that the member is responding well to treatment as indicated by less porphyria attacks and that the member does not have elevated transaminase levels.

Recommendation 8: Vote to Prior Authorize Ruzurgi® (Amifampridine)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Ruzurgi® (amifampridine) and recommends updating the current Firdapse® (amifampridine) prior authorization criteria (changes and additions noted in red):

Firdapse® (Amifampridine) and Ruzurgi® (Amifampridine) Approval Criteria:

1. An FDA approved diagnosis of Lambert-Eaton myasthenic syndrome (LEMS); and
2. LEMS diagnosis must be confirmed by 1 of the following:
   a. A high titer anti-P/Q-type voltage-gated calcium channel (VGCC) antibody assay; or
   b. A confirmatory electrodiagnostic study [e.g., repetitive nerve stimulation (RNS), needle electromyography (EMG), single-fiber electromyography (SFEMG)]; and
3. The requested medication must be prescribed by, or in consultation with, a neurologist or oncologist; and
4. Member must not have a history of seizures or be taking medications that lower the seizure threshold (e.g., bupropion, tramadol, amphetamines, theophylline); and
5. For Firdapse®, a patient-specific, clinically significant reason why the member cannot use Ruzurgi® must be provided; and
6. For Firdapse®, a quantity limit of 240 tablets per 30 days will apply. For Ruzurgi®, a quantity limit of 300 tablets per 30 days will apply; and
7. Initial approvals will be for 6 months. Consideration for continued authorization will require the prescriber to indicate that the member is responding well to treatment and continues to require treatment with the requested medication.

Recommendation 9: Annual Review of Leukemia Medications and 30-Day Notice to Prior Authorize Asparlas™ (Calaspargase Pegol-mknl), Daurismo™ (Glasdegib), Idhifa® (Enasidenib), Lumoxiti™ (Moxetumomab Pasudotox-tdfk), Tibsovo® (Ivosidenib), and Xospata® (Gilteritinib)

NO ACTION REQUIRED.

Recommendation 10: 30-Day Notice to Prior Authorize Azedra® (Iobenguane I-131)

NO ACTION REQUIRED.

Recommendation 11: Annual Review of Factor Replacement Products and 30-Day Notice to Prior Authorize Esperoct® [Antihemophilic Factor (Recombinant), Glycopegylated-exei]

NO ACTION REQUIRED.

Recommendation 12: Annual Review of Anti-Migraine Medications and 30-Day Notice to Prior Authorize Tosymra™ (Sumatriptan Nasal Spray), Reyvow™ (Lasmiditan), and Ubrelvy™ (Ubrogepant)

NO ACTION REQUIRED.

Recommendation 13: Annual Review of Anticonvulsants and 30-Day Notice to Prior Authorize Xcopri® (Cenobamate)

NO ACTION REQUIRED.

Recommendation 14: Annual Review of Osteoporosis Medications 30-Day Notice to Prior Authorize Evenity® (Romosozumab-aqqg)

NO ACTION REQUIRED.

Recommendation 15: Annual Review of Inhaled Short-Acting Beta$_2$ Agonists and 30-Day Notice to Prior Authorize ProAir® Digihaler™ (Albuterol Sulfate Inhalation Powder)

NO ACTION REQUIRED.

Recommendation 16: U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates

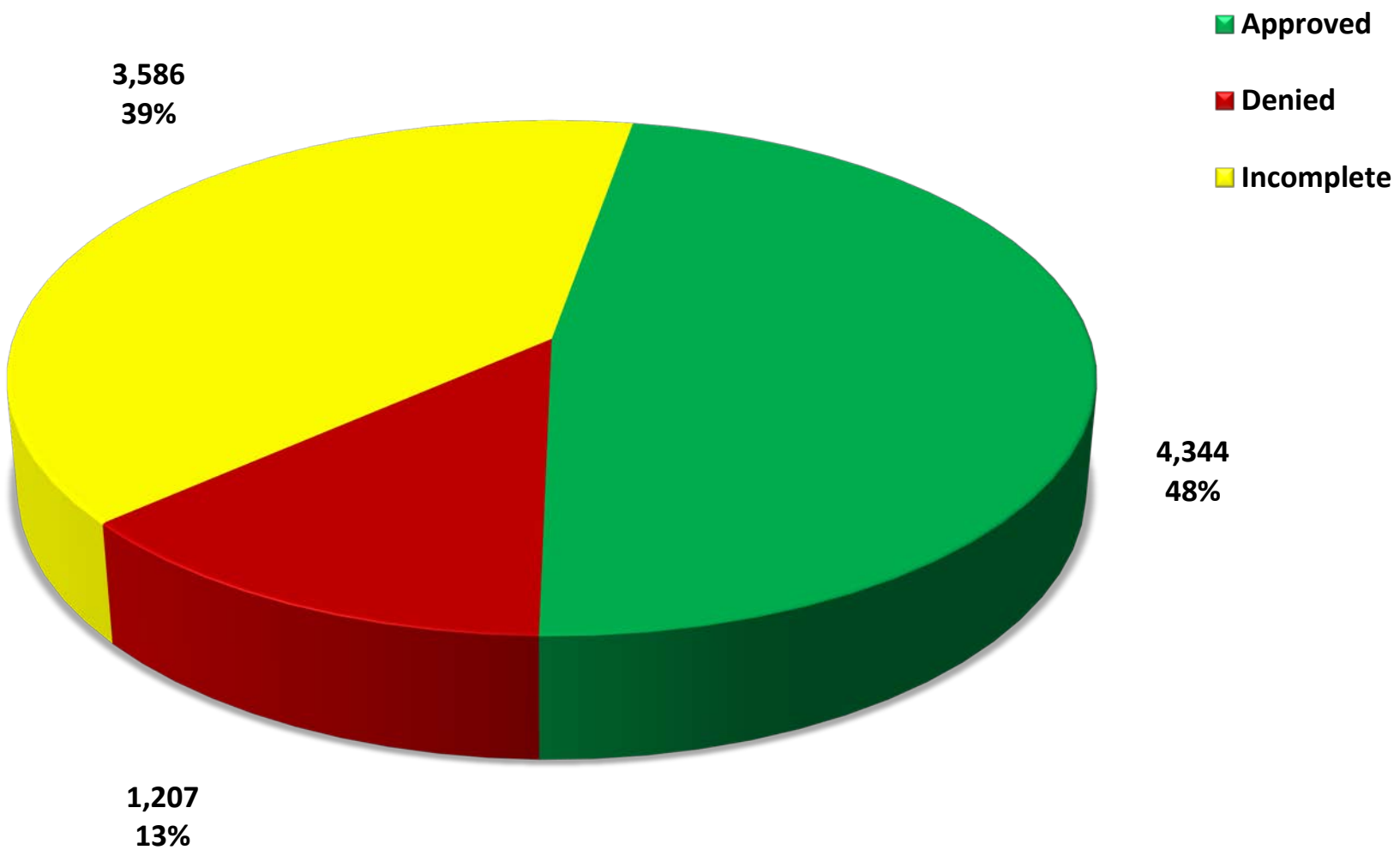
NO ACTION REQUIRED.

Recommendation 17: Future Business

NO ACTION REQUIRED.

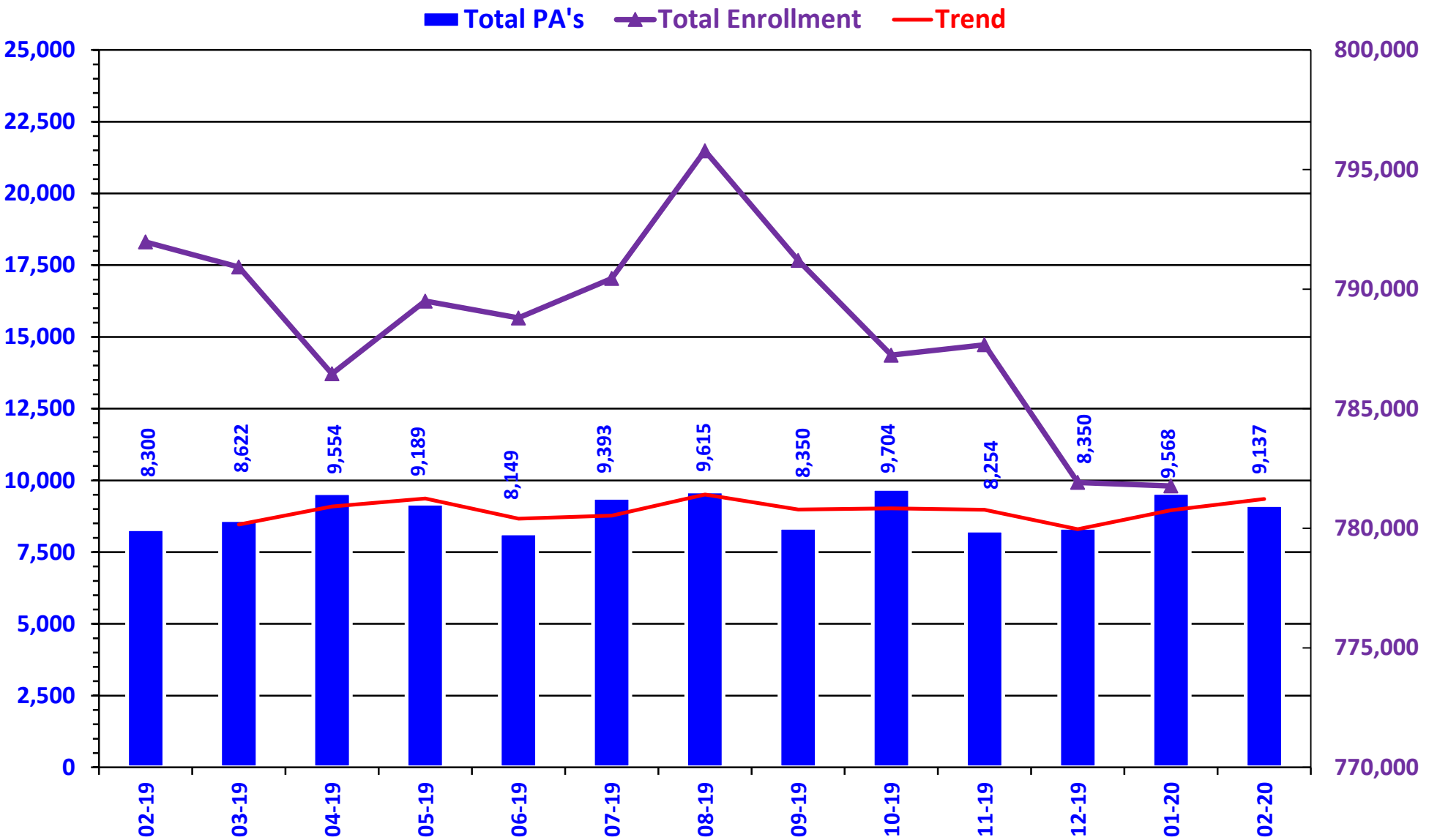
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: FEBRUARY 2020



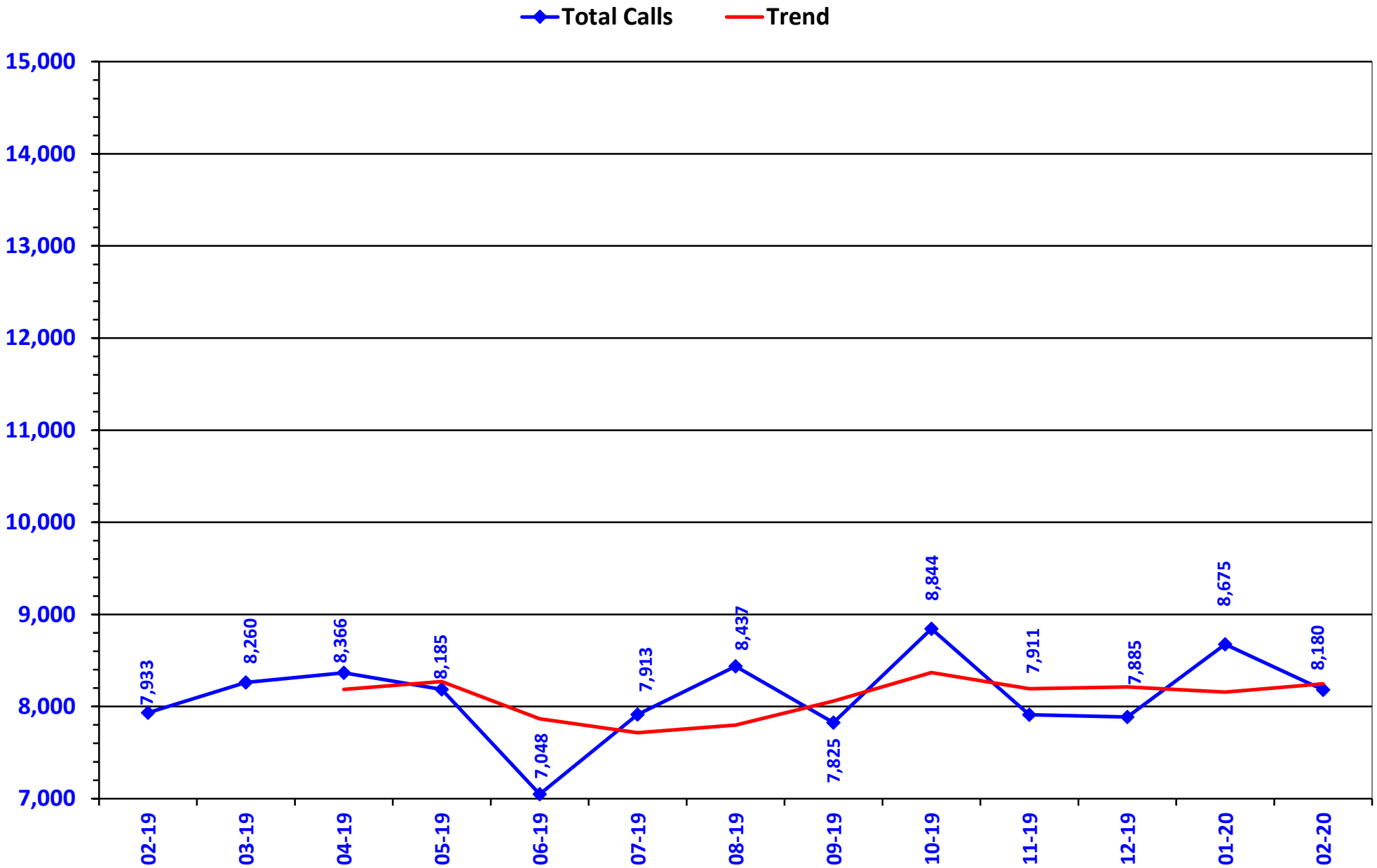
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: FEBRUARY 2019 – FEBRUARY 2020



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
FEBRUARY 2019 – FEBRUARY 2020



Prior Authorization Activity

2/1/2020 Through 2/29/2020

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	67	7	16	44	333
Analgesic - NonNarcotic	21	0	3	18	0
Analgesic, Narcotic	408	163	33	212	153
Antiasthma	96	28	20	48	295
Antibiotic	32	20	1	11	273
Anticonvulsant	204	90	21	93	302
Antidepressant	194	48	29	117	326
Antidiabetic	280	96	51	133	353
Antigout	10	4	2	4	360
Antihistamine	27	6	9	12	303
Antimigraine	202	38	80	84	177
Antineoplastic	101	67	4	30	180
Antiulcers	156	51	31	74	165
Anxiolytic	22	6	2	14	120
Atypical Antipsychotics	256	120	27	109	356
Biologics	185	94	27	64	290
Bladder Control	48	9	13	26	358
Blood Thinners	280	166	11	103	342
Botox	43	32	6	5	295
Buprenorphine Medications	90	26	7	57	42
Cardiovascular	72	31	7	34	287
Chronic Obstructive Pulmonary Disease	150	27	41	82	337
Constipation/Diarrhea Medications	158	26	56	76	263
Contraceptive	15	7	1	7	310
Dermatological	315	87	97	131	114
Diabetic Supplies	867	491	70	306	268
Endocrine & Metabolic Drugs	100	50	17	33	191
Erythropoietin Stimulating Agents	22	14	3	5	106
Fibromyalgia	28	4	2	22	191
Fish Oils	14	1	8	5	361
Gastrointestinal Agents	133	30	28	75	200
Genitourinary Agents	12	7	1	4	218
Glaucoma	16	3	3	10	54
Growth Hormones	177	137	8	32	140
Hematopoietic Agents	12	9	0	3	135
Hepatitis C	112	65	8	39	8
HFA Rescue Inhalers	77	3	6	68	256
Insomnia	39	2	5	32	129
Insulin	179	68	17	94	346
Miscellaneous Antibiotics	25	7	5	13	16
Multiple Sclerosis	41	18	8	15	242
Muscle Relaxant	55	8	17	30	29
Nasal Allergy	58	10	15	33	111
Neurological Agents	98	35	18	45	224
NSAIDs	31	2	8	21	186
Ocular Allergy	27	3	13	11	85
Ophthalmic Anti-infectives	12	0	2	10	0
Osteoporosis	28	7	9	12	329
Other*	280	67	60	153	283
Otic Antibiotic	19	3	8	8	15

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Pediculicide	34	1	13	20	19
Prenatal Vitamins	13	0	3	10	0
Respiratory Agents	61	44	1	16	165
Statins	21	9	4	8	224
Stimulant	775	373	67	335	350
Synagis	88	48	6	34	56
Testosterone	63	14	19	30	336
Topical Antifungal	27	3	5	19	105
Topical Corticosteroids	80	1	43	36	21
Vitamin	66	16	37	13	148
Pharmacotherapy	63	55	0	8	300
Emergency PAs	0	0	0	0	
Total	**7,185**	**2,857**	**1,132**	**3,196**	
Overrides					
Brand	53	35	4	14	307
Compound	16	12	0	4	74
Cumulative Early Refill	3	1	0	2	13
Diabetic Supplies	5	5	0	0	114
Dosage Change	350	331	1	18	13
High Dose	7	6	0	1	273
IHS-Brand	1	0	0	1	0
Ingredient Duplication	29	19	1	9	23
Lost/Broken Rx	83	78	2	3	15
MAT Override	254	207	5	42	67
NDC vs Age	263	159	32	72	232
NDC vs Sex	7	7	0	0	158
Nursing Home Issue	59	57	0	2	14
Opioid MME Limit	143	83	5	55	99
Opioid Quantity	49	40	2	7	159
Other*	59	52	3	4	17
Quantity vs. Days Supply	508	344	19	145	247
STBS/STBSM	24	19	1	4	69
Step Therapy Exception	6	6	0	0	283
Stolen	8	8	0	0	31
Third Brand Request	25	18	0	7	18
Overrides Total	**1,952**	**1,487**	**75**	**390**	
Total Regular PAs + Overrides	**9,137**	**4,344**	**1,207**	**3,586**	

Denial Reasons	
Unable to verify required trials.	2,669
Does not meet established criteria.	1,263
Lack required information to process request.	849
Other PA Activity	
Duplicate Requests	782
Letters	14,966
No Process	6
Changes to existing PAs	724
Helpdesk Initiated Prior Authorizations	730
PAs Missing Information	15

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

SoonerPsych Program Update

Oklahoma Health Care Authority
March 2020

Prescriber Mailing Summary

The SoonerPsych program is an educational quarterly mailing to prescribers treating members utilizing atypical antipsychotic medications. Each mailing includes a gauge showing prescribers how their practice compares to those of other SoonerCare prescribers of atypical antipsychotic medications regarding potential differences from evidence-based prescribing practices. Each mailing also includes an informational page with evidence-based material related to the mailing topics. Mailing topics are comprised of 4 modules: adherence, diagnosis, metabolic monitoring, and polypharmacy.

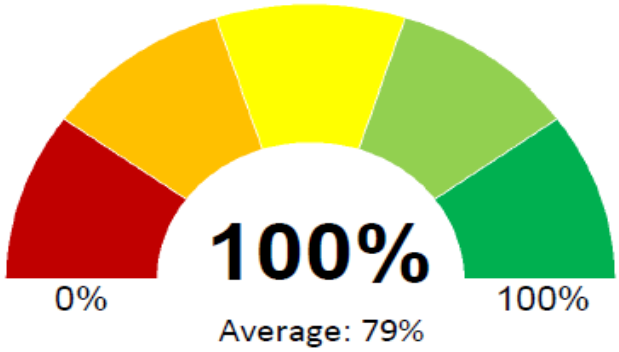
The SoonerPsych program has been using a "report card" format since April 2014. Beginning in April 2016, educational letters were sent to the same group of prescribers with all modules included in each mailing. The mailing list is updated approximately every 2 years, and included prescribers receive 4 letters per year to better inform them of their SoonerCare patients taking atypical antipsychotic medications and to make it more convenient to track patients and prescribing over time including any improvements or changes. Inclusion criteria requires the prescriber to have 5 or more SoonerCare patients taking atypical antipsychotic medications. The mailing list was recently updated in January 2020, and a total of 217 prescribers were selected for inclusion in the January 2020 mailing.

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

- **Adherence:** Adherence is defined as members whose proportion of days covered (PDC) or adherence calculated from pharmacy claims history for atypical antipsychotic medications was ≥80%.
- **Diagnosis:** Diagnosis is defined as members whose recent 12-month medical claims history included a diagnosis with a strong indication for prescribing an atypical antipsychotic medication.
- **Metabolic Monitoring:** Metabolic monitoring is defined as members whose recent 12-month medical claims history included glucose testing. Metabolic monitoring also evaluates the recent 12-month medical claims history for lipid testing for members with a diagnosis of hyperlipidemia.
- **Polypharmacy:** Polypharmacy is defined as members whose pharmacy claims history indicated concurrent use of 2 or more atypical antipsychotic medications for >90 days.

Example Gauge

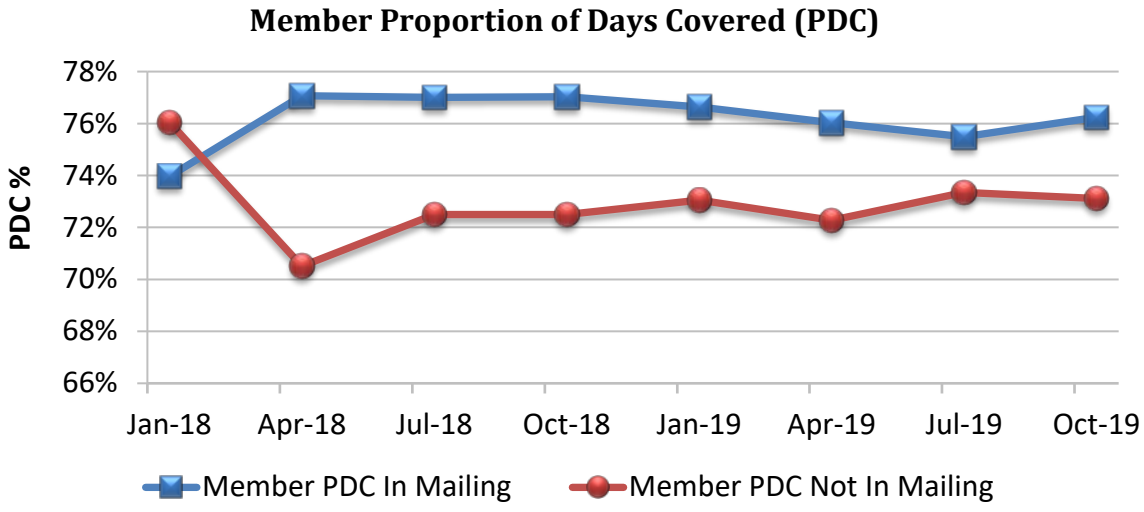
Each gauge includes the individual prescriber's performance in relation to the specific module as well as the average of other SoonerCare prescribers for comparison. The following is an example gauge included in the mailings.



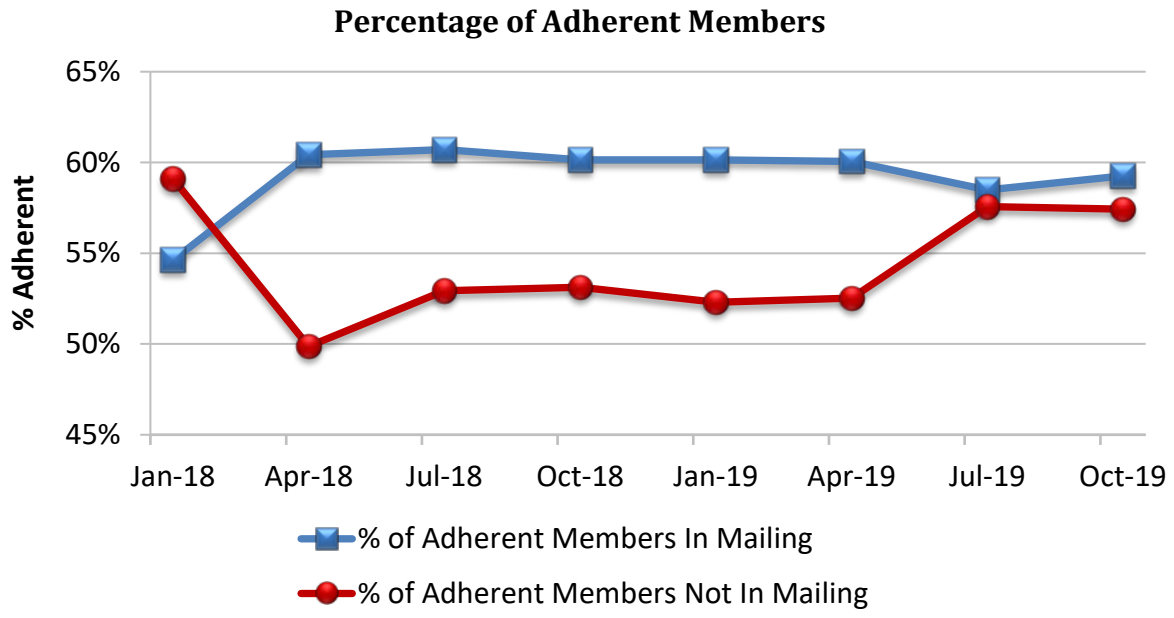
SoonerPsych Trends

The following graphs show the 2018 and 2019 SoonerPsych trends for member PDC, adherence, diagnosis, metabolic monitoring, and polypharmacy. Members whose prescribers are included in the SoonerPsych mailing are designated separately from those members whose prescribers are not included in the mailing. It is important to note that the prescriber mailing list was updated in April 2018 to include a larger number of prescribers and prescribers who were not previously receiving a mailing. Additionally, starting with the July 2019 mailing, the SoonerPsych data was adjusted for outliers, after input from the Drug Utilization Review (DUR) Board at the July 2019 DUR Board meeting, to show a more meaningful comparison of prescribers included in the mailing and prescribers not included in the mailing. Although SoonerPsych trends are tracked over time, it may be more meaningful to evaluate the mailings starting in April 2018 and going forward as a new data set since the prescriber mailing list was updated in April 2018 and again starting in July 2019 when the data was adjusted for outliers.

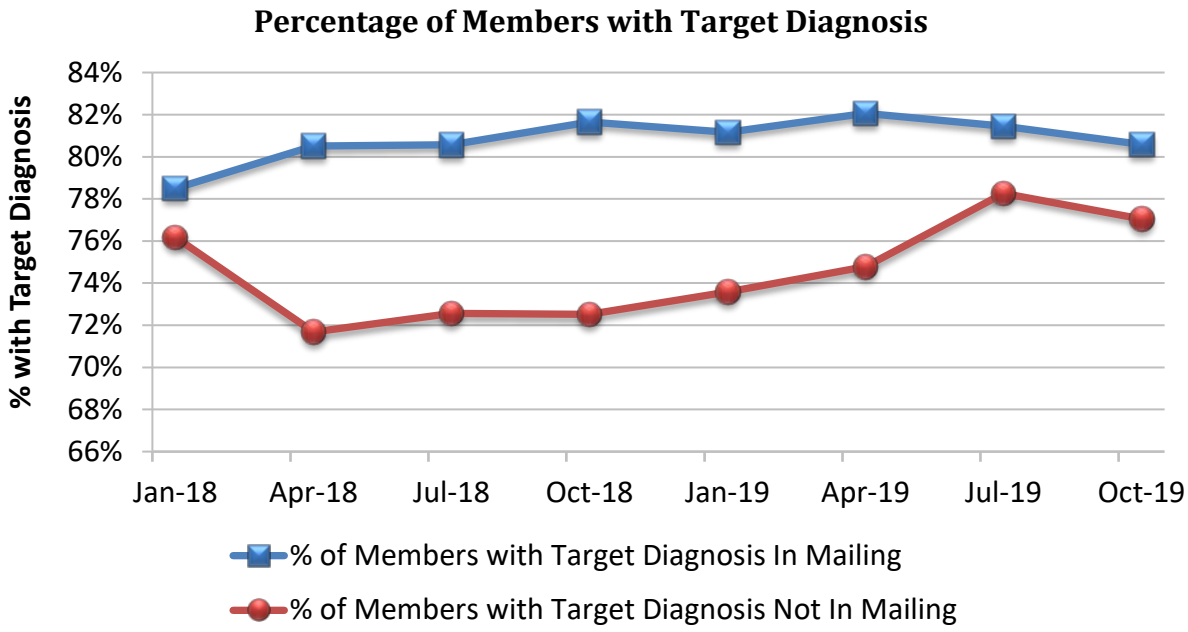
The following graph shows the 2018 and 2019 trends for member PDC. Please note, the vertical axis starts at a PDC of 66% in order to reflect small changes.



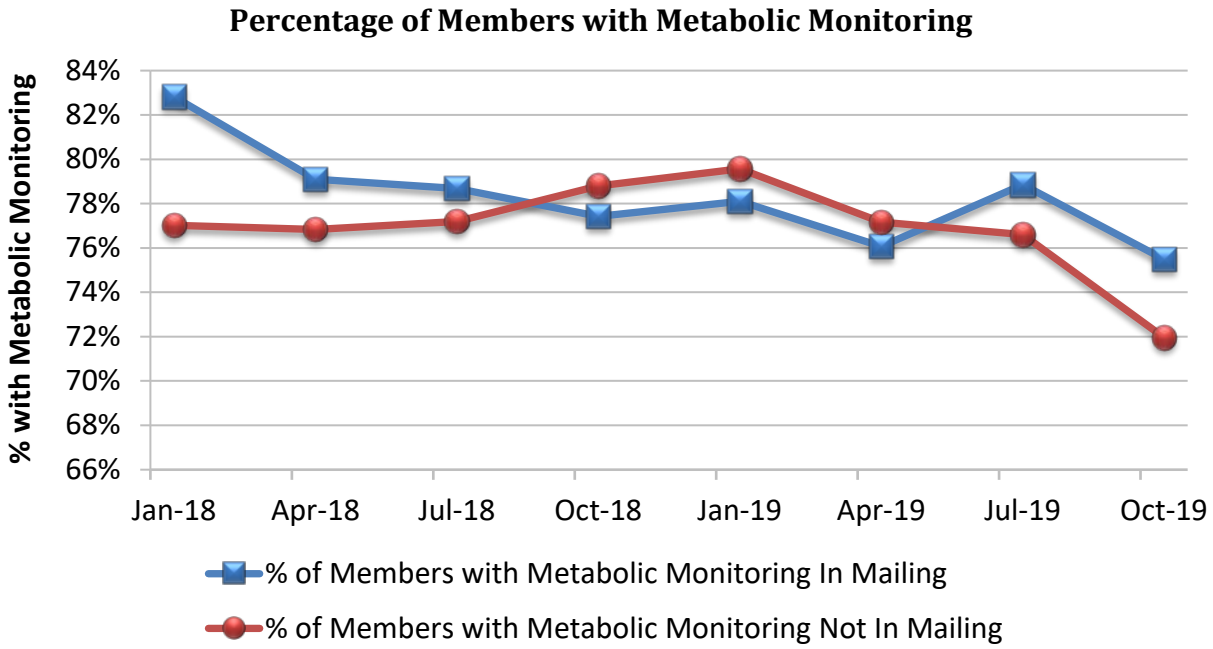
The following graph shows the SoonerPsych trends for the percentage of adherent members. Members are considered adherent if their PDC ≥80%. Please note, the vertical axis starts at 45% of members in order to reflect small changes. This data was included after input from the DUR Board in the December 2017 DUR meeting; the DUR Board indicated it would be an important measure for reporting.



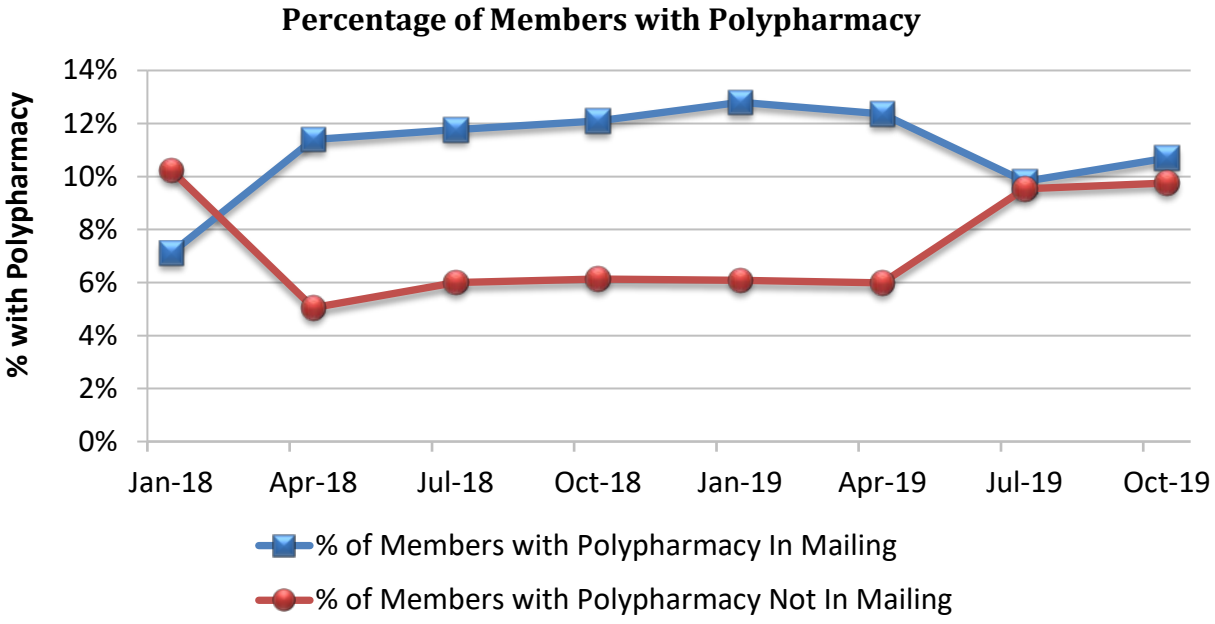
The following graph shows the SoonerPsych trends for the percentage of members whose recent 12-month medical claims history included a diagnosis with a strong indication for prescribing an antipsychotic medication. Please note, the vertical axis starts at 66% of members in order to reflect small changes.



The following graph shows the SoonerPsych trends for the percentage of members with appropriate metabolic monitoring while on an antipsychotic medication. Please note, the vertical axis starts at 66% of members in order to reflect small changes.



The following graph shows the SoonerPsych trends for the percentage of members with polypharmacy (concurrent use of 2 or more atypical antipsychotic medications for more than 90 days). Please note, unlike the previous graphs, the vertical axis starts at 0% of members and that a lower percentage is a better outcome (indicates less prescribing of concomitant atypical antipsychotic medications).



Conclusions

Recent 2018 and 2019 SoonerPsych trends indicate overall improvements in member PDC, the percentage of adherent members, and the percentage of members with a target diagnosis. The percentage of members with appropriate metabolic monitoring is similar for members whose prescribers received a mailing compared to those not included in the mailing in 2018 and 2019. Polypharmacy did not show positive trends in 2018 and 2019 for those prescribers included in the mailing; however, after adjusting the data for outliers starting in July 2019, the percentage of members with polypharmacy is similar for members whose prescribers received a mailing compared to those not included in the mailing. Continuing to adjust the data for outliers and following the results of the new prescriber list over time may provide more opportunities for additional prescriber-specific interventions. Overall, results indicate that consistently receiving evidence-based educational mailings reminds providers of evidence-based practices, and averts some potentially inappropriate prescribing. Recent changes to the mailing format (including all modules in each mailing, mailing to consistent prescribers, and updating the prescriber mailing list), as well as expanding the data collection process and adjusting the data for outliers, are intended to sustain improvements and reduce waning interventions. The College of Pharmacy will continue to work with the Oklahoma Health Care Authority to improve educational mailings with the goal of improving the quality of care for SoonerCare members utilizing atypical antipsychotic medications. Future results of the SoonerPsych educational mailing will be reviewed with the DUR Board as they become available.

Appendix C

Vote to Prior Authorize Xcopri® (Cenobamate)

Oklahoma Health Care Authority
March 2020

Introduction[1,2,3,4]

- **Xcopri® (cenobamate)** was approved by the U.S. Food and Drug Administration (FDA) in November 2019 for the treatment of adult patients with partial-onset seizures. Xcopri® is supplied as 12.5mg, 25mg, 50mg, 100mg, 150mg, and 200mg oral tablets, and the recommended initial dosage of cenobamate is 12.5mg once daily, titrated to the recommended maintenance dose of 200mg once daily (*refer to Xcopri® Prescribing Information for the recommended titration schedule).* The safety and effectiveness of cenobamate have not been established in pediatric patients. In clinical trials, the most common adverse reactions (incidence of ≥10% and greater than placebo) that occurred in cenobamate-treated patients were somnolence, dizziness, fatigue, diplopia, and headache. The efficacy of cenobamate for the treatment of partial-onset seizures was established in 2 multicenter, randomized, double-blind, placebo-controlled studies in adult patients. Cenobamate was statistically significant compared to placebo in the percent change from baseline in seizure frequency per 28 days. Cenobamate is currently pending controlled substance scheduling by the U.S. Drug Enforcement Administration (DEA), and cost information for Xcopri® (cenobamate) is not yet available.
- **Sabril® (vigabatrin)** was approved for an expanded indication by the FDA in January 2020 to include the adjunctive treatment of refractory complex partial seizures in patients 2 years of age and older who have responded inadequately to several alternative treatments; vigabatrin is not indicated as a first-line agent. Vigabatrin was previously approved for this indication in patients 10 years of age and older. Sabril® was first FDA approved in 2009 and is also indicated for the treatment of infantile spasms in infants 1 month to 2 years of age for whom the potential benefits outweigh the potential risk of vision loss.

Recommendations

The College of Pharmacy recommends the prior authorization of Xcopri® (cenobamate) with the following criteria:

Xcopri® (Cenobamate) Approval Criteria:

1. An FDA approved diagnosis of partial-onset seizures; and
2. Initial prescription must be written by a neurologist; and
3. Member must have failed therapy with at least 3 other anticonvulsants.

Additionally, the College of Pharmacy recommends updating the current approval criteria for Sabril® (vigabatrin) based on the expanded FDA approved indication (changes noted in red):

Sabril® (Vigabatrin) Approval Criteria:

1. An FDA approved diagnosis of 1 of the following:
    a. Refractory complex seizures in adults and pediatric patients ~~10~~ 2 years of age or older; or
    b. Infantile spasms in children 1 month to 2 years of age; and
2. Authorization of generic vigabatrin (in place of brand Sabril®) will require a patient-specific, clinically significant reason why the member cannot use the brand formulation (brand formulation is preferred); and
3. Members with refractory complex seizures must have previous trials of at least 3 other anticonvulsants; and
4. Prescription must be written by a neurologist; and
5. Member, prescriber, and pharmacy must all register in the Vigabatrin REMS Program and maintain enrollment throughout therapy.

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[1] SK Life Science. FDA Approves Xcopri® (Cenobamate Tablets), an Anti-Epileptic Drug (AED) from SK Biopharmaceuticals, Co., Ltd., and U.S. Subsidiary SK Life Science, Inc. Available online at: https://www.sklifescienceinc.com/pdf/FDA_Approves_XCOPRI_(cenobamate_tablets)_an_Anti-Epileptic_Drug_(AED)_from_SK_Biopharmaceuticals_Co._Ltd._and_U.S._Subsidiary_SK_Life_Science_Inc.pdf. Issued 11/21/2019. Last accessed 02/20/2020.

[2] Xcopri® (Cenobamate) Prescribing Information. SK Life Science, Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/212839s000lbl.pdf. Last revised 11/2019. Last accessed 02/20/2020.

[3] Levy S. FDA Approves New Indication for Lundbeck's Sabril®. *Drug Store News*. Available online at: https://drugstorenews.com/fda-approves-new-indication-lundbecks-sabril?utm_source=omeda&utm_medium=email&utm_campaign=NL_DSN+AM&utm_keyword=&oly_enc_id=6022E7647590A6Z. Issued 01/28/2020. Last accessed 02/20/2020.

[4] Sabril® (Vigabatrin) Prescribing Information. Lundbeck. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/020427s021,022006s023lbl.pdf. Last revised 01/2020. Last accessed 02/20/2020.

Appendix D

Vote to Prior Authorize Tosymra™ (Sumatriptan Nasal Spray), Reyvow™ (Lasmiditan), and Ubrelvy™ (Ubrogepant)

Oklahoma Health Care Authority
March 2020

Introduction[1,2,3,4]

Tosymra™ (sumatriptan nasal spray) , a serotonin $(5\text{-HT})_{1B/1D}$ receptor agonist (triptan), was approved by the U.S. Food and Drug Administration (FDA) in January 2019 for the acute treatment of migraine with or without aura in adults. It is supplied as a ready-to-use, single-dose, disposable unit delivering 10mg of sumatriptan. The recommended dose of Tosymra™ is 10mg administered as a single spray in 1 nostril. The maximum cumulative dose that may be given in a 24-hour period is 30mg, with doses of Tosymra™ separated by at least 1 hour. Tosymra™ may also be given at least 1 hour following a dose of another sumatriptan product. The efficacy of Tosymra™ was based on the relative bioavailability of Tosymra™ nasal spray compared to sumatriptan 4mg subcutaneous (sub-Q) injection in healthy adults. Tosymra™ should be used only if a clear diagnosis of migraine has been established. Additionally, Tosymra™ is not indicated for the preventive treatment of migraine nor for the treatment of cluster headache.

Cost Comparison:

Medication	Cost Per Dose	Cost Per Maximum Cumulative Dose*
Tosymra™ (sumatriptan) 10mg nasal spray	**$97.50**	**$292.50**
sumatriptan 20mg nasal spray	$41.53	$83.06
sumatriptan 6mg/0.5mL sub-Q injection	$32.29	$64.58

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.
sub-Q = subcutaneous
*Cost per maximum cumulative dose based on FDA recommended dosing in a 24-hour period.

Reyvow™ (lasmiditan), a 5-HT_{1F} receptor agonist, was approved by the FDA in October 2019 for the acute treatment of migraine with or without aura in adults. Reyvow™ is supplied as 50mg and 100mg tablets, and the recommended dose is 50mg, 100mg, or 200mg taken orally, as needed. No more than 1 dose should be taken in 24 hours. Reyvow™ is not indicated for the preventive treatment of migraine. The most common adverse reactions (incidence ≥5% and greater than placebo) in lasmiditan clinical studies were dizziness, fatigue, paresthesia, and sedation. The efficacy of lasmiditan in the acute treatment of migraine was demonstrated in 2 randomized, double-blind, placebo-controlled trials. In both studies, the percentage of patients achieving pain freedom and most bothersome symptom (MBS) freedom 2 hours after treatment was significantly greater among patients receiving lasmiditan at all doses compared to those receiving placebo. The Wholesale Acquisition Cost (WAC) for either the 50mg or 100mg Reyvow™ tablet is $80.00 per tablet.

Cost Comparison:

Medication	Cost Per Dose	Cost Per Maximum Cumulative Dose*
Reyvow™ (lasmiditan) 100mg tablets	**$80.00**	**$160.00**
rizatriptan 10mg tablets	$0.76	$2.28
sumatriptan 100mg tablets	$0.60	$1.20

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.
*Cost per maximum cumulative dose based on FDA recommended dosing in a 24-hour period.

Ubrelvy™ (ubrogepant), a calcitonin gene-related peptide (CGRP) receptor antagonist, was approved by the FDA in December 2019 for the acute treatment of migraine with or without aura in adults. It is supplied as 50mg and 100mg tablets in unit-dose packets, and each packet contains 1 tablet. Ubrelvy™ is available in boxes containing 6, 8, 10, 12, or 30 packets. Ubrelvy™ is not indicated for the preventive treatment of migraine. The recommended dose is 50mg or 100mg taken orally, as needed. If needed, a second dose may be administered at least 2 hours after the initial dose. The maximum dose in a 24-hour period is 200mg. The safety of treating more than 8 migraines in a 30-day period has not been established. The most common adverse reactions (incidence ≥2% and greater than placebo) in ubrogepant clinical studies were nausea and somnolence. Concomitant use of ubrogepant with strong CYP3A4 inhibitors is contraindicated. The efficacy of ubrogepant for the acute treatment of migraine was demonstrated in 2 randomized, double-blind, placebo-controlled trials. In both studies, the percentage of patients achieving headache pain freedom and MBS freedom 2 hours post-dose was significantly greater among patients receiving ubrogepant compared to those receiving placebo.

Cost Comparison:

Medication	Cost Per Dose	Cost Per Maximum Cumulative Dose*
Ubrelvy™ (ubrogepant) 100mg tablets	**$85.00**	**$170.00**
rizatriptan 10mg tablets	$0.76	$2.28
sumatriptan 100mg tablets	$0.60	$1.20

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.
*Cost per maximum cumulative dose based on FDA recommended dosing in a 24-hour period.

Emgality® (galcanezumab-gnlm), a CGRP antagonist, was approved by the FDA in June 2019 for the treatment of episodic cluster headache in adults. The effectiveness of Emgality® for the treatment of episodic cluster headache was demonstrated in a placebo-controlled, clinical trial of 106 patients. The trial measured the average number of cluster headaches per week for 3 weeks and compared the average change from baseline in the Emgality® and placebo groups. During the 3-week period, patients taking Emgality® experienced 8.7 fewer weekly cluster headache attacks than they did at baseline, compared to 5.2 fewer attacks for patients on placebo. Emgality® was first approved by the FDA in September 2018 for the preventive treatment of migraine in adults.

Recommendations

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

1. The placement of Tosymra™ (sumatriptan nasal spray), Reyvow™ (lasmiditan), and Ubrelvy™ (ubrogepant) into the Special Prior Authorization (PA) Tier with the following criteria (changes shown in red in the following Tier Chart and Special PA criteria)
2. Updating the current approval criteria for Emgality® (galcanezumab-gnlm) based on the new FDA approved indication (changes shown in red in the following criteria)

Anti-Migraine Medications			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
eletriptan (Relpax®) – **brand only**	naratriptan (Amerge®)	almotriptan (Axert®)	dihydroergotamine injection (D.H.E. 45®)
rizatriptan (Maxalt®, Maxalt MLT®)	zolmitriptan (Zomig®, Zomig-ZMT®, Zomig® nasal spray)	frovatriptan (Frova®)	dihydroergotamine nasal spray (Migranal®)
sumatriptan (Imitrex®)			eletriptan (Relpax®) – **generic**
sumatriptan/naproxen (Treximet®)			ergotamine sublingual tablet (Ergomar®)
			lasmiditan (Reyvow™)
			sumatriptan injection (Imitrex®)
			sumatriptan injection (Zembrace® SymTouch®)
			sumatriptan nasal powder (Onzetra® Xsail®)
			sumatriptan nasal spray (Imitrex®)
			sumatriptan nasal spray (Tosymra™)
			ubrogepant (Ubrelvy™)

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

Anti-Migraine Medications Tier-2 Approval Criteria:

1. A trial of all available Tier-1 products with inadequate response or a patient-specific, clinically significant reason why a Tier-1 product is not appropriate for the member; or
2. Documented adverse effect(s) to all available Tier-1 products; or
3. Previous success with a Tier-2 product within the last 60 days.

Anti-Migraine Medications Tier-3 Approval Criteria:

1. A trial of all available Tier-1 and Tier-2 products with inadequate response or a patient-specific, clinically significant reason why a lower tiered product is not appropriate for the member; or
2. Documented adverse effect(s) to all available Tier-1 and Tier-2 products; or
3. Previous success with a Tier-3 product within the last 60 days; and
4. Use of any non-oral formulation will require a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation.

Anti-Migraine Medications Special Prior Authorization (PA) Approval Criteria:

1. Use of any non-oral sumatriptan formulation will require a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation or lower-tiered triptan medications.
2. Use of Zembrace® SymTouch® or Tosymra™ will require a patient-specific, clinically significant reason why the member cannot use all available generic formulations of sumatriptan (tablets, nasal spray, and injection) or lower-tiered triptan medications.
3. Use of dihydroergotamine injection (D.H.E. 45®) will require a patient-specific, clinically significant reason why the member cannot use lower-tiered triptan medications.
4. Use of dihydroergotamine nasal spray (Migranal®) will require a patient-specific, clinically significant reason why the member cannot use lower-tiered triptan medications or dihydroergotamine injection (D.H.E. 45®).
5. Use of Ergomar® (ergotamine sublingual tablets) will require a patient-specific, clinically significant reason why the member cannot use lower-tiered triptan medications; and
    a. Member must not have any of the contraindications for use of Ergomar® (e.g., coadministration with a potent CYP 3A4 inhibitor, women who are or may become pregnant, peripheral vascular disease, coronary heart disease, hypertension, impaired hepatic or renal function, sepsis, hypersensitivity to any of the components); and
    b. A quantity limit of 20 tablets per 28 days will apply.
6. Use of generic eletriptan will require a patient-specific, clinically significant reason why the member cannot use the brand formulation of Relpax® (brand formulation is preferred).
7. Use of Reyvow™ (lasmiditan) or Ubrelvy™ (ubrogepant) will require a patient-specific, clinically significant reason why the member cannot use triptan medications.

Emgality® (Galcanezumab-gnlm) Approval Criteria [Episodic Cluster Headache Diagnosis]:

1. An FDA approved indication for the treatment of episodic cluster headache in adults; and
2. Member must be 18 years of age or older; and
3. Member has a diagnosis of episodic cluster headache as defined by the International Headache Society (IHS) International Classification of Headache Disorders (ICHD) guideline and meets the following criteria:

    a. Member has a history of episodic cluster headache with at least 2 cluster periods lasting from 7 days to 1 year (when untreated) and separated by pain-free remission periods of ≥1 month; and
4. Member is not frequently taking medications that are known to cause medication overuse headaches (MOH or rebound headaches) in the absence of intractable conditions known to cause chronic pain. MOH are a frequent cause of chronic headaches. A list of prescription or non-prescription medications known to cause MOH includes, but is not limited to:
    a. Decongestants (alone or in combination products) (≥10 days/month for >3 months); and
    b. Combination analgesics containing caffeine and/or butalbital (≥10 days/month for >3 months); and
    c. Opioids (≥10 days/month for >3 months); and
    d. Analgesic medications including acetaminophen or non-steroidal anti-inflammatory drugs (NSAIDs) (≥15 days/month for >3 months); and
    e. Ergotamine-containing medications (≥10 days/month for >3 months); and
    f. Triptans (≥10 days/month for >3 months); and
5. The member has failed prophylactic therapy with at least 1 other medication (e.g., verapamil, select anticonvulsants, glucocorticoids); and
6. Member must have been evaluated within the last 6 months by a neurologist for cluster headaches and the requested medication (e.g., Emgality®) recommended as treatment (not necessarily prescribed by a neurologist); and
7. Member will not use Emgality® concurrently with an alternative calcitonin gene-related peptide (CGRP) inhibitor; and
8. Prescriber must verify that member has been counseled on appropriate use, storage of the medication, and administration technique; and
9. Initial approvals will be for the duration of 3 months. Continuation approvals will be granted until the end of the cluster period if the prescriber documents that the member is responding well to treatment as indicated by a reduction in cluster headache attack frequency; and
10. A quantity limit of (3) 100mg/mL syringes per 30 days will apply.

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[1] Tosymra™ (sumatriptan nasal spray) Prescribing Information. Upsher-Smith Laboratories, LLC. Available online at: https://www.upsher-smith.com/wp-content/uploads/TOS-MI.pdf. Last revised 07/2019. Last accessed 02/20/2020.
[2] Reyvow™ (lasmiditan) Prescribing Information. Lilly USA, LLC. Available online at: http://pi.lilly.com/us/reyvow-uspi.pdf. Last revised 01/2020. Last accessed 02/20/2020.
[3] Ubrelvy™ (Ubrogepant) Prescribing Information. Allergan. Available online at: https://media.allergan.com/products/Ubrelvy_pi.pdf. Last revised 12/2019. Last accessed 02/20/2020.
[4] FDA News Release. FDA approves first treatment for episodic cluster headache that reduces the frequency of attacks. Available online at: https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-episodic-cluster-headache-reduces-frequency-attacks. Issued 06/04/2019. Last accessed 02/20/2020.

Appendix E

Vote to Prior Authorize Esperoct® [Antihemophilic Factor (Recombinant), Glycopegylated-exei]

Oklahoma Health Care Authority
March 2020

Introduction[1]

FDA Approval(s): Feburary 2019

Indication(s): For use in adults and children with hemophilia A for:

- On-demand treatment and control of bleeding episodes
- Perioperative management of bleeding
- Routine prophylaxis to reduce the frequency of bleeding episodes

Prolonged Half-Life: Esperoct® is a glycopegylated recombinant anti-hemophilic factor VIII (FVIII). The FVIII in Esperoct® is conjugated to a 40-kDa polyethylene glycol molecule which increases the half-life and decreases the clearance compared to the non-pegylated molecule. Esperoct® has a half-life ranging from 14.7 to 21.7 hours depending on the age of the patient. Factor VIII has an average half-life of 12 hours.

Cost Comparison:

Factor Replacement Product	Cost Per Unit	Cost for 4 Weeks of Prophylaxis Therapy
Esperoct® [antihemophilic factor (recombinant), glycopegylated-exei]¥	**$2.23***	**$34,788**
Advate® [antihemophilic factor (recombinant)]+	$1.29**	$10,836 - $21,672

Costs do not reflect rebated prices or net costs.
*Wholesale Acquistion Cost (WAC)
**Specialty Pharmaceutical Allowable Cost (SPAC)
¥Esperoct® [antihemophilic factor (recombinant), glycopegylated-exei] dosing 65 IU/kg twice weekly for a 30kg patient.
+Advate® dosing 20 to 40 IU/kg every other day for a 30kg patient.

Recommendations

The Oklahoma Health Care Authority recommends the prior authorization of Esperoct® [antihemophilic factor (recombinant), glycopegylated-exei] with the following criteria (changes noted in red):

Eloctate®, Adynovate®, Afstyla®, Jivi®, Esperoct®, Alprolix®, Idelvion®, and Rebinyn®
Approval Criteria:

1. An FDA approved indication; and
2. Requested medication must be prescribed by a hematologist specializing in hemophilia, or a mid-level practitioner with a supervising physician that is a hematologist specializing in hemophilia; and
3. A patient-specific, clinically significant reason why the member cannot use the following:
    a. Hemophilia A: Advate® or current factor VIII replacement product; or

   b. Hemophilia B: Benefix® or current factor IX replacement product; and
4. A half-life study must be performed to determine the appropriate dose and dosing interval; and
5. Initial approvals will be for the duration of the half-life study. If the half-life study shows significant benefit in prolonged half-life, subsequent approvals will be for the duration of 1 year.

[1] Esperoct® Prescribing Information. Novo Nordisk, Inc. Available online at: https://www.fda.gov/vaccines-blood-biologics/esperoct. Last revised 07/19/2019. Last accessed 01/16/2020.

Appendix F

Vote to Prior Authorize ProAir® Digihaler™ (Albuterol Sulfate Inhalation Powder)

Oklahoma Health Care Authority
March 2020

Introduction[1]

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

- **ProAir® Digihaler™ (albuterol sulfate inhalation powder):** In December 2018, the FDA approved ProAir® Digihaler™ (albuterol sulfate inhalation powder), a digital inhaler with built-in sensors which connects to a companion mobile application (app) and provides inhaler use information to patients with asthma. ProAir® Digihaler™ is indicated for the treatment or prevention of bronchospasm in patients 4 years of age and older with reversible obstructive airway disease, and for the prevention of exercise-induced bronchospasm in patients 4 years of age and older. ProAir® Digihaler™ contains a built-in electronic module that automatically detects, records, and stores data on inhaler events, including peak inspiratory flow rate (L/min). ProAir® Digihaler™ may be used with, and transmits information to, a mobile app, but does not need to be connected to the mobile app in order for patients to use the inhaler.

Recommendations

The College of Pharmacy recommends the placement of ProAir® Digihaler™ (albuterol sulfate inhalation powder) into Tier-2 of the Short-Acting Beta$_2$ Agonist Product Based Prior Authorization (PBPA) category with the following criteria (changes noted in red):

Short-Acting Beta$_2$ Agonists	
Tier-1	**Tier-2**
albuterol HFA (ProAir® HFA)*	albuterol HFA (generic)
albuterol HFA (Proventil® HFA)*	**albuterol inhalation powder (ProAir® Digihaler™)¥**
albuterol HFA (Ventolin® HFA)*	levalbuterol HFA (generic)
albuterol inhalation powder (ProAir® RespiClick®)	
levalbuterol HFA (Xopenex® HFA)*	

*Brand preferred.
¥Additional criteria applies.
Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC is unavailable.

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

Short-Acting Beta$_2$ Agonists Tier-2 Approval Criteria:

1. An FDA approved or clinically accepted indication; and
2. A patient-specific, clinically significant reason why the member cannot use all available Tier-1 medications must be provided.

ProAir® Digihaler™ (Albuterol Sulfate Inhalation Powder) Approval Criteria:

1. An FDA approved or clinically accepted indication; and
2. A patient-specific, clinically significant reason why the member requires the ProAir® Digihaler™ formulation over all available Tier-1 medications must be provided; and
3. The prescriber agrees to closely monitor member adherence; and
4. The member should be capable and willing to use the Companion Mobile App and follow the *Instructions for Use* and ensure the ProAir® Digihaler™ Companion Mobile App is compatible with their specific smartphone; and
5. The member's phone camera must be functional and able to scan the inhaler QR code and register the ProAir® Digihaler™ inhaler; and
6. Approvals will be for the duration of 3 months. For continuation consideration, documentation demonstrating positive clinical response and member compliance greater than 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.

[1] Teva Pharmaceutical Industries, Ltd. Teva Announces FDA Approval of First and Only Digital Inhaler with Built-In Sensors-ProAir® Digihaler™ (Albuterol Sulfate 117mcg) Inhalation Powder. *Business Wire*. Available online at: https://apnews.com/c4eda18019434172848f5f5ab6857cf0. Issued 12/21/2018. Last accessed 02/24/2020.

Appendix G

Vote to Prior Authorize Evenity® (Romosozumab-aqqg)

Oklahoma Health Care Authority
March 2020

Introduction[1]

Evenity® (romosozumab-aqqg) is a sclerostin inhibitor indicated for the treatment of osteoporosis in postmenopausal women at high risk for fracture or in patients who have failed or are intolerant to other available osteoporosis therapies. Romosozumab has a *Boxed Warning* for potential risk of myocardial infarction (MI), stroke, and cardiovascular (CV) death. Evenity® is available as a 105mg/1.17mL solution supplied in single-use prefilled syringes. The recommended dose of romosozumab is 210mg [administered as (2) 105mg subcutaneous (sub-Q) injections] once every month for 12 doses. Romosozumab should be administered sub-Q in the abdomen, thigh, or upper arm by a health care provider. Patients should be adequately supplemented with calcium and vitamin D during treatment with romosozumab. The Wholesale Acquisition Cost (WAC) of Evenity® is $912.49 per 105mg pre-filled syringe. This results in an approximate cost per 12-month treatment of $21,899.87. The anabolic effect of romosozumab wanes after 12 monthly doses of therapy; therefore, the duration of romosozumab use should be limited to 12 months. If osteoporosis therapy remains warranted after 12 months, continued therapy with an anti-resorptive agent should be considered.

Recommendations

The College of Pharmacy recommends the placement of Evenity® (romosozumab-aqqg) into the Special Prior Authorization (PA) Tier of the Osteoporosis Medications Product Based Prior Authorization (PBPA) category with the following criteria:

Evenity® (Romosozumab-aqqg) Approval Criteria:

1. An FDA approved diagnosis of osteoporosis in postmenopausal women at high risk for fracture; and
2. Member meets 1 of the following:
    a. History of osteoporotic fracture; or
    b. Multiple risk factors for fracture (e.g., T-score ≤-2.5 at the total hip or femoral neck, smoking, corticosteroid use, rheumatoid arthritis); or
    c. Failed or are intolerant to other available osteoporosis therapies; and
3. Prescriber must verify member has not had a myocardial infarction or stroke within the preceding year; and
4. Prescriber must verify calcium levels will be monitored and pre-existing hypocalcemia will be corrected prior to starting therapy; and
5. Prescriber must verify that the member will take adequate calcium and vitamin D supplements during treatment with Evenity® to reduce the risk of hypocalcemia; and
6. Evenity® must be administered by a health care provider; and
7. Approvals will be for a maximum total duration of 1 year of therapy.

Osteoporosis Medications		
Tier-1	**Tier-2**	**Special PA**
alendronate tabs (Fosamax®)	alendronate + vitamin D tabs (Fosamax Plus D®)	abaloparatide inj (Tymlos®)
calcium + vitamin D*	risedronate tabs (Actonel®)	alendronate effervescent tabs (Binosto®)
ibandronate tabs (Boniva®)		alendronate soln (Fosamax®)
zoledronic acid inj (Reclast®)		alendronate 40mg tabs (Fosamax®)
		denosumab inj (Prolia®)
		ibandronate inj (Boniva® IV)
		risedronate 30mg tabs (Actonel®)
		risedronate DR tabs (Atelvia®)
		romosozumab-aqqg (Evenity®)
		teriparatide inj (Forteo®)

tabs = tablets; inj = injection; soln = solution; DR = delayed-release; PA = prior authorization

*Must be used in combination with a bisphosphonate to count as a trial.

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

[1] Evenity® (romosozumab-aqqg) Prescribing Information. Amgen CA. Available online at: https://www.pi.amgen.com/~/media/amgen/repositorysites/pi-amgen-com/evenity/evenity_pi.ashx. Last revised 12/2019. Last accessed 01/02/2020.

Appendix H

Vote to Prior Authorize Asparlas™ (Calaspargase Pegol-mknl), Daurismo™ (Glasdegib), Idhifa® (Enasidenib), Lumoxiti® (Moxetumomab Pasudotox-tdfk), Tibsovo® (Ivosidenib), and Xospata® (Gilteritinib)

Oklahoma Health Care Authority
March 2020

Introduction[1]

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

- **August 2017:** The FDA approved Idhifa® (enasidenib) for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with an isocitrate dehydrogenase-2 (IDH2) mutation.
- **September 2018:** The FDA approved Lumoxiti® (moxetumomab pasudotox-tdfk), a CD22-directed cytotoxin, for the treatment of adult patients with relapsed or refractory hairy cell leukemia (HCL) who have received at least 2 prior systemic therapies, including treatment with a purine nucleoside analog (PNA).
- **November 2018:** The FDA approved Daurismo™ (glasdegib) in combination with low-dose cytarabine (LDAC), for the treatment of newly-diagnosed AML in patients who are 75 years of age or older or who have comorbidities that preclude intensive induction chemotherapy.
- **November 2018:** The FDA approved Xospata® (gilteritinib) for treatment of adult patients who have relapsed or refractory AML with a FMS-related tyrosine kinase 3 (FLT3) mutation.
- **December 2018:** The FDA approved Asparlas™ (calaspargase pegol-mknl), an asparagine-specific enzyme, as a component of a multi-agent chemotherapeutic regimen for the treatment of acute lymphoblastic leukemia (ALL) in pediatric and young adult patients 1 month to 21 years of age. Asparlas™ provides for a longer interval between doses compared to other available pegaspargase products.
- **May 2019:** The FDA approved Tibsovo® (ivosidenib) for the treatment of newly-diagnosed AML with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation in patients who are at least 75 years of age or who have comorbidities that preclude the use of intensive induction chemotherapy.

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

- **March 2018:** The FDA approved Tasigna® (nilotinib) for the treatment of pediatric patients 1 year of age or older with newly-diagnosed Philadelphia chromosome positive chronic myeloid leukemia in chronic phase (Ph+ CML-CP) and for the treatment of Ph+ CML-CP resistant or intolerant to prior tyrosine kinase inhibitor (TKI) therapy.
- **May 2019:** The FDA approved Venclexta® (venetoclax) for the treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) in combination with obinutuzumab (Gazyva®).

- **May 2019:** The FDA approved the addition of overall survival (OS) data in the labeling for Xospata® (gilteritinib). Approval was based on the ADMIRAL trial in which 371 adult patients with relapsed or refractory AML with specified mutations were randomized (2:1) to receive gilteritinib 120mg once daily (N=247) over continuous 28-day cycles or prespecified salvage chemotherapy (N=124). The median OS was 9.3 months for patients receiving gilteritinib and 5.6 months for those in the chemotherapy arm (P=0.0004).
- **November 2019:** The FDA approved Calquence® (acalabrutinib) for the treatment of adults with CLL or SLL.

Product Summaries[2,3,4,5,6,7]

Asparlas™ (Calaspargase Pegol-mknl):

- **Therapeutic Class:** Asparagine-specific enzyme
- **Indication(s):** As a component of a multi-agent chemotherapeutic regimen for the treatment of ALL in pediatric and young adult patients 1 month to 21 years of age
- **How Supplied:** 3,750 units/5mL sterile solution in a single-dose vial (SDV)
- **Dose:** 2,500 units/m^2 intravenously (IV) no more frequently than every 21 days
- **Cost:** Wholesale Acquisition Cost (WAC) of $4,800.00 per SDV; cost will vary due to body surface area-based dosing and duration variability

Daurismo™ (Glasdegib):

- **Therapeutic Class:** Hedgehog pathway inhibitor
- **Indication(s):** For use in combination with LDAC, for the treatment of newly-diagnosed AML in adult patients who are 75 years of age or older or who have comorbidities that preclude the use of intensive induction chemotherapy
- **How Supplied:** 25mg and 100mg oral tablets
- **Dose:** 100mg orally once daily on days 1 to 28 in combination with cytarabine 20mg subcutaneously (sub-Q) twice daily on days 1 to 10 of each 28-day cycle
- **Cost:** WAC of $296.19 per 25mg tablet and $592.38 per 100mg tablet; $16,586.64 per 28 days based on recommended dose of 100mg once daily

Idhifa® (Enasidenib):

- **Therapeutic Class:** IDH2 inhibitor
- **Indication(s):** Treatment of adult patients with relapsed or refractory AML with an IDH2 mutation
- **How Supplied:** 50mg and 100mg oral tablets
- **Dose:** 100mg orally once daily
- **Cost:** WAC of $900.99 for either 50mg tablet or 100mg tablet; $27,029.70 per 30 days based on recommended dose of 100mg once daily

Lumoxiti® (Moxetumomab Pasudotox-tdfk):

- **Therapeutic Class:** CD22-directed cytotoxin
- **Indication(s):** Treatment of adult patients with relapsed/refractory HCL who have received 2 prior systemic therapies, including treatment with a PNA

- **How Supplied:** 1mg lyophilized powder in a SDV
- **Dose:** 0.04mg/kg IV on days 1, 3, and 5 of a 28-day cycle
- **Cost:** WAC of $2,114.58 per SDV; cost will vary due to weight-based dosing and duration variability

Tibsovo® (Ivosidenib):

- **Therapeutic Class:** IDH1 inhibitor
- **Indication(s):** Treatment of AML with a susceptible IDH1 mutation in newly-diagnosed adult patients who are 75 years of age or older or who have comorbidities that preclude use of intensive induction chemotherapy, and in adult patients with relapsed or refractory AML
- **How Supplied:** 250mg oral tablets
- **Dose:** 500mg orally once daily
- **Cost:** WAC of $457.01 per 250mg tablet; $27,420.60 per 30 days based on recommended dose of 500mg once daily

Xospata® (Gilteritinib):

- **Therapeutic Class:** Kinase inhibitor
- **Indication(s):** Treatment of adult patients who have relapsed or refractory AML with a FLT3 mutation
- **How Supplied:** 40mg oral tablets
- **Dose:** 120mg orally once daily
- **Cost:** WAC of $262.50 per 40mg tablet; $23,625.00 per 30 days based on recommended dose of 120mg once daily

Recommendations

- Update the prior authorization criteria to reflect new FDA approved; changes can be seen in the following criteria listed in red (only criteria with updates listed)
- The prior authorization of Asparlas™ (calaspargase pegol-mknl), Daurismo™ (glasdegib), Idhifa® (enasidenib), Lumoxiti® (moxetumomab pasudotox-tdfk), Tibsovo® (ivosidenib), and Xospata® (gilteritinib) with the following criteria listed in red

Asparlas™ (Calaspargase Pegol-mknl) Approval Criteria [Acute Lymphoblastic Leukemia (ALL) Diagnosis]:

1. A patient-specific, clinically significant reason why the member cannot use pegaspargase must be provided; and
2. Member must be 1 month to 21 years of age.

Calquence® (Acalabrutinib) Approval Criteria [Mantle Cell Lymphoma (MCL) Diagnosis]:

1. As a single-agent ~~in members who have received ≥1 prior therapy~~.

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

1. As a single-agent ~~in relapsed/refractory disease~~.

Daurismo™ (Glasdegib) Approval Criteria [Acute Myeloid Leukemia (AML) Diagnosis]:

1. Newly diagnosed AML in members 75 years of age or older or in adult members who have significant comorbidities that preclude use of intensive chemotherapy [severe cardiac disease, ECOG performance status ≥2, or serum creatinine (SCr) >1.3]; and
2. In combination with low-dose cytarabine (LDAC).

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

1. As a single-agent for relapsed/refractory disease; or
2. In combination with chlorambucil, bendamustine, ibrutinib, or venetoclax for first-line therapy; and
3. When obinutuzumab is used in combination with venetoclax, maximum approval duration will be 6 treatment cycles of obinutuzumab.

Idhifa® (Enasidenib) Approval Criteria [Acute Myeloid Leukemia (AML) Diagnosis]:

1. Newly diagnosed AML in members 75 years of age or older or in adult members who have comorbidities that preclude use of intensive chemotherapy; and
    a. As a single-agent; and
    b. IDH2 mutation; or
2. Relapsed/refractory AML; and
    a. As a single-agent; and
    b. IDH2 mutation.

Lumoxiti® (Moxetumomab Pasudotox-tdfk) Approval Criteria [Hairy Cell Leukemia (HCL) Diagnosis]:

1. Treatment of relapsed or refractory HCL in adults; and
2. Member has received at least 2 prior systemic therapies, including treatment with a purine nucleoside analog (PNA); and
3. Creatinine clearance (CrCl) ≥30mL/minute/1.73m^2; and
4. As a single-agent.

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

1. Member must have 1 of the following:
    a. Newly diagnosed chronic, accelerated, or blast phase CML; or
    b. Philadelphia Chromosome Positive (Ph+) CML chronic phase (CP) resistant or intolerant to prior tyrosine-kinase inhibitor (TKI) therapy; or
    c. Post-hematopoietic stem cell transplantation.

Tibsovo® (Ivosidenib) Approval Criteria [Acute Myeloid Leukemia (AML) Diagnosis]:

1. Newly diagnosed AML in members 75 years of age or older or in adult members who have comorbidities that preclude use of intensive chemotherapy; and
    a. As a single-agent; and
    b. IDH1 mutation; or
2. Relapsed/refractory AML; and
    a. As a single-agent; and

b. IDH1 mutation.

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

1. Untreated disease in combination with obinutuzumab for a maximum duration of 12 months; or
2. Relapsed/refractory disease in combination with rituximab or as a single-agent.

Xospata® (Gilteritinib) Approval Criteria [Acute Myeloid Leukemia (AML) Diagnosis]:

1. Relapsed/refractory AML; and
2. FLT3 mutation; and
3. As a single-agent.

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[1] FDA: Hematology/Oncology (Cancer) Approvals & Safety Notifications. Available online at: https://www.fda.gov/drugs/resources-information-approved-drugs/hematologyoncology-cancer-approvals-safety-notifications. Last revised 01/09/2020. Last accessed 02/12/2020.

[2] Asparlas™ Prescribing Information. Servier Pharmaceuticals. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/761102s000lbl.pdf. Last revised 12/2018. Last accessed 02/12/2020.

[3] Daurismo™ Prescribing Information. Pfizer. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/210656s000lbl.pdf. Last revised 11/2018. Last accessed 02/12/2020.

[4] Idhifa® Prescribing Information. Celgene Corporation. Available online at: https://media2.celgene.com/content/uploads/idhifa-pi.pdf. Last revised 09/2019. Last accessed 02/12/2020.

[5] Lumoxiti® Prescribing Information. AstraZeneca. Available online at: https://www.azpicentral.com/lumoxiti/lumoxiti.pdf#page=1. Last revised 01/2019. Last accessed 02/12/2020.

[6] Tibsovo® Prescribing Information. Agios Pharmaceuticals. Available online at: https://www.tibsovopro.com/pdf/prescribinginformation.pdf. Last revised 05/2019. Last accessed 02/12/2020.

[7] Xospata® Prescribing Information. Astellas Pharma. Available online at: https://astellas.us/docs/xospata.pdf. Last revised 05/2019. Last accessed 02/12/2020.

Appendix I

Vote to Prior Authorize Azedra® (Iobenguane I-131)

Oklahoma Health Care Authority
March 2020

Introduction[1]

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

- **July 2018:** The FDA approved Azedra® (iobenguane I-131) for the treatment of adult and pediatric patients (12 years of age and older) with iobenguane scan-positive, unresectable, locally advanced or metastatic pheochromocytoma or paraganglioma (PPGL) who require systemic anticancer therapy.

Azedra® (Iobenguane I-131) Product Summary[2]

Azedra® (Iobenguane I-131):

- **Therapeutic Class:** Radioactive therapeutic agent
- **Indication(s):** Treatment of adult and pediatric patients 12 years of age and older with locally advanced or metastatic pheochromocytoma or PPGL
- **How Supplied:** 555MBq/mL (15mCi/mL) of I-131 (as iobenguane I-131) and 0.006mg/mL of iobenguane in a 30mL single-dose vial (SDV); supplied in dosimetric (2mL) and therapeutic (22.5mL) presentations
- **Dose:** Administered intravenously (IV) as a dosimetric dose followed by 2 therapeutic doses administered 90 days apart:
  - Dosimetric Dose: 185 to 222MBq (5 to 6mCi) if >50kg or 3.7MBq/kg (0.1mCi/kg) if ≤50kg
  - Therapeutic Dose: 18,500MBq (500mCi) if >62.5kg or 296MBq/kg (8mCi/kg) if ≤62.5kg
- **Cost:** Wholesale Acquisition Cost (WAC) of $9,060.00 per dosimetric dose vial and $101,925.00 per therapeutic dose vial; treatment cost will vary depending on patient weight

Recommendations

Azedra® (Iobenguane I-131) Approval Criteria [Pheochromocytoma or Paraganglioma (PPGL) Diagnosis]:

1. Adult and pediatric members 12 years of age and older; and
2. Iobenguane scan positive; and
3. Unresectable, locally advanced or metastatic pheochromocytoma or PPGL requiring systemic anticancer therapy.

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[1] FDA. Hematology/Oncology (Cancer) Approvals & Safety Notifications. Available online at: https://www.fda.gov/drugs/resources-information-approved-drugs/hematologyoncology-cancer-approvals-safety-notifications. Last revised 01/09/2020. Last accessed 02/11/2020.

[2] Azedra® (iobenguane I-131) Prescribing Information. Progenics Pharmaceuticals, Inc. Available online at: https://azedra.com/full-prescribing-information.pdf. Last revised 08/2018. Last accessed 02/11/2020.

Appendix J

Calendar Year 2019 Annual Review of Lymphoma Medications and 30-Day Notice to Prior Authorize Aliqopa™ (Copanlisib), Brukinsa™ (Zanubrutinib), Polivy™ (Polatuzumab Vedotin-piiq), and Ruxience™ (Rituximab-pvvr)

Oklahoma Health Care Authority
March 2020

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

Lymphoma is a general term for cancers that develop in the lymphatic system. Lymphomas that do not start in white blood cells (WBCs) are called non-Hodgkin's lymphoma (NHL). NHL consists of a diverse group of neoplasms derived from B-cell progenitors, mature B-cells, mature T-cells, T-cell progenitors, or natural killer (NK) cells. The majority of NHL types develop in B-cells and the most common forms of B-cell NHL include diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL), mantle cell lymphoma (MCL), and marginal zone lymphoma (MZL). The clinical presentation of NHL varies widely depending on the type of lymphoma and the areas involved. Common presentations include lymphadenopathy, hepatosplenomegaly, fever, weight loss, and night sweats. Some NHLs behave indolently with waxing and waning lymphadenopathy for years, while others are highly aggressive and result in death within weeks if left untreated. NHL is the seventh most common cancer in the nation and is slightly more common in Caucasian men. In 2019, there were an estimated 74,200 new diagnoses of NHL and 19,970 deaths due to NHL in the United States.

Hodgkin's lymphoma (HL) is a type of lymphoma that arises from germinal center or post-germinal center B-cells. Almost all HL cases contain Reed-Sternberg cells, a specific type of cancer cell not found in NHL. Most patients with HL can be treated successfully, even in advanced stages. HL is divided into 2 major types, based on the appearance and immunophenotype of the tumor cells: classic HL (cHL) and nodular lymphocyte-predominant HL (NLPHL). Most patients with cHL present with painless localized peripheral lymphadenopathy. HL has a bimodal age distribution and is most common in young adults (15 to 40 years of age) and older adults (older than 55 years of age). Males are slightly more likely to develop HL. In 2019, there were an estimated 8,100 new diagnoses of HL and 1,000 deaths due to HL in the United States.

T-cell lymphomas can develop in lymphoid tissues or outside of lymphoid tissues. A similar lymphocyte called a NK cell shares many features with T-cells and when NK cells become cancerous, the cancer is called NK or NK/T-cell lymphoma and is generally grouped with other T-cell lymphomas. T-cell lymphomas account for approximately 7% of all NHLs in the United States; each particular subtype of T-cell lymphoma is very uncommon. They can be aggressive or indolent. Lymphomas that arise from mature T-cells are sometimes categorized together under the general term peripheral T-cell lymphoma (PTCL). Almost all types of T-cell lymphomas fall under the category of PTCL. The following are among the PTCLs: peripheral T-

cell lymphoma, not otherwise specified (PTCL, NOS); anaplastic large cell lymphoma (ALCL), primary systemic type; angioimmunoblastic T-cell lymphoma (AITL); extranodal NK/T-cell lymphoma, nasal type; subcutaneous panniculitis-like T-cell lymphoma; enteropathy associated T-cell lymphoma; and hepatosplenic T-cell lymphoma. PTCL, NOS accounts for the largest number of patients with PTCL in western countries, accounting for approximately 30% of PTCL and approximately 4% of NHLs overall. It is likely that this group of PTCL, NOS tumors represents a conglomerate of many not yet identified PTCL subtypes. The incidence of PTCL, NOS in the United States was approximately 0.4 cases per 100,000 population in 2006. In the United States, the incidence is highest among blacks, lower among non-Hispanic whites, Hispanic whites, and Asian/Pacific Islanders, and lowest among American Indian/Alaskan natives. The median age at diagnosis is 60 years, and the diagnosis is more common in men than women. Most patients with PTCL, NOS present with generalized lymphadenopathy with or without extranodal disease. ALCL accounts for approximately 1% of all NHLs. Symptoms associated with ALCL include fever, backache, painless swelling of lymph nodes, loss of appetite, itching, skin rash, and tiredness. ALCL can be systemic or cutaneous; systemic ALCL is typically in an advanced stage at diagnosis and can progress rapidly. The systemic subtype is classified as anaplastic lymphoma kinase (ALK)-positive or ALK-negative, depending on whether or not it contains an abnormal ALK fusion protein that results from a genetic event. The non-systemic subtype is called primary cutaneous ALCL and has a good prognosis. AITL is a rare, aggressive type accounting for approximately 7% of all patients with T-cell lymphomas in the United States. Most patients are diagnosed with advanced stage disease and are middle-aged or elderly. Symptoms include fever, night sweats, skin rash, itching, and some autoimmune disorders (autoimmune hemolytic anemia and immune thrombocytopenia). Cutaneous T-cell lymphomas (CTCL) account for 2 to 3% of all NHL cases and generally affect adults. CTCL describes a group of typically indolent lymphomas that appear on the skin; mycosis fungoides (MF) is the most common type of CTCL.

Current Prior Authorization Criteria

Adcetris® (Brentuximab Vedotin) Approval Criteria [Anaplastic Large Cell Lymphoma (ALCL), Primary Cutaneous Diagnosis]:

1. As a single-agent in members with multifocal lesions or regional nodes either as primary treatment or in relapsed/refractory disease; or
2. In combination with cyclophosphamide, doxorubicin, and prednisone (CHP) for primary treatment or relapsed/refractory disease with regional nodes.

Adcetris® (Brentuximab Vedotin) Approval Criteria [Anaplastic Large Cell Lymphoma (ALCL), Systemic Diagnosis]:

1. In previously untreated disease in combination with cyclophosphamide, doxorubicin, and prednisone; or
2. In members who have received ≥1 line of therapy as a single-agent.

Adcetris® (Brentuximab Vedotin) Approval Criteria [Classical Hodgkin's Lymphoma (cHL) Diagnosis]:

1. In previously untreated Stage III or IV disease in combination with doxorubicin, vinblastine, and dacarbazine; or
2. In relapsed/refractory disease after failure of ≥2 multi-agent chemotherapy regimens in non-autologous stem cell transplant (SCT) candidates or after failure of autologous SCT as a single-agent; or
3. In relapsed/refractory disease if not previously used in combination with multi-agent chemotherapy; or
4. Consolidation following autologous SCT in members at high risk of relapse or progression.

Adcetris® (Brentuximab Vedotin) Approval Criteria [Diffuse Large B-Cell Lymphoma (DLBCL) or High Grade Lymphoma Diagnosis]:

1. As a single-agent; and
2. CD30+ disease; and
3. DLBCL relapsed/refractory disease in non-autologous stem cell transplant (SCT) candidates; or
4. In members who have transformed to DLBCL from follicular lymphoma or marginal zone lymphoma and received ≥2 lines of therapy for indolent or transformed disease.

Adcetris® (Brentuximab Vedotin) Approval Criteria [Primary Cutaneous Lymphomas – Mycosis Fungoides (MF)/Sézary Syndrome (SS) Diagnosis]:

1. As a single-agent as primary treatment or relapsed/refractory disease.

Adcetris® (Brentuximab Vedotin) Approval Criteria [Peripheral T-Cell Lymphoma (PTCL) Diagnosis]:

1. Treatment of previously untreated CD30+ disease in combination with cyclophosphamide, doxorubicin, and prednisone; or
2. In members who have received ≥1 line of therapy as a single-agent.

Adcetris® (Brentuximab Vedotin) Approval Criteria [Adult T-Cell Leukemia/Lymphoma Diagnosis]:

1. CD30+ disease; and
2. Member meets 1 of the following:
    a. In combination with cyclophosphamide, doxorubicin, and prednisone (CHP) in nonresponders to first-line therapy for chronic/smoldering subtype; or
    b. In combination with CHP for first-line therapy for acute or lymphoma subtype; or
    c. In combination with CHP for continued treatment in responders to first-line therapy for acute or lymphoma subtype; or
    d. In members who have received ≥1 line of therapy as a single-agent.

Adcetris® (Brentuximab Vedotin) Approval Criteria [T-Cell Lymphoma, Extranodal NK/T-Cell Lymphoma, Nasal Type Diagnosis]:

1. CD30+ disease; and

2. As a single-agent; and
3. Relapsed/refractory disease following additional therapy with an alternate combination chemotherapy regimen not previously used.

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

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

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

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

Beleodaq® (Belinostat) Approval Criteria [Anaplastic Large Cell Lymphoma (ALCL), Primary Cutaneous Diagnosis]:

1. As a single-agent for primary treatment or relapsed refractory with multifocal lesions, or cutaneous ALCL with regional nodes.

Beleodaq® (Belinostat) Approval Criteria [Primary Cutaneous Lymphomas – Mycosis Fungoides (MF)/Sézary Syndrome (SS) Diagnosis]:

1. Primary treatment in Stage IV non Sézary or visceral disease (solid organ) with or without radiation therapy for local control; or
2. Primary treatment for large cell transformation with generalized cutaneous or extracutaneous lesions with or without skin-directed therapy; or
3. As a single-agent (with or without skin-directed therapy) in relapsed/refractory disease.

Beleodaq® (Belinostat) Approval Criteria [Peripheral T-Cell Lymphoma (PTCL) Diagnosis]:

1. As a single-agent in relapsed/refractory disease.

Beleodaq® (Belinostat) Approval Criteria [Adult T-Cell Leukemia/Lymphoma Diagnosis]:

1. As a single-agent in relapsed/refractory disease.

Beleodaq® (Belinostat) Approval Criteria [T-Cell Lymphoma, Extranodal NK/T-Cell Lymphoma, Nasal Type Diagnosis]:

1. As a single-agent; and
2. Relapsed/refractory disease following additional therapy with an alternate combination chemotherapy regimen not previously used.

Calquence® (Acalabrutinib) Approval Criteria [Mantle Cell Lymphoma (MCL) Diagnosis]:

1. As a single-agent in members who have received ≥1 prior therapy.

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

1. As a single-agent in relapsed/refractory disease.

Copiktra® (Duvelisib) Approval Criteria [Follicular Lymphoma (FL) Diagnosis]:

1. Relapsed/refractory FL; and
2. Progression of disease following 2 or more lines of systemic therapy; and
3. As a single-agent.

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

1. Relapsed/refractory CLL or SLL; and
2. Progression of disease following 2 or more lines of systemic therapy; and
3. As a single-agent.

Folotyn® (Pralatrexate) Approval Criteria [Adult T-Cell Leukemia/Lymphoma Diagnosis]:

1. As a single-agent in relapsed/refractory disease.

Folotyn® (Pralatrexate) Approval Criteria [Anaplastic Large Cell Lymphoma (ALCL), Primary Cutaneous Diagnosis]:

1. As a single-agent in members with multifocal lesions or regional nodes either as primary treatment or in relapsed/refractory disease.

Folotyn® (Pralatrexate) Approval Criteria [Peripheral T-Cell Lymphoma (PTCL) Diagnosis]:

1. As a single-agent in relapsed/refractory disease.

Folotyn® (Pralatrexate) Approval Criteria [T-Cell Lymphoma, Extranodal NK/T-Cell Lymphoma, Nasal Type Diagnosis]:

1. As a single-agent; and
2. Relapsed/refractory disease following additional therapy with an alternate combination chemotherapy regimen not previously used.

Folotyn® (Pralatrexate) Approval Criteria [Primary Cutaneous Lymphomas – Mycosis Fungoides (MF)/Sézary Syndrome (SS) Diagnosis]:

1. As a single-agent as primary treatment or in relapsed/refractory disease.

Istodax® (Romidepsin) Approval Criteria [Primary Cutaneous Lymphomas – Mycosis Fungoides (MF)/Sézary Syndrome (SS) Diagnosis]:

1. As a single-agent as primary treatment or in relapsed/refractory disease.

Istodax® (Romidepsin) Approval [Anaplastic Large Cell Lymphoma (ALCL), Primary Cutaneous Diagnosis]:

1. As a single-agent in members with multifocal lesions or regional nodes either as primary treatment or in relapsed/refractory disease.

Istodax® (Romidepsin) Approval [Peripheral T-Cell Lymphoma (PTCL) Diagnosis]:

1. As a single-agent in relapsed/refractory disease.

Istodax® (Romidepsin) Approval [T-Cell Lymphoma, Extranodal NK/T-Cell Lymphoma, Nasal Type Diagnosis]:

1. As a single-agent; and
2. Relapsed/refractory disease following additional therapy with an alternate combination chemotherapy regimen not previously used.

Poteligeo® (Mogamulizumab-kpkc) Approval Criteria [Primary Cutaneous Lymphomas – Mycosis Fungoides (MF)/Sézary Syndrome (SS) Diagnosis]:

1. As a single-agent as primary treatment or in relapsed/refractory disease.

Poteligeo® (Mogamulizumab-kpkc) Approval Criteria [Adult T-Cell Leukemia/Lymphoma Diagnosis]:

1. As a single-agent in relapsed/refractory disease.

Truxima® (Rituximab-abbs) Approval Criteria:

1. An FDA approved diagnosis; and
2. A patient-specific, clinically significant reason why the member cannot use Rituxan® (rituximab) must be provided.

Yescarta® (Axicabtagene) Approval Criteria [Lymphoma Diagnosis]:

1. A diagnosis of large B-cell lymphoma [including diffuse large B cell lymphoma (DLBCL), high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma (FL)]; and
2. Member must be 18 years of age or older; and
3. Relapsed/refractory disease; and
4. Member must not have primary central nervous system lymphoma; and
5. Member must have had 2 or more lines of therapy; and
6. Health care facilities must be on the certified list to administer chimeric antigen receptor (CAR) T-cells, must be trained in the management of cytokine release syndrome (CRS) and neurologic toxicities, and must comply with the REMS requirements.

Zevalin® (Ibritumomab Tiuxetan) Approval Criteria [Follicular Lymphoma (FL) (Grade 1-2) Diagnosis]:

1. As a single-agent; and
2. Relapsed/refractory disease.

Zevalin® (Ibritumomab Tiuxetan) Approval Criteria [Follicular Lymphoma (FL) or Marginal Zone Lymphoma (MZL) Transformed to Diffuse Large B-Cell Lymphoma (DLBCL) Diagnosis]:

1. As a single-agent; and
2. Member meets 1 of the following:
    a. Minimal or no chemotherapy prior to histologic transformation to DLBCL (FISH for MYC and BCL2 and/or BCL6 must show no translocation) and have partial response, no response, or progressive disease after chemoimmunotherapy; or
    b. Member must have received ≥2 prior therapies of chemoimmunotherapy for indolent or transformed disease.

Zolinza® (Vorinostat) Approval Criteria [Primary Cutaneous Lymphomas – Mycosis Fungoides (MF)/Sézary Syndrome (SS) Diagnosis]:

1. As a single-agent as primary treatment or in relapsed/refractory disease.

Approval criteria for Gazyva® (obinutuzumab), Imbruvica® (ibrutinib), Kymriah® (tisagenlecleucel), Venclexta® (venetoclax), and Zydelig® (idelalisib) for indications other than lymphoma can be found in the February 2020 Drug Utilization Review (DUR) Board packet. These medications are reviewed annually with the leukemia medications.

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

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

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

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

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

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

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

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

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

1. As third-line or greater therapy for members who have transformed to non-germinal center DLBCL.

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

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

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

1. A diagnosis of non-germinal center DLBCL; and

2. As second-line or subsequent therapy; and
3. Member is not a candidate for high-dose therapy.

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

1. As second-line or subsequent therapy in members with partial response, persistent, or progressive disease; and
2. Non-germinal center B-cell type.

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

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

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

1. A diagnosis of large B-cell lymphoma [including diffuse large B-cell lymphoma (DLBCL), high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma (FL)]; and
2. Relapsed/refractory disease; and
3. Member must be 18 years of age or older; and
4. Member must not have primary central nervous system lymphoma; and
5. Member must have had 2 or more lines of therapy; and
6. Health care facilities must be on the certified list to administer chimeric antigen receptor (CAR) T-cells, must be trained in the management of cytokine release syndrome (CRS) and neurologic toxicities, and must comply with the REMS requirements.

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

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

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

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

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

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

The following approval criteria for Keytruda® (pembrolizumab) and Opdivo® (nivolumab) includes only criteria for indications of lymphoma. Complete prior authorization criteria for Keytruda® (pembrolizumab) and Opdivo® (nivolumab) can be found in the November 2019 DUR Board packet. These medications are reviewed annually with the skin cancer medications.

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

1. A diagnosis of relapsed or refractory classical HL (cHL); and
    a. Exception: lymphocyte-predominant HL
2. Pembrolizumab must be used as a single-agent; and
3. Member has not previously failed other PD-1 inhibitors [e.g., Opdivo® (nivolumab)].

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

1. A diagnosis of PMBCL in adult or pediatric members; and
2. Member must have refractory disease or pembrolizumab must be used in members who have relapsed after 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 PD-1 inhibitors [e.g., Opdivo® (nivolumab)].

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

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

Utilization of Lymphoma Medications: Calendar Year 2019

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

Comparison of Calendar Years: Pharmacy Claims

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2018	9	46	$524,267.13	$11,397.11	$366.11	2,942	1,432
2019	12	89	$968,145.39	$10,878.04	$377.59	3,506	2,564
% Change	**33.30%**	**93.50%**	**84.70%**	**-4.60%**	**3.10%**	**19.20%**	**79.10%**
Change	**3**	**43**	**$443,878.26**	**-$519.07**	**$11.48**	**564**	**1,132**

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

Calendar Year 2019 Utilization: Medical Claims

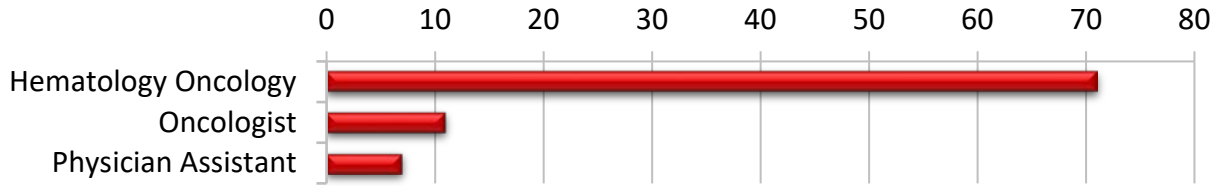
Calendar Year	*Total Members	†Total Claims	Total Cost	Cost/ Claim	Claims/ Member
2019	144	663	$7,123,159.57	$10,743.83	4.60

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

Demographics of Members Utilizing Lymphoma Medications: Pharmacy Claims

- Due to the limited number of members utilizing lymphoma medications, detailed demographic information could not be provided.

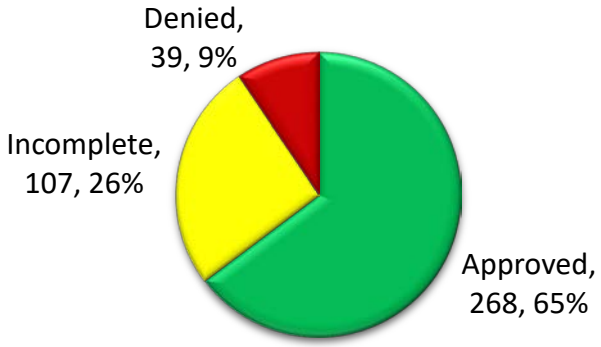
Top Prescriber Specialties of Lymphoma Medications By Number of Claims: Pharmacy Claims



Prior Authorization of Lymphoma Medications

There were 414 prior authorization requests submitted for lymphoma medications during calendar year 2019. The following chart shows the status of the submitted petitions for calendar year 2019.

Status of Petitions



Market News and Updates[9,10,11]

Anticipated Patent Expiration(s):

- Istodax® (romidepsin): August 2021
- Folotyn® (pralatrexate): May 2025
- Beleodaq® (belinostat): October 2027
- Zolinza® (vorinostat): March 2028
- Aliqopa™ (copanlisib): March 2032
- Copiktra® (duvelisib): May 2032
- Venclexta® (venetoclax): September 2033
- Zydelig® (idelalisib): September 2033
- Imbruvica® (ibrutinib): October 2033
- Brukinsa™ (zanubrutinib): April 2034
- Calquence® (acalabrutinib): July 2036

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

- **September 2017:** The FDA granted accelerated approval to Aliqopa™ (copanlisib) for the treatment of adult patients with relapsed FL who have received at least 2 prior systemic therapies.
- **June 2019:** The FDA granted accelerated approval to Polivy™ (polatuzumab vedotin-piiq), a CD79b-directed antibody-drug conjugate indicated in combination with bendamustine and a rituximab product for adult patients with relapsed or refractory DLBCL, not otherwise specified, after at least 2 prior therapies.
- **July 2019:** The FDA approved Ruxience™ (rituximab-pvvr), a biosimilar to Rituxan® (rituximab), for the treatment of adult patients with NHL, chronic lymphocytic leukemia (CLL), and granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA).
- **November 2019:** The FDA granted accelerated approval to Brukinsa™ (zanubrutinib) for the treatment of MCL for adult patients who have received at least 1 prior therapy.

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

- **May 2019*:** The FDA approved Venclexta® (venetoclax) for the treatment of adult patients with CLL or small lymphocytic lymphoma (SLL) in combination with obinutuzumab (Gazyva®).
- **May 2019:** The FDA approved Revlimid® (lenalidomide) in combination with a rituximab product for previously treated FL and previously treated MZL.
- **November 2019*:** The FDA approved Calquence® (acalabrutinib) for the treatment of adults with CLL or SLL.
- **January 2020:** FDA approved Keytruda® (pembrolizumab) for the treatment of patients with Bacillus Calmette-Guerin (BCG)-unresponsive, high-risk, non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors who are ineligible for or have elected not to undergo cystectomy.

*These new FDA approved indications were previously reviewed with the leukemia medications at the February 2020 DUR Board meeting.

Product Summaries[12,13,14,15]

Aliqopa™ (Copanlisib):

- **Therapeutic Class:** Kinase inhibitor
- **Indication(s):** Treatment of adult patients with relapsed FL who have received at least 2 prior systemic therapies
- **How Supplied:** 60mg lyophilized solid in a single-dose vial (SDV)
- **Dose:** 60mg intravenously (IV) on days 1, 8, and 15 of a 28-day treatment cycle on an intermittent schedule (3 weeks on, 1 week off)
- **Cost:** Wholesale Acquisition Cost (WAC) of $4,665.28 per SDV; $13,995.84 per 28 days based on recommended dosing

Brukinsa™ (Zanubrutinib):

- **Therapeutic Class:** Kinase inhibitor
- **Indication(s):** Treatment of adult patients with MCL who have received at least 1 prior therapy

- **How Supplied:** 80mg oral capsules
- **Dose:** 160mg orally twice daily or 320mg orally once daily
- **Cost:** WAC of $107.79 per 80mg capsule; $12,934.80 per 30 days based on recommended dosing of 160mg twice daily or 320mg once daily

Polivy™ (Polatuzumab Vedotin-piiq):

- **Therapeutic Class:** CD79b-directed antibody-drug conjugate
- **Indication(s):** For use in combination with bendamustine and a rituximab product for the treatment of adult patients with relapsed or refractory DLBCL, not otherwise specified, after at least 2 prior therapies
- **How Supplied:** 140mg lyophilized powder in a SDV
- **Dose:** 1.8mg/kg IV every 21 days for 6 cycles
- **Cost:** WAC of $15,000 per SDV; cost will vary due to weight-based dosing

Ruxience™ (Rituximab-pvvr):

- **Therapeutic Class:** CD20-directed cytolytic antibody; biosimilar to Rituxan® (rituximab)
- **Indication(s):** Treatment of adult patients with NHL, CLL, and GPA/MPA
- **How Supplied:** 100mg/10mL or 500mg/50mL solution for IV infusion in a SDV
- **Dose:**
  - NHL: 375mg/m^2 IV infusion; *see Ruxience™ Prescribing Information for dosing schedules specific to type of NHL being treated*
  - CLL: 375mg/m^2 in the first cycle and 500mg/m^2 in cycles 2 through 6, in combination with fludarabine and cyclophosphamide (FC), administered every 28 days
  - GPA and MPA: For induction, 375mg/m^2 once weekly for 4 weeks with glucocorticoids; then (2) 500mg IV infusions separated by 2 weeks; then 500mg every 6 months thereafter
- **Cost:** WAC of $71.68 per mL; cost will vary depending on patient weight, diagnosis, and treatment duration

Recommendations

- Update the prior authorization criteria to reflect new FDA approved indications; changes can be seen in the following criteria listed in red (only criteria with updates listed)
- The prior authorization of Aliqopa™ (copanlisib), Brukinsa™ (zanubrutinib), Polivy™ (polatuzumab vedotin-piiq), and Ruxience™ (rituximab-pvvr) with the following criteria listed in red

Aliqopa™ (Copanlisib) Approval Criteria [Follicular Lymphoma (FL) Diagnosis]:

1. A diagnosis of relapsed/refractory FL; and
2. Member must have failed at least 2 prior systemic therapies.

Brukinsa™ (Zanubrutinib) Approval Criteria [Mantle Cell Lymphoma (MCL) Diagnosis]:

1. Adult members with a diagnosis of MCL; and
2. Member must have received at least 1 prior therapy.

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.

Polivy™ (Polatuzumab Vedotin-piiq) Approval Criteria [Diffuse Large B-Cell Lymphoma (DLBCL) or High Grade Lymphoma Diagnosis]:

1. Relapsed/refractory DLBCL or high grade B-cell lymphoma after at least 2 prior therapies; and
2. Used in combination with bendamustine and rituximab; and
3. Member is not a candidate for transplant.

Ruxience (Rituximab-pvvr) Approval Criteria:

1. An FDA approved diagnosis; and
2. A patient-specific, clinically significant reason why the member cannot use Rituxan® (rituximab) must be provided.

Utilization Details of Lymphoma Medications: Calendar Year 2019

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
IBRUTINIB PRODUCTS					
IMBRUVICA TAB 420MG	31	6	$374,552.57	5.17	$12,082.34
IMBRUVICA CAP 140MG	14	2	$86,103.21	7	$6,150.23
IMBRUVICA TAB 280MG	11	3	$132,904.15	3.67	$12,082.20
IMBRUVICA TAB 560MG	9	2	$108,752.31	4.5	$12,083.59
SUBTOTAL	**65**	**13**	**$702,312.24**	**5**	**$10,804.80**
ACALABRUTINIB PRODUCTS					
CALQUENCE CAP 100MG	9	1	$126,643.99	9	$14,071.55
SUBTOTAL	**9**	**1**	**$126,643.99**	**9**	**$14,071.55**
IDELALISIB PRODUCTS					
ZYDELIG TAB 150MG	8	1	$85,793.16	8	$10,724.15
SUBTOTAL	**8**	**1**	**$85,793.16**	**8**	**$10,724.15**
VENETOCLAX PRODUCTS					
VENCLEXTA TAB 100MG	4	1	$23,447.26	4	$5,861.82
VENCLEXTA TAB START PK	1	1	$2,534.36	1	$2,534.36
SUBTOTAL	**5**	**2**	**$25,981.62**	**2.5**	**$5,196.32**
VORINOSTAT PRODUCTS					
VORINOSTAT CAP 100 MG	1	1	$15,016.97	1	$15,016.97
SUBTOTAL	**1**	**1**	**$15,016.97**	**1**	**$15,016.97**
DUVELISIB PRODUCTS					
COPIKTRA CAP 15MG	1	1	$12,397.41	1	$12,397.41
SUBTOTAL	**1**	**1**	**$12,397.41**	**1**	**$12,397.41**
TOTAL	**89**	**12***	**$968,145.39**	**7.42**	**$10,878.04**

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

Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBERS	COST/ CLAIM
BRENTUXIMAB VEDOTIN J9042	17	6	$212,533.36	2.83	$12,501.96
PEMBROLIZUMAB J9271	337	79	$3,628,649.00	4.27	$10,767.50
NIVOLUMAB J9299	309	62	$3,281,977.21	4.98	$10,621.29
TOTAL	**663^**	**147***	**$7,123,159.57**	**4.51**	**$10,743.83**

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

[1] Freedman AS, Friedberg JW, Aster JC. Clinical presentation and diagnosis of non-Hodgkin lymphoma. *UpToDate*. Available online at: https://www.uptodate.com/contents/clinical-presentation-and-diagnosis-of-non-hodgkin-lymphoma?search=non%20hodgkins%20lymphoma&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1. Last revised 09/27/2018. Last accessed 02/21/2020.

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[4] MD Anderson Cancer Center. Non-Hodgkin's Lymphoma. Available online at: https://www.mdanderson.org/cancer-types/non-hodgkins-lymphoma.html. Last accessed 02/21/2020.

[5] MD Anderson Cancer Center. Hodgkin's Lymphoma. Available online at: https://www.mdanderson.org/cancer-types/hodgkins-lymphoma.html. Last accessed 02/21/2020.

[6] Aster JC, Pozdnyakova O. Epidemiology, pathologic features, and diagnosis of classic Hodgkin lymphoma. *UpToDate*. Available online at: https://www.uptodate.com/contents/epidemiology-pathologic-features-and-diagnosis-of-classic-hodgkin-lymphoma?search=hodgkins%20disease%20adult&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2. Last revised 06/11/2018. Last accessed 02/21/2020.

[7] Freedman AS, Aster JC. Clinical manifestations, pathologic features, and diagnosis of peripheral T cell lymphoma, not otherwise specified. *UpToDate*. Available online at: https://www.uptodate.com/contents/clinical-manifestations-pathologic-features-and-diagnosis-of-peripheral-t-cell-lymphoma-not-otherwise-specified?search=t-cell%20lymphoma&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2. Last revised 04/12/2019. Last accessed 02/24/2020.

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[10] FDA: Hematology/Oncology (Cancer) Approvals & Safety Notifications. Available online at: https://www.fda.gov/drugs/resources-information-approved-drugs/hematologyoncology-cancer-approvals-safety-notifications. Last revised 01/09/2020. Last accessed 01/14/2020.

[11] Pfizer. FDA Approves Pfizer's Biosimilar, Ruxience™ (rituximab-pvvr), for Certain Cancers and Autoimmune Conditions. Available online at: https://www.pfizer.com/news/press-release/press-release-detail/fda_approves_pfizer_s_biosimilar_ruxience_rituximab_pvvr_for_certain_cancers_and_autoimmune_conditions. Issued 07/23/2019. Last accessed 02/19/2020.

[12] Aliqopa™ Prescribing Information. Bayer Healthcare Pharmaceuticals. Available online at: http://labeling.bayerhealthcare.com/html/products/pi/Aliqopa_PI.pdf. Last revised 02/2020. Last accessed 02/19/2020.

[13] Brukinsa™ Prescribing Information. BeiGene. Available online at: https://www.brukinsa.com/prescribing-information.pdf. Last revised 11/2019. Last accessed 02/19/2020.

[14] Polivy™ Prescribing Information. Genentech. Available online at: https://www.gene.com/download/pdf/polivy_prescribing.pdf. Last revised 06/2019. Last accessed 02/19/2020.

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Appendix K

Calendar Year 2019 Annual Review of Lutathera® (Lutetium Lu-177 Dotatate) and Vitrakvi® (Larotrectinib)

Oklahoma Health Care Authority
March 2020

Introduction[1,2,3,4]

Gastroenteropancreatic Neuroendocrine Tumors (GEP-NETs):
GEP-NETs are complex neoplasms that present many clinical challenges. GEP-NETs, also known as carcinoids and islet cell tumors, are tumors derived from neuroendocrine cells that occur anywhere along the gastrointestinal (GI) tract and comprise a heterogeneous family of neoplasms with a wide and complex spectrum of clinical behavior. These tumors have been considered rare diseases; however, data from the United States Surveillance Epidemiology and End Results show an increase of more than 400% in the incidence of GEP-NETs over a period of 29 years (1.09 per 100,000 population in 1973 to 5.25 per 100,000 population in 2004). GEP-NETs are more prevalent than many other tumors of the GI tract, including stomach and pancreatic carcinomas combined. The age at diagnosis is generally younger than for carcinomas (5^{th} decade), and GEP-NETs may arise sporadically or as a result of hereditary predisposition. GEP-NETs have traditionally been divided into foregut, midgut, and hindgut tumors. Survival is dependent on stage and histology. In January 2018, the U.S. Food and Drug Administration (FDA) approved Lutathera® (lutetium Lu-177 dotatate) for the treatment of adult patients with somatostatin receptor-positive GEP-NETs.

Neurotrophic Tyrosine Receptor Kinase (*NTRK*) Gene Fusions:
The underlying genomic profile of a tumor has become increasingly important in oncology. Genomic alterations, such as *NTRK* gene fusions, are an area of focus. In tropomyosin receptor kinase (TRK) fusion cancer, the *NTRK* gene fuses with an unrelated gene, causing overexpression of the TRK protein. TRK fusion cancer is rare, but occurs in a broad range of tumor types with varying prevalence across both adult and pediatric patient populations. In November 2018, Vitrakvi® (larotrectinib) was approved by the FDA for use in adults and children with any solid tumor with an *NTRK* gene fusion without a known acquired resistance mutation, that is either metastatic or where surgical resection is likely to result in severe morbidity, and who have no other satisfactory alternative treatments or whose cancer has progressed following treatment. This represents the first new cancer drug to be approved based on a DNA test, instead of based on the tissue of origin.

Current Prior Authorization Criteria

Lutathera® (Lutetium Lu-177 Dotatate) Approval Criteria [Gastroenteropancreatic Neuroendocrine Tumor (GEP-NET) Diagnosis]:

1. A diagnosis of progressive locoregional advanced disease or metastatic disease; and
2. Positive imaging of somatostatin receptor; and

3. Must be used as second-line or subsequent therapy following progression on octreotide or lanreotide; or
4. May be used first-line for treatment of pheochromocytoma/paraganglioma.

Vitrakvi® (Larotrectinib) Approval Criteria [Solid Tumors with Neurotrophic Receptor Tyrosine Kinase (*NTRK*) Gene Fusion Diagnosis]:

1. Diagnosis of a solid tumor with a *NTRK* gene fusion without a known acquired resistance mutation; and
2. Disease is metastatic or surgical resection (or radioactive iodine refractory if thyroid carcinoma) is contraindicated; and
3. Documentation of no satisfactory alternative treatments or progression following acceptable alternative treatments.

Utilization of Lutathera® (Lutetium Lu-177 Dotatate) and Vitrakvi® (Larotrectinib): Calendar Year 2019

Calendar Year 2019 Utilization: Medical Claims

Calendar Year	*Total Members	+Total Claims	Total Cost	Cost/ Claim	Total Units
2019	1	2	$95,000.00	$47,500.00	400

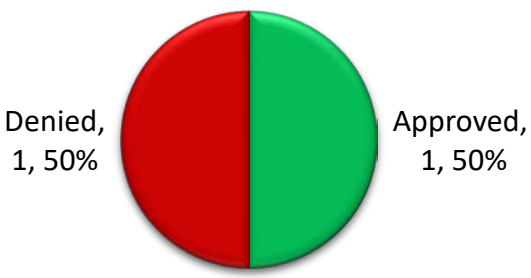
*Total number of unduplicated members. +Total number of unduplicated claims.
Cost do not reflect rebated prices or net costs.

- The medical claims information provided is for Lutathera® (lutetium Lu-177 dotatate). Due to the limited number of members utilizing Lutathera® during calendar year 2019, detailed demographic information could not be provided. There was no SoonerCare utilization of Vitrakvi® (larotrectinib) for calendar year 2019.

Prior Authorization of Lutathera® (Lutetium Lu-177 Dotatate) and Vitrakvi® (Larotrectinib)

There were 2 prior authorization requests submitted for Lutathera® (lutetium Lu-177 dotatate) during calendar year 2019. There were no prior authorization requests submitted for Vitrakvi® (larotrectinib) for calendar year 2019. The following chart shows the status of the submitted petitions for Lutathera® (lutetium Lu-177 dotatate) for calendar year 2019.

Status of Petitions



Market News and Updates[5]

Anticipated Patent Expiration(s):

- Vitrakvi® (larotrectinib): November 2035

Recommendations

No changes are recommended to the current Lutathera® (lutetium Lu-177 dotatate) or Vitrakvi® (larotrectinib) prior authorization criteria at this time.

[1] Díez M, Teulé A, Salazar R. Gastroenteropancreatic neuroendocrine tumors: diagnosis and treatment. *Ann Gastroenterol* 2013; 26(1):29-36.

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Appendix L

Calendar Year 2019 Annual Review of Multiple Sclerosis (MS) Medications and 30-Day Notice to Prior Authorize Mayzent® (Siponimod), Mavenclad® (Cladribine), and Vumerity™ (Diroximel Fumarate)

Oklahoma Health Care Authority
March 2020

Current Prior Authorization Criteria

Multiple Sclerosis (MS) Interferon Medications Approval Criteria:

1. An FDA approved diagnosis of clinically isolated syndrome, relapsing forms of MS, or secondary progressive forms of MS; and
2. Authorization of Tier-2 medications requires previous failure of preferred Tier-1 medication(s) defined as:
   a. Occurrence of an exacerbation after 6 months; or
   b. Significant increase in magnetic resonance imaging (MRI) lesions after 6 months; or
   c. Adverse reactions or intolerable side effects; and
3. Approvals will not be granted for concurrent use with other disease-modifying therapies; and
4. Compliance will be checked for continued approval every 6 months.

Multiple Sclerosis (MS) Interferon Medications	
Tier-1	**Tier-2**
interferon β - 1a (Avonex®)	interferon β - 1a (Rebif®)
interferon β - 1b (Betaseron®)	interferon β - 1a (Plegridy®)
	interferon β - 1b (Extavia®)

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.

Ampyra® (Dalfampridine) Approval Criteria:

1. An FDA approved indication to improve walking in adult members with multiple sclerosis (MS); and
2. Kurtzke Expanded Disability Status Scale (EDSS) score between 3 and 7.5; and
3. Initial approvals will be for the duration of 90 days. If the member has responded well to treatment and the prescriber states that the member has shown improvement or the drug was effective, the member may receive authorization for 1 year; and
4. A quantity limit of 60 tablets for 30 days will apply; and
5. Ampyra® may be used with other MS therapies.

Aubagio® (Teriflunomide) Approval Criteria:

1. An FDA approved diagnosis of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease; and

2. Approvals will not be granted for concurrent use with other disease-modifying therapies; and
3. All of the following will be required for initiation of treatment:
    a. Verification that female members are not pregnant and are currently using reliable contraception; and
    b. Verification that the member has no active infection(s); and
    c. Complete blood counts (CBC) and verification that levels are acceptable to the prescriber; and
    d. Liver function tests (LFTs) and verification that levels are acceptable to the prescriber; and
    e. Blood pressure (BP) measurement and verification that BP is being monitored; and
    f. Verification that the member does not have tuberculosis (TB), or completion of standard medical treatment for members with TB; and
4. Initial approvals of Aubagio® will be for 6 months, after which time all of the following will be required for further approval:
    a. Medication compliance; and
    b. Repeat CBC and verification that counts are acceptable to the prescriber; and
    c. Repeat LFTs and verification that levels are acceptable to the prescriber; and
    d. Verification that female members are not pregnant and will continue using reliable contraception; and
    e. Verification that BP and signs of renal failure are being monitored; and
5. Compliance will be checked for continued approval every 6 months; and
6. A quantity limit of 30 tablets per 30 days will apply.

Copaxone® (Glatiramer Acetate) Approval Criteria:

1. An FDA approved diagnosis of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults; and
2. Approvals for the 40mg strength of Copaxone® will require a patient-specific, clinically significant reason why the member cannot use the 20mg strength; and
3. Approvals for the generic formulation of either strength of Copaxone®, including Glatopa®, will require a patient-specific, clinically significant reason why the member cannot use the brand formulation (brand formulation is preferred); and
4. Compliance will be checked for continued approval every 6 months.

Gilenya® (Fingolimod) Approval Criteria:

1. An FDA approved diagnosis of relapsing forms of multiple sclerosis (MS)*, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults; and
   (*The manufacturer of Gilenya® has provided a supplemental rebate to remove the requirement of "at least 1 relapse in the previous 12 months, or transitioning from existing MS therapy"; however, Gilenya® will follow the original criteria if the manufacturer chooses not to participate in supplemental rebates); and
2. Approvals will not be granted for concurrent use with other disease-modifying therapies; and

3. The first dose should be observed in the prescriber's office for signs and symptoms of bradycardia for 6 hours after the first dose; and
4. Verification from the prescriber that member has no active infection(s); and
5. Complete blood counts (CBC) and verification that levels are acceptable to the prescriber; and
6. LFTs and verification that levels are acceptable to the prescriber; and
7. Compliance will be checked for continued approval every 6 months.

Lemtrada® (Alemtuzumab) Approval Criteria:

1. An FDA approved diagnosis of relapsing forms of multiple sclerosis (MS), to include relapsing remitting disease and active secondary progressive disease in adults; and
2. Member must have had an inadequate response to 2 or more medications indicated for the treatment of MS; and
    a. Lemtrada® must be administered in a setting with appropriate equipment and personnel to manage anaphylaxis or serious infusion reactions. The prescriber must agree that the member will be monitored for 2 hours after each infusion; and
2. The prescriber must agree to monitor complete blood counts (CBC) with differential, serum creatinine levels, and urinalysis with urine cell counts at periodic intervals for 48 months after the last dose of Lemtrada®; and
3. The prescriber must agree that baseline and yearly skin examinations will be performed while the member is utilizing Lemtrada® therapy; and
4. Member, prescriber, pharmacy, and health care facility must all enroll in the Lemtrada® REMS Program and maintain enrollment throughout therapy.

Ocrevus® (Ocrelizumab) Approval Criteria:

1. An FDA approved diagnosis of primary progressive forms of multiple sclerosis (MS) or relapsing forms of MS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults; and
2. Approvals will not be granted for concurrent use with other disease modifying therapies; and
3. Ocrevus® must be administered in a setting with appropriate equipment and personnel to manage anaphylaxis or serious infusion reactions. The prescriber must agree that the member will be monitored for 1 hour after each infusion; and
4. Prescriber must verify hepatitis B virus (HBV) testing has been performed prior to initiating Ocrevus® therapy and member does not have active HBV; and
5. Verification from the prescriber that member has no active infection(s); and
6. Verification from the prescriber that female members are not currently pregnant and will use contraception while receiving Ocrevus® therapy and for 6 months after the last infusion of Ocrevus®; and
7. Compliance will be checked for continued approval.

Tecfidera® (Dimethyl Fumarate) Approval Criteria:

1. An FDA approved diagnosis of clinically isolated syndrome, relapsing forms of MS, or secondary progressive forms of MS; and

2. Approvals will not be granted for concurrent use with other disease-modifying therapies; and
3. Verification from the prescriber that member has no active infection(s); and
4. Complete blood counts (CBC) and verification that levels are acceptable to the prescriber; and
5. Serum aminotransferase, alkaline phosphatase, and total bilirubin levels and verification that levels are acceptable to the prescriber; and
6. Compliance will be checked for continued approval every 6 months; and
7. A quantity limit of 60 tablets per 30 days will apply.

Tysabri® (Natalizumab) Approval Criteria:

1. An FDA approved diagnosis of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults or Crohn's disease; and
2. For a diagnosis of MS, the following criteria will apply:
   a. Prescriber must be a neurologist or be an advanced care practitioner with a supervising prescriber that is a neurologist; and
   b. Approvals will not be granted for concurrent use with other disease-modifying therapies; or
3. For a diagnosis of Crohn's disease, the following criteria will apply:
   a. Treatment with at least 2 different first-line therapeutic categories for Crohn's disease that have failed to yield an adequate clinical response, or a patient-specific, clinically significant reason why the member cannot use all available first- and second-line alternatives must be provided; and
4. Prescriber, infusion center, and member must enroll in the TOUCH Prescribing Program; and
5. Compliance will be checked for continued approval every 6 months.

Utilization of MS Medications: Calendar Year 2019

Comparison of Calendar Years: Pharmacy Claims

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2018	193	1,411	$8,526,806.36	$6,043.09	$208.68	43,714	40,861
2019	163	1,168	$6,926,266.04	$5,930.02	$202.19	40,072	34,256
% Change	**-15.50%**	**-17.20%**	**-18.80%**	**-1.90%**	**-3.10%**	**-8.30%**	**-16.20%**
Change	**-30**	**-243**	**-$1,600,540.32**	**-$113.07**	**-$6.49**	**-3,642**	**-6,605**

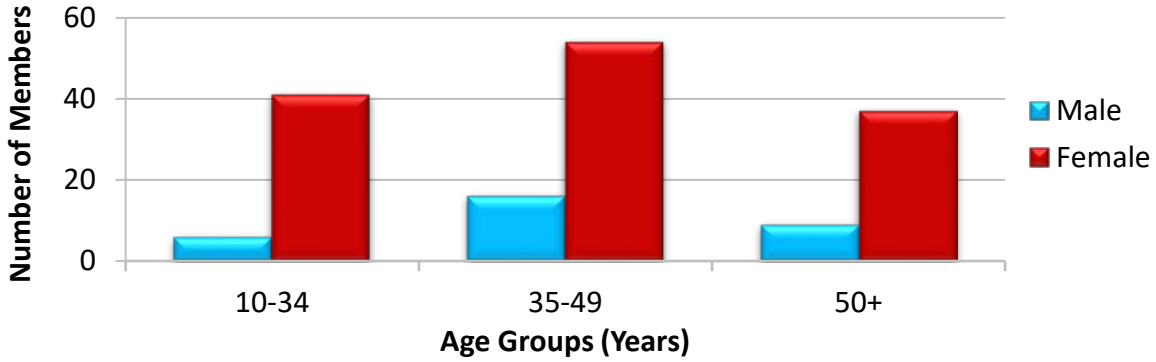
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

Comparison of Calendar Years: Medical Claims

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Claims/ Member
2018	46	198	$2,159,987.12	$10,909.03	4.3
2019	48	184	$2,066,399.32	$11,230.43	3.8
% Change	**0.04%**	**-0.07%**	**-0.04%**	**0.03%**	**-0.12%**
Change	**2**	**-14**	**-$93,584.80**	**$321.40**	**-0.5**

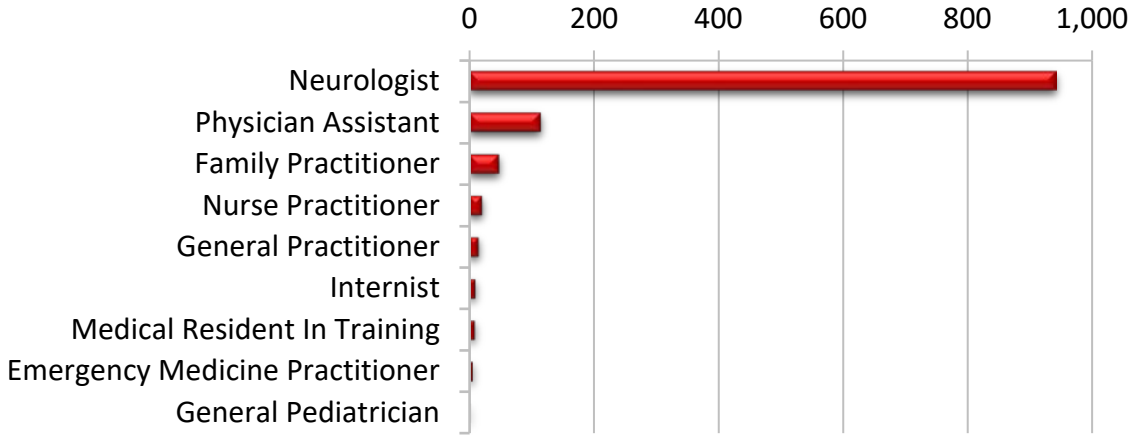
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

Demographics of Members Utilizing MS Medications: Pharmacy Claims



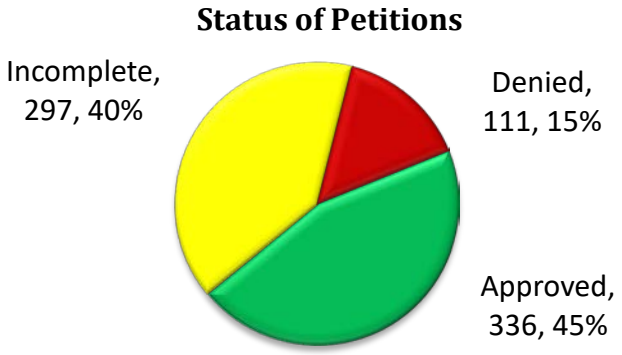
- All members younger than 21 years of age were verified to have a diagnosis of MS in their diagnosis history, and their MS therapies were prescribed by a specialist in neurology.

Top Prescriber Specialties of MS Medications by Number of Claims: Pharmacy Claims



Prior Authorization of MS Medications

There were 744 prior authorization requests submitted for 209 unique members for MS medications during calendar year 2019. The following chart shows the status of the submitted petitions for calendar year 2019.



Market News and Updates[1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27]

Anticipated Patent Expiration(s):

- Mavenclad® (cladribine): October 2026
- Tecfidera® (dimethyl fumarate): February 2028
- Mayzent® (siponimod): November 2030
- Gilenya® (fingolimod): September 2032
- Vumerity™ (diroximel fumarate): September 2033
- Aubagio® (teriflunomide): February 2034

Generic Formulation Update(s):

- **December 2018:** The U.S. Food and Drug Administration (FDA) granted Lupin tentative approval for a generic formulation of Tecfidera® (dimethyl fumarate). This is the first FDA approval of a generic formulation of dimethyl fumarate. Full approval would not be expected until after patent expiration of Tecfidera® in June 2020.
- **December 2019:** The FDA approved 3 applications for first time generics of Gilenya® (fingolimod) capsules for the treatment of relapsing forms of multiple sclerosis (MS) in adult patients.

New FDA Approval(s):

- **January 2019:** Banner Life Sciences announced that Bafiertam™ (monomethyl fumarate), a prodrug to Tecfidera® (dimethyl fumarate), received tentative FDA approval for the treatment of relapsing forms of MS. Bafiertam™ is expected to be available as delayed-release 95mg oral capsules. According to the FDA, Bafiertam™ met the required safety, efficacy, quality, and bioequivalence standards for tentative approval. Full approval, however, is expected after patent expiration of Tecfidera® in June 2020 or sooner depending on the outcome of pending litigation with Biogen, the manufacturer of Tecfidera®. Bafiertam™ will be brought to the Drug Utilization Review (DUR) Board for review after full approval has been granted by the FDA.
- **March 2019:** Mayzent® (siponimod) was FDA approved for the treatment of adults with relapsing forms of MS, including secondary progressive multiple sclerosis (SPMS) with active disease, relapsing-remitting multiple sclerosis (RRMS), and clinically isolated syndrome (CIS). CIS is defined as a first episode of neurologic symptoms that lasts at

least 24 hours and is caused by inflammation or demyelination in the central nervous system (CNS). SPMS is a debilitating form of MS characterized by progressive and irreversible neurological disability. Mayzent® is a next generation, selective sphingosine-1-phosphate (S1P) receptor modulator that selectively binds to S1P1 and S1P5 receptors. In relation to the S1P1 receptor, it prevents the lymphocytes from egressing the lymph nodes and as a consequence, from entering the CNS of patients with MS. This leads to the anti-inflammatory effects of siponimod. Mayzent® also enters the CNS and directly binds to the S1P5 and S1P1 sub-receptors on specific cells in the CNS (oligodendrocytes and astrocytes) to promote remyelination and prevent inflammation.

- **March 2019:** Mavenclad® (cladribine) was FDA approved to treat relapsing forms of MS in adults, to include RRMS and active SPMS. Mavenclad® is not recommended for MS patients with CIS. Because of its safety profile, the use of Mavenclad® is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternate drug indicated for the treatment of MS. Mavenclad® has a *Boxed Warning* for an increased risk of malignancy and fetal harm. Mavenclad® is not to be used in patients with current malignancy.
- **July 2019:** The FDA updated the prescribing information to clarify the approved indications for Avonex® (interferon β - 1a), Copaxone® (glatiramer acetate), Ocrevus® (ocrelizumab), Plegridy® (interferon β - 1a), Rebif® (interferon β - 1a), and Tecfidera® (dimethyl fumarate) for the treatment of relapsing forms of MS, to include CIS, RRMS, and active SPMS, in adults. Similarly, the FDA updated the prescribing information in August 2019 for Betaseron® (interferon β – 1b), Extavia® (interferon β – 1b), Gilenya® (fingolimod), and Tysabri® (natalizumab) and in September 2019 updated the prescribing information for Aubagio® (teriflunomide). The current prior authorization (PA) criteria for Aubagio®, Avonex®, Betaseron®, Copaxone®, Extavia®, Gilenya®, Ocrevus®, Plegridy®, Rebif®, Tecfidera®, and Tysabri® have been updated to include this clarification (shown in red in the *Current Prior Authorization Criteria* section at the beginning of this report).
- **October 2019:** The FDA updated the prescribing information to clarify the approved indications for Lemtrada® (alemtuzumab) for the treatment of relapsing forms of MS, to include RRMS and active SPMS disease in adults. The current PA criteria for Lemtrada® have been updated to include this clarification (shown in red in the *Current Prior Authorization Criteria* section at the beginning of this report).
- **October 2019:** Vumerity™ (diroximel fumarate) was FDA approved for the treatment of relapsing forms of MS, to include CIS, RRMS, and active SPMS. Once in the body, Vumerity™ rapidly converts to monomethyl fumarate (MMF), the same active metabolite of dimethyl fumarate (Tecfidera®). The FDA approval of Vumerity™ was based on a New Drug Application (NDA) submitted under the 505(b)(2) filing pathway, which included data from pharmacokinetic bridging studies comparing Vumerity™ and Tecfidera® to establish bioequivalence, and relied, in part, on the FDA's findings of safety and efficacy for Tecfidera®.

Safety Update(s):

- **July 2019:** The European Medicines Agency (EMA) has recommended that Gilenya® (fingolimod) must not be used in pregnant women or in women able to have children

who are not using effective contraception. If a woman becomes pregnant while using Gilenya®, the medicine must be stopped and the pregnancy closely monitored. These updated recommendations follow a review of available data triggered by post-marketing reports suggesting that infants born to mothers treated with fingolimod during pregnancy have a 2-fold increased risk of major congenital malformations compared with the rate observed in the general population [which is 2-3%, according to the European network of population-based registries for the epidemiological surveillance of congenital anomalies (EUROCAT)]. The most frequently reported major malformations in infants exposed to fingolimod *in utero* are congenital heart diseases (e.g., atrial and ventricular septal defects, tetralogy of Fallot), renal abnormalities, and musculoskeletal abnormalities.

- **January 2020:** The EMA issued its final decision to support the recommendation to restrict the use of Lemtrada® (alemtuzumab) due to reports of rare but serious side effects, including death. The review of Lemtrada® was initiated in April 2019 and carried out by the Pharmacovigilance Risk Assessment Committee (PRAC). Lemtrada® should now only be used to treat RRMS if the disease is highly active despite treatment with at least 1 disease-modifying therapy (DMT) or if the disease is worsening rapidly. Lemtrada® must also no longer be used in patients with certain heart, circulation or bleeding disorders, or in patients who have autoimmune disorders other than MS. The medication should only be given in a hospital with ready access to intensive care facilities and specialists who can manage serious adverse reactions. Previously in November 2018, the FDA issued a Safety Announcement regarding rare but serious cases of stroke and tears in the lining of the arteries in the head and neck that have occurred in MS patients receiving Lemtrada® (alemtuzumab). The FDA has added a warning about these risks to the prescribing information in the product label as well as adding a *Boxed Warning* regarding the risk of stroke.

Guideline Update(s):

- **August 2019:** A practice guideline update by the American Academy of Neurology (AAN) for vaccine-preventable infections and immunization in MS was published in *Neurology.* This practice guideline updates previous guidance from 2002 and incorporates new evidence, vaccines, and DMTs. From that review, the panel developed the following recommendations for clinicians:
  - Discuss the evidence about immunizations in MS with patients and ask about their opinions and preferences.
  - Recommend patients follow all local vaccine standards, unless there are specific contraindications, and weigh local vaccine-preventable disease risks.
  - Counsel patients about infection risks of specific immunosuppressive or immunomodulating (ISIM) drugs according to prescribing information and vaccinate patients as needed at least 4 to 6 weeks before starting ISIM therapy. ISIM drugs include alemtuzumab (Lemtrada®), dimethyl fumarate (Tecfidera®), fingolimod (Gilenya®), mitoxantrone, natalizumab (Tysabri®), ocrelizumab (Ocrevus®), rituximab (Rituxan®), and teriflunomide (Aubagio®).
  - Recommend yearly influenza vaccines unless there is a specific contraindication.

- Screen for infections before starting ISIM treatment, including hepatitis, tuberculosis, and varicella zoster virus, according to prescribing information and treat patients who test positive for latent infections.
- In patients at high risk for infection, screen and (if necessary) treat even when prescribing information does not call for it; consult infectious disease or other specialists about treating patients who screen positive for latent infection before treating them with ISIM drugs.
- Recommend against using live-attenuated vaccines in patients using ISIM therapies.
- Delay vaccinating patients who are experiencing an MS relapse.

Pipeline Update(s):

- **Evobrutinib:** In September 2019, Merck KGaA announced the initiation of 2 global pivotal Phase 3 trials (EVOLUTION RMS 1 and 2) to study the efficacy and safety of evobrutinib, an oral, highly selective Bruton's Tyrosine Kinase (BTK) inhibitor in adult patients with relapsing multiple sclerosis (RMS). Evobrutinib is entering Phase 3 trials following the results of the Phase 2 clinical trial, which met its primary endpoint over 24 weeks of treatment, where the total cumulative number of T1 gadolinium-enhancing (Gd+) lesions was reduced with evobrutinib compared with placebo. The reduction of T1 Gd+ lesions was observed at 12 weeks, the first time point at which MRI data was available, and maintained through 48 weeks with evobrutinib 75mg once daily (QD) and 75mg twice daily (BID). Further data show that the effect on relapse reduction observed at Week 24 was maintained through 48 weeks. EVOLUTION RMS 1 and 2 are multicenter, randomized, parallel-group, double-blind, active-controlled studies comparing evobrutinib BID with interferon (IFN) β - 1a given intramuscularly once a week. The primary endpoint of both studies is annualized relapse rate (ARR) at week 96. Secondary endpoints include time to first occurrence of 12- and 24-week confirmed Expanded Disability Status Scale (EDSS) progression and total number of T1 Gd+ lesions and new or enlarging T2 lesions assessed by magnetic resonance imaging. Trial recruitment is currently underway with the goal of 1,900 patients enrolled, and the target completion is June 2023.
- **Ibudilast:** In October 2017, results of a Phase 2 trial of ibudilast, an investigational phosphodiesterase type 4 and 10 enzyme (PDE-4 and PDE-10) inhibitor, revealed that ibudilast may slow the loss of brain tissue in progressive MS patients. The Phase 2 SPRINT-MS trial evaluated the efficacy of ibudilast in 255 adult patients with primary MS or SPMS. Patients must have shown clear signs of disability progression in the 2 years before enrollment and were randomly assigned to ibudilast or placebo. Patients were followed for 96 weeks, with doctor's evaluations and imaging assessments of patients' brains performed every 24 weeks. Brain shrinkage was evaluated using a measure known as brain parenchymal fraction (BPF). Compared to placebo, ibudilast treatment was associated with a 48% slowing in the rate of atrophy progression. Approximately 92% of the ibudilast-treated participants experienced adverse events, versus 88% in the placebo group, with the most common being nausea, diarrhea, abdominal pain, and

vomiting. Ibudilast is in ongoing studies for 4 other disease states. Phase 3 trial plans for progressive MS have not been released.

- **Ozanimod:** In October 2018, Celgene Corporation announced results from 2 post hoc analyses of data from the Phase 3 SUNBEAM and RADIANCE Part B trials, which evaluated the efficacy of ozanimod, an oral sphingosine 1-phosphate 1 and 5 (S1PR1 and S1PR5) receptor modulator, versus Avonex® (IFN β - 1a) in patients with RRMS. A post hoc analysis of 12-month data from SUNBEAM examined the effect of ozanimod on cognitive processing speed, based on performance on the Symbol Digit Modalities Test (SDMT). More patients exhibited clinically meaningful (≥4-point) improvements in processing speed at month 12 with ozanimod 1mg [rate ratio: 1.3; 95% confidence interval (CI): 1.05, 1.55] and 0.5mg (rate ratio: 1.2; 95% CI: 0.94, 1.40) versus IFN. A second post hoc analysis regarding ARR and MRI lesions examined the effect of ozanimod in patients with early RRMS compared with patients with more advanced disease. Early RRMS was defined based on a composite baseline profile, including 3 years or less since diagnosis, an EDSS of ≤3.5, and the use of 1 or no DMTs. ARR was lower at 12 months for both early and more advanced RRMS with ozanimod 1mg (early ARR=0.149; advanced ARR=0.217) and ozanimod 0.5mg (early ARR=0.200; advanced ARR=0.277) compared with IFN (early ARR=0.285; advanced ARR=0.363). In the SUNBEAM and RADIANCE clinical trials, the most common adverse reactions (≥5%) experienced (that were higher with ozanimod than with IFN) were upper respiratory tract infections, urinary tract infections, increases of alanine aminotransferase, and increases of gamma-glutamyl transferase. Celgene previously received a refuse to file letter from the FDA for an NDA for ozanimod regarding insufficient data in February 2018. In June 2019, the FDA accepted the NDA for review, and the EMA also accepted the marketing authorization application for review in the European Union. Under the Prescription Drug User Fee Act, the FDA has set its action date as March 25, 2020. A regulatory decision from the EMA is expected in the first half of 2020.
- **Temelimab:** GeNeuro announced collaboration for a new clinical trial of temelimab in MS with clinical researchers of Karolinska Institutet and the Academic Specialist Center (ASC), Stockholm, Sweden. The trial will be conducted at Center for Neurology of ASC, the largest MS center in Sweden with approximately 2,400 patients. The 1-year trial will enroll patients whose disability progresses without relapses and will document the safety and tolerability of temelimab following higher doses, as well as efficacy based on the latest biomarkers associated with disease progression. Temelimab is a monoclonal antibody designed to neutralize a pathogenic envelope protein, pHERV-W Env, which has been shown to activate microglia in the brain resulting in an aggressive phenotype attacking myelin, and to impair the remyelination capacity of the brain through the inhibition of oligodendrocyte precursor cell differentiation. This collaboration follows the data from GeNeuro's ANGEL-MS clinical trial results, which demonstrated positive results at 2 years on key markers associated with disease progression. The study aims to start enrolling patients in the first quarter of 2020.
- **Ublituximab:** In September 2019, TG Therapeutics presented the first look at the ULTIMATE I & II Phase 3 trial design and demographic data and updated Phase 2 extension trial data for ublituximab, an investigational B-cell targeting therapy, in

relapsing MS patients. The ULTIMATE I & II trials are expected to elucidate the therapeutic potential of a 1 hour, 450mg infusion of ublituximab in patients with RMS. Topline results are expected in the second half of 2020.

Other News:

- **June 2019:** The Institute for Clinical and Economic Review (ICER) released a Final Evidence Report and Report-at-a-Glance assessing the comparative clinical effectiveness and value of siponimod (Mayzent®) for the treatment of SPMS. Siponimod was recently approved by the FDA for the treatment of relapsing forms of MS, including active SPMS. However, ICER's assessment focuses on the clinical and cost-effectiveness of siponimod just for patients with SPMS (both active and non-active), which was the population studied in the Phase 3 trial. ICER's report was reviewed at the May 2019 public meeting of the Midwest Comparative Effectiveness Public Advisory Council (Midwest CEPAC), one of ICER's three independent evidence appraisal committees. During the meeting, the majority of the panel voted that the evidence demonstrated siponimod to be clinically superior to best supportive care for patients with active SPMS, though some panel members noted that they still had concerns about trial methodology. Panel members unanimously found that the evidence was insufficient to demonstrate that siponimod is superior to best supportive care for patients with non-active SPMS. At its current list price of $88,561 per year, siponimod exceeds commonly accepted thresholds for cost-effectiveness of $50,000-$150,000 per quality-adjusted life years (QALY) gained, when compared to best supportive care in patients with SPMS. Consistent with ICER's value assessment framework, because the incremental cost ratio for siponimod in the SPMS population exceeds $175,000 per QALY, it was deemed "low long-term value for money" without a formal vote by the panel. ICER recommends payers may wish to specifically consider granting preferential formulary status to fingolimod when its generic formulation comes to the market.
- **September 2019:** A retrospective analysis found higher-efficacy infusible therapies had a disproportionally larger effect in RRMS patients younger than 45 years of age. The review compared oral (fingolimod or dimethyl fumarate) versus infusible (natalizumab or rituximab) therapies, tracking 1,004 patients with RRMS at the University of Colorado Rocky Mountain MS Center for 24 months or until drug discontinuation. Researchers assessed patient records for disease activity, defined as clinical relapses, new T2 lesions, or Gd+ lesions, and also looked at a composite of these measures. Participants started treatment with 1 of the 4 drugs from January 2010 to October 2013. Overall, 509 patients were on oral treatment and 495 were on infusible treatment. At baseline, the infusible treatment group was younger (mean age 38.6 years) than the oral treatment group (mean age 42.5 years). In the oral treatment group, 36.4% of patients experienced disease activity, compared with 21.2% in the infusible treatment group. Oral treatment patients who experienced disease activity were younger, had few years of disease duration, and were more likely to have Gd+ lesions on baseline MRI than those who did not experience disease activity. Infusible treatment patients who experienced disease activity also were younger and were more likely to have Gd+ lesions on baseline MRI. Oral treatment patients who were younger than 45 years of age had greater odds of overall (composite) disease activity, clinical relapses, new T2 lesions,

or Gd+ lesions than those 45 years of age or older. Infusible treatment patients younger than 45 years of age, however, showed similar trends on these measures as patients 45 years of age and older. The odds of experiencing disease activity with oral versus infusible treatment was greater in patients younger than age 45 [odds ratio (OR) 2.67, P<0.001] than in patients 45 years of age and older (OR 1.60, P=0.069) in an unadjusted analysis. After propensity matching and controlling for covariates, disease activity with oral versus infusible drugs was nearly 2 times higher in younger patients (OR 2.18, P=0.002) than in older patients (OR 1.16, P=0.675).

- **September 2019:** A case-control study of active-duty United States military personnel showed levels of serum neurofilament light (sNfL) increased 6 years before the clinical onset of MS. In serum samples drawn a median of 6 years before clinical onset of the disease, sNfL levels were higher in people who eventually developed MS than in matched controls (median 16.7pg/mL vs 15.2pg/mL, P=0.04), reported Kjetil Bjornevik, MD, PhD, of Harvard T. H. Chan School of Public Health in Boston, at the ECTRIMS congress. The findings were published simultaneously in *JAMA Neurology*. Bjornevik and colleagues evaluated serum neurofilament light chain, a specific marker of neuroaxonal degeneration, as a potential indicator of a pre-symptomatic phase in MS. They studied active-duty United States military personnel who had at least 1 serum sample stored in the Department of Defense Serum Repository identifying 245 MS patients from 2010 and 2011 samples. The mean age of these patients was 27.5 years at baseline and 76.7% were men. sNfL concentrations were measured using an ultrasensitive single-molecule array assay. sNfL levels were higher in studied patients with MS compared with their matched control individuals in samples drawn a median of 6 years (range 4-10 years) before the clinical onset. A within-person increase in presymptomatic sNfL levels was associated with higher MS risk (rate ratio for ≥5pg/mL increase: 7.50; 95% CI: 1.72-32.80). The clinical onset was associated with a marked increase in sNfL levels (median: 25.0; IQR: 17.1-41.3 vs 45.1; IQR: 27.0-102.7pg/mL for presymptomatic and post onset MS). The levels of sNfL were increased 6 years before the clinical MS onset, indicating that MS may have a prodromal phase lasting several years and that neuroaxonal damage occurs during this phase.
- **November 2019:** Biogen, the manufacturer of Tecfidera® (dimethyl fumarate) and Vumerity™ (diroximel fumarate), announced the results from the Phase 3 EVOLVE-MS-2 study demonstrating the improved patient-assessed gastrointestinal (GI) tolerability of Vumerity™, a new FDA-approved treatment for relapsing forms of MS, compared to Tecfidera® (dimethyl fumarate). Once in the body, Vumerity™ rapidly converts to MMF, the same active metabolite of Tecfidera®. EVOLVE-MS-2 is the first study to directly compare the GI tolerability of 2 relapsing MS treatments. In this study involving RRMS patients, Vumerity™ was associated with significantly shorter duration, severity, and daily impact of five key GI symptoms, compared to Tecfidera®. Results for the primary endpoint show patients treated with Vumerity™ self-reported 46% fewer days with intensity scores of ≥2 on the Individual Gastrointestinal Symptom and Impact Scale (IGISIS), compared to Tecfidera® [adjusted rate ratio (95% CI): 0.54 (0.39−0.75); p=0.0003]. IGISIS is a novel and exploratory scale used by patients in the study to self-assess the intensity and duration of key GI symptoms, including nausea, vomiting, upper

and lower abdominal pain, and diarrhea. Additionally, lower investigator-reported incidences of GI adverse effects (AEs) with Vumerity™ (34%) compared to Tecfidera® (49.0%) were reported. Overall AEs occurred in 78.3% of patients with Vumerity™ and 83.7% with Tecfidera®. Most AEs were mild or moderate in severity. The overall proportion of patients with AEs leading to study discontinuation were 1.6% for Vumerity™ and 5.6% for Tecfidera®.

Mayzent® (Siponimod) Product Summary[28,29]

Indication(s): Mayzent® (siponimod) is a S1P receptor modulator indicated for the treatment of relapsing forms of MS, to include CIS, RRMS, and active SPMS, in adults.

Dosing:

- Mayzent® is supplied as a 0.25mg and 2mg oral tablets.
- Assessments should be done prior to the initiation of treatment with Mayzent® which include CYP2C9 genotype determination, complete blood count (CBC), ophthalmic evaluation, cardiac evaluation, review of current or prior medications, vaccinations, and liver function tests.
- Titration is required for treatment initiation. If 1 titration dose is missed for more than 24 hours, treatment needs to be reinitiated with Day 1 of the titration regimen.
- Mayzent® should be initiated with a 5-day titration:
  - Day 1: 0.25mg once daily
  - Day 2: 0.25mg once daily
  - Day 3: 0.50mg once daily (2x 0.25mg tablets)
  - Day 4: 0.75mg once daily (3x 0.25mg tablets)
  - Day 5: 1.25mg once daily (5x 0.25mg tablets)
- Patients with a CYP2C9*1/*3 or *2/*3 genotype should initiate Mayzent® with a 4-day titration:
  - Day 1: 0.25mg once daily
  - Day 2: 0.25mg once daily
  - Day 3: 0.50mg once daily (2x 0.25mg tablets)
  - Day 4: 0.75mg once daily (3x 0.25mg tablets)
- The recommended maintenance dosage of Mayzent® is 2mg once daily.
- The recommended maintenance dosage in patients with CYP2C9*1/*3 or *2/*3 genotype is 1mg once daily.
- First-dose monitoring is recommended for patients with sinus bradycardia, first- or second-block degree (Mobitz type I) atrioventricular (AV) block, or a history of myocardial infarction (MI) or heart failure (HF).

Mechanism of Action: Siponimod is a S1P receptor modulator. Siponimod binds with high affinity to S1P receptors 1 and 5 and blocks the capacity of lymphocytes to egress from lymph nodes, reducing the number of lymphocytes in peripheral blood. The mechanism by which siponimod exerts therapeutic effects in MS is unknown, but may involve reduction of lymphocyte migration into the CNS.

Contraindication(s):

- Patients with a CYP2C9*3/*3 genotype
- Patients who experienced MI, unstable angina, stroke, transient ischemic attack (TIA), decompensated HF requiring hospitalization, or Class III/IV HF in the last 6 months
- Presence of Mobitz type II second-degree, third-degree AV block, or sick sinus syndrome, unless patient has a functioning pacemaker

Warnings and Precautions:

- Infections: Mayzent® may increase the risk of infections. A CBC should be obtained before initiating treatment. The patient should be monitored for infection during treatment. Mayzent® should not be started in patients with active infection.
- Macular Edema: An ophthalmic evaluation is recommended before starting treatment and if there is any change in vision while taking Mayzent®. Diabetes mellitus and uveitis increase the risk of macular edema during treatment with Mayzent®.
- Bradyarrhythmia and Atrioventricular Conduction Delays: Mayzent® may result in a transient decrease in heart rate (HR); for this reason titration is required for treatment initiation. The patient's resting HR with concomitant beta-blocker use should be considered prior to initiation of treatment with Mayzent®; a cardiologist consultation before concomitant use with other drugs that decrease heart rate should be obtained.
- Respiratory Effects: Mayzent® may cause a decline in pulmonary function. Pulmonary function (e.g., spirometry) should be assessed if clinically indicated.
- Liver Injury: Liver enzyme results should be obtained before initiation with Mayzent®. Patients with severe hepatic impairment should be closely monitored. Mayzent® should be discontinued if significant liver injury occurs.
- Increased Blood Pressure (BP): BP should be monitored during treatment.
- Fetal Risk: Women of childbearing potential should use effective contraception during treatment and for 10 days after stopping Mayzent®.

Drug Interactions:

- Vaccines: Live attenuated vaccines should be avoided during and for up to 4 weeks after treatment with Mayzent®.
- CYP2C9 and CYP3A4 Inhibitors: Concomitant use of Mayzent® with CYP2C9 and CYP3A4 inhibitors results in increased siponimod exposure; concomitant use of Mayzent® with moderate CYP2C9 and moderate or strong CYP3A4 inhibitors is not recommended.
- CYP2C9 and CYP3A4 Inducers: Concomitant use of Mayzent® with CYP2C9 and CYP3A4 inducers results in decreased siponimod exposure; concomitant use of Mayzent® with moderate CYP2C9 and strong CYP3A4 inducers is not recommended.
- Anti-Neoplastic, Immune-Modulating, or Immunosuppressive Therapies: Caution should be used during concomitant administration because of the risk of additive immune effects during such therapy and in the weeks following administration. Because of the characteristics and duration of Lemtrada® (alemtuzumab) immune suppressive effects, initiating treatment with Mayzent® after alemtuzumab is not recommended.

Adverse Reactions: The most common adverse reactions (incidence >10%) are headache, hypertension, and transaminase increases.

Efficacy: The efficacy of Mayzent® was established in a double-blind, time-to-event study in 1,651 patients with SPMS. Patients were randomized to receive either Mayzent® 2mg or placebo, beginning with a dose titration. The primary endpoint of the study was the time to 3-month confirmed disability progression (CDP). Other key secondary endpoints included the confirmed worsening in timed 25-foot walk and the ARR.

- Mayzent® was superior to placebo in reducing the risk of CDP, based on a time-to-event analysis (Hazard Ratio: 0.79; P<0.0134). Overall, 26% of patients had CDP with Mayzent® vs. 32% with placebo.
- Mayzent® did not significantly delay the time to 20% deterioration in the timed 25-foot walk vs. placebo.
- Patients treated with Mayzent® had a 55% relative reduction in annualized relapse rate, vs. patients on placebo (P<0.0001). The annualized relapse rate was 0.071 for Mayzent® vs. 0.160 for placebo.

Cost Comparison:

Medication	Cost Per Unit	Cost Per Month	Cost Per Year
Mayzent® (siponimod) 2mg capsule	**$255.80**	**$7,674.00[+]**	**$92,088.00[+]**
Gilenya® (fingolimod) 0.5mg capsule	$288.74	$8,662.20[*]	$103,946.40[*]

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
Unit = capsule
[+] Mayzent® cost per month and cost per year based on the recommended maintenance dosage of 2mg once daily.
[*] Gilenya® cost per month and cost per year based on the recommended dosage for adults and pediatric patients (10 years of age and older) weighing more than 40kg of 0.5mg once daily.

Mavenclad® (Cladribine) Product Summary[30,31]

Indication(s): Mavenclad® (cladribine) is a purine antimetabolite indicated for the treatment of relapsing forms of MS, to include RRMS and active SPMS, in adults. Because of its safety profile, use of Mavenclad® is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternate drug indicated for the treatment of MS.

- Limitation(s) of Use: Mavenclad® is not recommended for use in patients with CIS because of its safety profile.

Dosing:

- Mavenclad® is supplied as a 10mg oral tablet.
- Assessments should be done prior to the initiation of treatment with Mavenclad® which include cancer screening, pregnancy test, CBC, ruling out certain infections, and liver function tests (LFTs).
- Mavenclad® is a cytotoxic drug.
- Mavenclad® tablets are taken orally, with water, and swallowed whole without chewing.
- Mavenclad® can be taken with or without food.
- The recommended cumulative dosage of Mavenclad® is 3.5mg/kg administered orally and divided into 2 treatment courses (1.75mg/kg per treatment course). Each treatment course is divided into 2 treatment cycles.
    - Administration of first treatment course:
        - First course/first cycle: Start any time.

    - First course/second cycle: Administer Mavenclad® 23 to 27 days after the last dose of the first course/first cycle.
  - Administration of the second treatment course:
    - Second course/first cycle: Administer Mavenclad® at least 43 weeks after the last dose of first course/second cycle.
    - Second course/second cycle: Administer Mavenclad® 23 to 27 days after the last dose of second course/first cycle.
- Administer the cycle dosage as 1 or 2 tablets once daily over 4 or 5 consecutive days. The maximum dose is 2 tablets per day; more than 2 tablets daily should not be administered.
- Following the administration of 2 treatment courses, Mavenclad® should not be administered during the next 2 years. Treatment during these 2 years may further increase the risk of malignancy. The safety and efficacy of reinitiating Mavenclad® >2 years after completing 2 treatment courses has not been studied.
- Mavenclad® administration should be separated from any other drug by at least 3 hours during the 4 to 5 treatment days.
- If a dose is missed, patients should not take double or extra doses.
- If a dose is not taken on the scheduled day, then the patient must take the missed dose on the following day and extend the number of days in the treatment cycle (if 2 consecutive doses are missed, the treatment cycle is extended 2 days).

Mechanism of Action: The mechanism by which cladribine exerts its therapeutic effects in patients with MS has not been fully elucidated but is thought to involve cytotoxic effects on B and T lymphocytes through impairment of DNA synthesis, resulting in depletion of lymphocytes.

Contraindication(s):
- Patients with current malignancy
- Pregnant women, and women and men of reproductive potential who do not plan to use effective contraception during Mavenclad® dosing and for 6 months after the last dose in each treatment course
- HIV infection
- Active chronic infections (e.g., hepatitis, tuberculosis)
- History of hypersensitivity to cladribine
- Women intending to breastfeed on a Mavenclad® treatment day and for 10 days after the last dose

Warnings and Precautions:
- <u>Lymphopenia:</u> Lymphocyte counts should be monitored before, during, and after treatment.
- <u>Infections:</u> Patients should be screened for latent infections; delaying treatment should be considered until infection is fully controlled. Patients who are antibody-negative to varicella zoster virus should be vaccinated prior to treatment. Anti-herpes prophylaxis should be administered in patients with lymphocyte counts <200 cells per microliter. Patients should be monitored for infections.

- Hematologic Toxicity: CBC should be monitored before, during and after treatment.
- Graft-Versus-Host-Disease with Blood Transfusion: Irradiation of cellular blood components is recommended.
- Liver Injury: LFTs should be obtained prior to treatment. Mavenclad® should be discontinued if clinically significant injury is suspected.

Drug Interactions:

- Immunosuppressive Drugs: Consider overlapping effects on immune system, when used sequentially. Concomitant use not recommended.
- Hematotoxic Drugs: Patients should be monitored for additive effects on the hematological profile.
- Antiviral and Antiretroviral Drugs: Concomitant use should be avoided.
- BCRP or ENT/CNT inhibitors: May alter bioavailability of cladribine. Concomitant use should be avoided.

Adverse Reactions: The most common adverse reactions (incidence >20%) are upper respiratory tract infection, headache, and lymphopenia.

Efficacy: The efficacy of Mavenclad® was established in a double-blind study in 1,326 patients with relapsing forms of MS. Patients were randomized to receive placebo or a cumulative oral dosage of Mavenclad® 3.5mg/kg or Mavenclad® 5.25mg/kg over the 96-week study period in 2 treatment courses. The primary outcome was the ARR.

- The ARR was 0.14 and 0.33 for patients receiving Mavenclad® 3.5mg/kg and placebo, respectively ($P<0.001$). The relative risk reduction was 58%.
- The proportion of patients without a relapse was 81% vs. 63% for Mavenclad® 3.5mg/kg and placebo, respectively (nominal $P<0.05$).
- The Mavenclad® 5.25mg/kg cumulative dose did not add any clinically meaningful benefit, but was associated with a higher incidence in grade 3 lymphopenia or higher.

Cost:

Medication	Cost Per Unit	Cost Per 2 Courses
Mavenclad® (cladribine) 10mg tablet	**$7,107.14**	**$284,285.60***

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
Unit = tablet
*Mavenclad® is available in a box of 4, 5, 6, 7, 8, 9, and 10 tablets packaged in a child-resistant day pack containing 1 or 2 tablets in a blister card. The maximum dose is 10 tablets per cycle. The recommended cumulative dosage of Mavenclad® is 3.5mg/kg administered orally and divided into 2 treatment courses (1.75mg/kg per treatment course). Each treatment course is divided into 2 treatment cycles. Following the administration of 2 treatment courses, Mavenclad® should not be administered during the next 2 years.

Vumerity™ (Diroximel Fumarate) Product Summary[32,33]

Indication(s): Vumerity™ (diroximel fumarate) is indicated for the treatment of relapsing forms of MS, to include CIS, RRMA, and active SPMS, in adults.

Dosing:

- Vumerity™ is supplied as a 231mg delayed-release capsule.

- A CBC (including lymphocyte count) and serum aminotransferase, alkaline phosphatase, and total bilirubin should be obtained prior to treatment with Vumerity™.
- The starting dosage for Vumerity™ is 231mg orally BID for 7 days.
- After 7 days, the maintenance dose is 462mg [(2) 231mg capsules] orally BID.
- Temporary dosage reductions to 231mg BID may be considered for individuals who do not tolerate the maintenance dosage. The recommended maintenance dose of 462mg BID should be resumed within 4 weeks. Discontinuation of Vumerity™ should be considered for patients unable to tolerate return to the maintenance dosage.
- Vumerity™ should be swallowed whole and intact. Vumerity™ should not be crushed, chewed, or capsules opened and contents sprinkled on food.
- If taken with food, a high-fat, high-calorie meal/snack should be avoided with the administration of Vumerity™. The meal/snack should contain ≤700 calories and ≤30 grams of fat.
- Co-administration of Vumerity™ with alcohol should be avoided.

Mechanism of Action: The mechanism by which diroximel fumarate exerts its therapeutic effect in MS is unknown. MMF, the active metabolite of diroximel fumarate, has been shown to activate the nuclear factor (erythroid-derived 2)-like 2 (Nrf2) pathway *in vitro* and *in vivo* in animals and humans. The Nrf2 pathway is involved in the cellular response to oxidative stress. MMF has been identified as a nicotinic acid receptor agonist *in vitro*.

Contraindication(s):
- Known hypersensitivity to diroximel fumarate, dimethyl fumarate, or to any of the excipients of Vumerity™
- Co-administration with dimethyl fumarate

Warnings and Precautions:
- Anaphylaxis and Angioedema: Vumerity™ should be discontinued and should not be restarted if these occur.
- Progressive Multifocal Leukoencephalopathy (PML): Vumerity™ should be withheld at the first sign or symptom suggestive of PML.
- Lymphopenia: A CBC including lymphocyte count should be obtained before initiating Vumerity™, after 6 months, and every 6 to 12 months thereafter. Consider interruption of Vumerity™ if lymphocyte counts $<0.5 \times 10^9$/L persist for more than 6 months.
- Liver Injury: Serum aminotransferase, alkaline phosphatase, and total bilirubin levels should be obtained before initiating Vumerity™ and during treatment, as clinically indicated. Vumerity™ should be discontinued if clinically significant liver injury induced by Vumerity™ is suspected.

Adverse Reactions: The most common adverse reactions [incidence for dimethyl fumarate (which has the same active metabolite as Vumerity™) ≥10% and ≥2% more than placebo] were flushing, abdominal pain, diarrhea, and nausea.

Efficacy: Vumerity™ was approved via the 505(b)(2) filing pathway. It included data from pharmacokinetic bridging studies comparing Vumerity™ and Tecfidera® to establish bioequivalence, and relied, in part, on the FDA's findings of safety and efficacy for Tecfidera®.

Cost Comparison:

Medication	Cost Per Unit	Cost Per Month	Cost Per Year
Vumerity™ (diroximel fumarate) 231mg capsule	**$60.27**	**$7,232.40+**	**$86,788.80+**
Tecfidera® (dimethyl fumarate) 240mg capsule	$137.93	$8,275.80*	$99,309.60*

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
Unit = capsule, tablet, or mL
+ Vumerity™ cost per month and cost per year based on maintenance dose of 462mg [(2) 231mg capsules] twice daily.
* Tecfidera® cost per month and cost per year based on maintenance dose of 240mg twice daily.

Recommendations

The College of Pharmacy recommends the prior authorization of Mayzent® (siponimod), Mavenclad® (cladribine), and Vumerity™ (diroximel fumarate) with the following criteria:

Mayzent® (Siponimod) Approval Criteria:

1. An FDA approved diagnosis of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease; and
2. Member must have been assessed for CYP2C9 genotype:
    a. Members with a CYP2C9*3/*3 genotype will not generally be approved; or
    b. Members with a CYP2C9*1/*3 or *2/*3 genotype will not be approved for doses exceeding 1mg per day; or
    c. All other genotypes CYP2C9*1/*1, *1/*2, or *2/*2 will be approved for 2mg per day; and
3. Member must not have any contraindication for use of siponimod including:
    a. CYP2C9*3/*3 genotype; or
    b. Experienced myocardial infarction (MI), unstable angina, stroke, transient ischemic attack (TIA), decompensated heart failure (HF) requiring hospitalization, or class III/IV HF in the last 6 months; or
    c. Presence of Mobitz type II second-degree, third-degree atrioventricular (AV) block, or sick sinus syndrome, unless member has a functioning pacemaker; and
4. Member must not have received prior treatment with alemtuzumab; and
5. Verification from the prescriber that member has no active infection(s); and
6. Complete blood counts (CBC) and verification that levels are acceptable to the prescriber; and
7. Liver function tests (LFTs) and verification that levels are acceptable to the prescriber; and
8. Ophthalmic evaluation and verification that member will be monitored for changes in vision throughout therapy; and
9. Verification from the prescriber that the member has been assessed for medications and conditions that cause reduction in heart rate (HR) or AV conduction delays and that the member will be followed with appropriate monitoring per package labeling; and
10. Verification from the prescriber that the member has been assessed for previous confirmed history of chickenpox or vaccination against varicella. Members without

history of chickenpox or varicella vaccination should receive a full course of the varicella vaccine prior to commencing treatment with Mayzent®; and
11. Verification from the prescriber that members with sinus bradycardia (HR <55 beats per minute), first- or second-degree AV block (Mobitz type I), or a history of HF or MI will be monitored following the first dose for a minimum of 6 hours; and
12. Female members of reproductive potential must not be pregnant and must have a negative pregnancy test prior to initiation of therapy; and
13. Female members of reproductive potential must be willing to use effective contraception during treatment with Mayzent® and for at least 10 days after discontinuing treatment; and
14. Member must have had an inadequate response to Gilenya® (fingolimod) or a patient-specific, clinically significant reason why fingolimod is not appropriate for the member must be provided; and
15. Compliance will be checked for continued approval every 6 months; and
16. Quantity limits according to package labeling will apply.

Mavenclad® (Cladribine) Approval Criteria:

1. An FDA approved diagnosis of relapsing forms of multiple sclerosis (MS), to include relapsing remitting disease and active secondary progressive disease in adults; and
2. Requests for use in patients with clinically isolated syndrome (CIS) will not generally be approved; and
3. Member must have had at least 1 relapse in the previous 12 months; and
4. Member must have had an inadequate response to 2 or more medications indicated for the treatment of MS; and
5. Prescriber must confirm that the member does not have any contraindications for use of cladribine; and
6. Prescriber must confirm that the member does not have an active malignancy; and
7. Prescriber must confirm that females members of reproductive potential must not be pregnant and must have a negative pregnancy test prior to initiation of therapy; and
8. Prescriber must attest that female and male members of reproductive potential plan to use effective contraception during cladribine dosing and for 6 months after the last dose in each treatment course; and
9. Complete blood counts (CBC) and verification that levels are acceptable to the prescriber; and
10. Verification from the prescriber that member has no active infection(s); and
11. Liver function tests (LFTs) and verification that levels are acceptable to the prescriber; and
12. 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; and
13. Quantity limits according to package labeling will apply.

Vumerity™ (Diroximel Fumarate) Approval Criteria:

1. An FDA approved diagnosis relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease; and
2. Approvals will not be granted for concurrent use with other disease-modifying therapies; and
3. Verification from the prescriber that member has no serious active infection(s); and
4. Complete blood counts (CBC) and verification that levels are acceptable to the prescriber; and
5. Serum aminotransferase, alkaline phosphatase, and total bilirubin levels and verification that levels are acceptable to the prescriber; and
6. Verification from the prescriber that member does not have moderate or severe renal impairment; and
7. Verification from the prescriber that the member has been counseled on proper administration of Vumerity™ including caloric and fat intake limits at the time of dosing; and
8. Compliance will be checked for continued approval every 6 months; and
9. A quantity limit of 120 capsules per 30 days will apply.

Utilization Details of MS Medications: Calendar Year 2019

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
INTERFERON BETA-1A PRODUCTS					
AVONEX PEN KIT 30MCG	24	4	$160,314.16	$237.85	$6,679.76
REBIF REBIDO INJ 44MCG/0.5ML	21	3	$160,366.64	$272.73	$7,636.51
REBIF INJ 22MCG/0.5ML	16	1	$59,576.05	$194.69	$3,723.50
REBIF REBIDO INJ 22MCG/0.5ML	15	2	$115,778.60	$257.29	$7,718.57
REBIF INJ 44MCG/0.5ML	12	3	$91,265.00	$271.62	$7,605.42
REBIF REBIDO INJ TITRATN	2	2	$15,237.02	$253.95	$7,618.51
AVONEX PREFL KIT 30MCG	1	1	$6,745.59	$240.91	$6,745.59
SUBTOTAL	**91**	**16**	**$609,283.06**	**$249.50**	**$6,695.42**
INTERFERON BETA-1B PRODUCTS					
BETASERON INJ 0.3MG	55	7	$328,932.77	$213.59	$5,980.60
SUBTOTAL	**55**	**7**	**$328,932.77**	**$213.59**	**$5,980.60**
PEGINTERFERON BETA-1A PRODUCTS					
PLEGRIDY INJ 125MCG/0.5ML	20	3	$138,520.38	$247.36	$6,926.02
PLEGRIDY INJ STARTER	1	1	$6,932.62	$247.59	$6,932.62
SUBTOTAL	**21**	**4**	**$145,453.00**	**$247.37**	**$6,926.33**
DALFAMPRIDINE PRODUCTS					
DALFAMPRIDIN TAB 10MG ER	174	25	$26,240.63	$5.03	$150.81
AMPYRA TAB 10MG	44	13	$119,010.37	$90.16	$2,704.78

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
SUBTOTAL	**218**	**38**	**$145,251.00**	**$22.21**	**$666.29**
TERIFLUNOMIDE PRODUCTS					
AUBAGIO TAB 14MG	101	16	$703,245.95	$243.51	$6,962.83
AUBAGIO TAB 7MG	9	2	$60,832.85	$241.40	$6,759.21
SUBTOTAL	**110**	**18**	**$764,078.80**	**$243.34**	**$6,946.17**
GLATIRAMER ACETATE PRODUCTS					
COPAXONE INJ 20MG/ML	176	31	$1,216,824.32	$225.34	$6,913.77
COPAXONE INJ 40MG/ML	131	22	$740,212.65	$201.58	$5,650.48
GLATIRAMER INJ 40MG/ML	4	1	$5,555.53	$46.30	$1,388.88
SUBTOTAL	**311**	**54**	**$1,962,592.50**	**$213.51**	**$6,310.59**
FINGOLIMOD PRODUCTS					
GILENYA CAP 0.5MG	158	22	$1,252,510.91	$264.24	$7,927.28
SUBTOTAL	**158**	**22**	**$1,252,510.91**	**$264.24**	**$7,927.28**
DIMETHYL FUMARATE PRODUCTS					
TECFIDERA CAP 240MG	169	28	$1,320,530.98	$260.46	$7,813.79
TECFIDERA MIS STARTER	11	10	$85,532.70	$259.19	$7,775.70
SUBTOTAL	**180**	**38**	**$1,406,063.68**	**$260.38**	**$7,811.46**
NATALIZUMAB PRODUCTS					
TYSABRI INJ 300/15ML	14	2	$83,888.40	$214.00	$5,992.03
SUBTOTAL	**14**	**2**	**$83,888.40**	**$214.00**	**$5,992.03**
CLADRIBINE PRODUCTS					
MAVENCLAD PAK 10MG(6)	2	1	$85,300.42	$1,470.70	$42,650.21
SUBTOTAL	**2**	**1**	**$85,300.42**	**$1,470.70**	**$42,650.21**
OCRELIZUMAB PRODUCTS					
OCREVUS INJ 300/10ML	4	4	$113,787.06	$1,094.11	$28,446.77
SUBTOTAL	**4**	**4**	**$113,787.06**	**$1,094.11**	**$28,446.77**
SIPONIMOD PRODUCTS					
MAYZENT TAB 2MG	4	2	$29,124.44	$242.70	$7,281.11
SUBTOTAL	**4**	**2**	**$29,124.44**	**$242.70**	**$7,281.11**
TOTAL	**1,168**	**163***	**$6,926,266.04**	**$202.19**	**$5,930.02**

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

Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
ALEMTUZUMAB PRODUCTS					
LEMTRADA INJ 10MG/1ML (J0202)	6	2	$138,074.04	3	$23,012.34
NATALIZUMAB PRODUCTS					
TYSABRI INJ 300MG/15ML (J2323)	133	20	$739,788.78	6.65	$5,562.32

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
OCRELIZUMAB PRODUCTS					
OCREVUS INJ 300MG/10ML (J2350)	45	26	$1,188,536.50	1.73	$26,411.92
TOTAL	**184[+]**	**48***	**$2,066,399.32**	**3.8**	**$11,230.43**

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

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Appendix M

30-Day Notice to Prior Authorize Tepezza™ (Teprotumumab-trbw)

Oklahoma Health Care Authority
March 2020

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

Thyroid eye disease, also known as Graves' ophthalmopathy or Graves' eye disease, is a rare orbital inflammatory disease, which can be sight-threatening, debilitating, and disfiguring. Thyroid eye disease is caused by retro-orbital inflammation to which orbital fibroblast activation is a key contributor; fibroblast activation is presumed to occur secondary to stimulatory auto-antibodies [anti-thyroid stimulating hormone (TSH) receptor (anti-TSHR) and anti-insulin-like growth factor-1 (anti-IGF-1)]. These fibroblasts express the TSHR and produce extracellular matrix components and pro-inflammatory molecules. Inflammation of the extraocular muscles can lead to restricted eye movements and proptosis. The optic nerve can be compressed, which can cause optic neuropathy resulting in permanent vision loss.

Ophthalmic symptoms of thyroid eye disease include dry eyes, red eyes, diplopia, pain on eye movement, and cosmetic changes. The most common clinical signs of thyroid eye disease are eyelid retraction, proptosis (exophthalmos), and optic neuropathy. The ocular symptoms of thyroid eye disease can be incapacitating, leading to the progressive inability to perform important daily activities, such as driving or working. The 2 most serious signs of thyroid eye disease are optic neuropathy and exposure keratopathy, which are considered ocular emergencies as both can abruptly lead to blindness. Thyroid eye disease is typically self-limiting: the disease commences with an active (inflammatory) phase with rapidly worsening symptoms and signs, reaches a point of maximum severity, then improves to an inactive phase but does not resolve to baseline.

Most patients with thyroid eye disease have biochemical evidence of hyperthyroidism, with the most common cause being Graves' disease; however, thyroid eye disease may occur in patients who have hypothyroidism (most commonly Hasimoto's thyroiditis) or euthyroidism. The timing of the presentation of thyroid eye disease may differ between patients, occurring simultaneously with thyroid dysfunction or either preceding or following thyroid dysfunction. Visual field analysis, orthoptic assessment, optometric assessment, orbital imaging, and laboratory tests (thyroid function tests and thyroid auto-antibodies) are used in the evaluation and diagnosis of thyroid eye disease.

The incidence of thyroid eye disease is 16 per 100,000 females and 2.9 per 100,000 males. The higher prevalence in females relates to the higher incidence of hyperthyroidism in females. Risk factors for thyroid eye disease include female gender, middle age, and smoking. In autoimmune cases of Graves' disease or Hasimoto's thyroiditis, there is also an increased prevalence and relative risk for coexisting autoimmune disorders.

There are very limited treatment options for thyroid eye disease. Thyroid function control should be the primary approach to treatment, as normal thyroid function is associated with a reduction in the severity of thyroid eye disease. Treatment of thyroid eye disease should be multidisciplinary, and general supportive measures (e.g., ocular lubricants, head elevation) for thyroid eye disease should be considered for immediate use. In the active phase of thyroid eye disease, systemic corticosteroids are most effective early in this phase. Orbital radiotherapy can be used as an adjunctive therapy to improve ocular motility during active disease, and surgical orbital decompression is required in rare cases of acute progressive optic neuropathy or exposure keratopathy. Surgery for the improvement of cosmetic appearance and symptoms should be avoided if possible until the inactive phase; surgical options include decompression, motility surgery, and lid surgery. In January 2020, the U.S. Food and Drug Administration (FDA) approved Tepezza™ (teprotumumab-trbw), the first FDA-approved treatment for thyroid eye disease. Teprotumumab is a fully human monoclonal antibody (mAb) and a targeted inhibitor of the IGF-1 receptor (IGF-1R).

Market News and Updates[7,8]

New FDA Approval(s):

- **January 2020:** The FDA approved Horizon Therapeutics' Tepezza™ (teprotumumab-trbw) for the treatment of adults with thyroid eye disease. Teprotumumab was granted Priority Review, Orphan Drug, Fast Track, and Breakthrough Therapy designations by the FDA.

Pipeline:

- **Teprotumumab:** A 48-week, open-label, Phase 3 extension study is ongoing with Tepezza™ (teprotumumab-trbw) to evaluate whether certain patients with thyroid eye disease may benefit from retreatment or longer treatment with teprotumumab. Horizon is also currently evaluating Tepezza™ (teprotumumab-trbw) in an exploratory Phase 1 study for diffuse cutaneous scleroderma.

Tepezza™ (Teprotumumab-trbw) Product Summary[9]

Indication(s): Tepezza™ (teprotumumab-trbw) is an IGF-1R inhibitor indicated for the treatment of thyroid eye disease in adult patients.

Dosing:

- Tepezza™ is supplied as a single-dose vial (SDV) containing 500mg of teprotumumab as a sterile, preservative-free, lyophilized powder for reconstitution. The reconstituted teprotumumab solution must be further diluted prior to intravenous (IV) infusion.
- Teprotumumab should be administered by IV infusion every 3 weeks, and the recommended dosage of teprotumumab is 10mg/kg for the initial dose, followed by 20mg/kg for 7 additional infusions.
- The diluted teprotumumab solution should be administered IV over 90 minutes for the first 2 infusions. If well tolerated, the minimum time for subsequent infusions can be reduced to 60 minutes. If not well tolerated, the minimum time for subsequent

infusions should remain at 90 minutes (*refer to Tepezza™ Prescribing Information for specific reconstitution, preparation, and administration instructions*).
- Tepezza™ SDVs should be refrigerated in the original carton until time of use.

Mechanism of Action: Teprotumumab, an IGF-1R inhibitor, is a fully human IgG1 mAb that binds to IGF-1R and blocks its activation and signaling. The mechanism of action for teprotumumab in patients with thyroid eye disease has not been fully characterized.

Contraindications: None.

Safety:
- **Infusion Reactions:** Teprotumumab may cause infusion reactions. Infusion reactions have been reported in approximately 4% of patients treated with teprotumumab and may occur during any of the infusions or within 1.5 hours after an infusion. Reported infusion reactions are usually mild or moderate in severity and can usually be successfully managed with corticosteroids and antihistamines. In patients who experience an infusion reaction, consideration should be given to pre-medicating with an antihistamine, antipyretic, corticosteroid, and/or administering all subsequent infusions at a slower infusion rate.
- **Exacerbation of Preexisting Inflammatory Bowel Disease (IBD):** Teprotumumab may cause an exacerbation of preexisting IBD. Patients with IBD should be monitored for flare of disease. If IBD exacerbation is suspected, discontinuation of teprotumumab should be considered.
- **Hyperglycemia:** Hyperglycemia or increased blood glucose may occur in patients treated with teprotumumab. In clinical trials, 10% of patients (2/3 of whom had pre-existing diabetes or impaired glucose tolerance) experienced hyperglycemia. Patients should be monitored for elevated blood glucose and symptoms of hyperglycemia while on treatment with teprotumumab. Patients with pre-existing diabetes should be under appropriate glucose control before receiving teprotumumab. Hyperglycemic episodes should be controlled with medication for glycemic control, if necessary.
- **Pregnancy:** Based on findings in animals and its mechanism of action inhibiting IGF-1R, teprotumumab may cause fetal harm when administered to a pregnant woman. Adequate and well-controlled studies with teprotumumab have not been conducted in pregnant women. In utero teprotumumab exposure in cynomolgus monkeys dosed once weekly with teprotumumab throughout pregnancy resulted in external and skeletal abnormalities. Teprotumumab exposure may lead to an increase in fetal loss. Therefore, teprotumumab should not be used in pregnancy, and appropriate forms of contraception should be implemented prior to initiation, during treatment, and for 6 months following the last dose of teprotumumab. If a patient becomes pregnant during treatment, teprotumumab should be discontinued and the patient should be advised of the potential risk to the fetus.
- **Lactation:** There is no information on the presence of teprotumumab in human milk, the effects on the breastfed infant, or the effects on milk production.
- **Females and Males of Reproductive Potential:** Based on its mechanism of action of inhibiting IGF-1R, teprotumumab may cause fetal harm when administered to a

pregnant woman. Females of reproductive potential should be advised to use effective contraception prior to initiation, during treatment with teprotumumab, and for 6 months after the last dose of teprotumumab.

- **Pediatric Use:** The safety and effectiveness of teprotumumab have not been established in pediatric patients.
- **Geriatric Use:** Of the 171 patients in the 2 randomized trials, 15% were 65 years of age or older; the number of patients 65 years of age or older was similar between treatment groups. No overall differences in efficacy or safety were observed between patients 65 years of age or older and younger patients.

Adverse Reactions: In randomized, placebo-controlled clinical studies, the most common adverse reactions (occurred ≥5% and more frequently than placebo) following teprotumumab treatment were muscle spasms, nausea, alopecia, diarrhea, fatigue, hyperglycemia, hearing impairment, dysgeusia, headache, and dry skin.

Efficacy: The efficacy of teprotumumab was evaluated in 2 randomized, double-masked, placebo-controlled studies (Study 1 and Study 2) in 171 patients with thyroid eye disease. Patients had a clinical diagnosis of thyroid eye disease with symptoms and were euthyroid or had thyroxine and free triiodothyronine levels <50% above or below normal limits. Prior surgical treatment for thyroid eye disease was not permitted. Proptosis ranged from 16 to 33mm and 125 patients (73%) had diplopia at baseline. Patients were randomized to receive teprotumumab or placebo in a 1:1 ratio; a total of 84 patients were randomized to teprotumumab and 87 patients were randomized to placebo. Patients were given IV infusions (10mg/kg for the first infusion and 20mg/kg for the remaining 7 infusions) every 3 weeks for a total of 8 infusions. The proptosis responder rate at week 24 was defined as the percentage of patients with ≥2mm reduction in proptosis in the study eye from baseline, without deterioration in the non-study eye (≥2mm increase) in proptosis. The following table (Table 1) summarizes the efficacy results in Study 1 and Study 2. Following discontinuation of treatment in Study 1, 53% of patients (16 of 30 patients) who were proptosis responders at week 24 maintained proptosis response 51 weeks after the last teprotumumab infusion.

Table 1. Efficacy Results in Patients with Thyroid Eye Disease (Study 1 and Study 2)

	Study 1			Study 2		
	Teprotumumab (N=42)	Placebo (N=45)	Difference (95% CI)	Teprotumumab (N=41)	Placebo (N=42)	Difference (95% CI)
Proptosis responder rate at week 24, % (n)	71% (30)	20% (9)	51% (33, 69)	83% (34)	10% (4)	73% (59, 88)
Proptosis (mm) average change from baseline through week 24, LS Mean (SE)	-2.5 (0.2)	-0.2 (0.2)	-2.3 (-2.8, -1.8)	-2.8 (0.2)	-0.5 (0.2)	-2.3 (-2.8, -1.8)

N = number of patients per treatment group; % = percentage; n = number proptosis responders; CI = confidence interval; LS = least squares; SE = standard error

Cost: The Wholesale Acquisition Cost (WAC) of Tepezza™ (teprotumumab-trbw) is $14,900 per 500mg SDV. Treatment cost will vary depending on patient weight. The cost of treatment for a 70kg patient would be $342,700 for the recommended 8 total infusions.

Recommendations

The College of Pharmacy recommends the prior authorization of Tepezza™ (teprotumumab-trbw) with the following criteria:

Tepezza™ (Teprotumumab-trbw) Approval Criteria:

1. An FDA approved indication for the treatment of thyroid eye disease in adult members 18 years of age and older; and
    a. Member must be experiencing eye symptoms related to thyroid eye disease; and
    b. Member must have thyroid blood levels in the normal range; and
2. Female members must not be pregnant and must have a negative pregnancy test prior to initiation of therapy; and
3. Female members of reproductive potential must be willing to use effective contraception prior to initiation, during treatment with Tepezza™, and for at least 6 months after the last dose of Tepezza™; and
4. Member must not have had prior surgical treatment for thyroid eye disease; or
    a. A prior authorization request with patient-specific information may be submitted for consideration of Tepezza™ for members who have had prior surgical treatment for thyroid eye disease, including but not limited to patient-specific, clinically significant information regarding the member's prior surgery and the need for Tepezza™; and
5. Medical supervision by an ophthalmologist for the treatment of thyroid eye disease; and
    a. The name of the ophthalmologist recommending treatment with Tepezza™ must be provided on the prior authorization request; and
6. Tepezza™ must be administered as an intravenous (IV) infusion at the recommended infusion rate per package labeling, with appropriate pre-medication(s) based on the member's risk of infusion reactions; and
7. Tepezza™ must be administered by a health care professional. Prior authorization requests must indicate how Tepezza™ will be administered; and
    a. Tepezza™ must be shipped via cold chain supply to the facility where the member is scheduled to receive treatment; or
    b. Tepezza™ must be shipped via cold chain supply to the member's home and administered by a home health care provider and the member (or the member's caregiver) must be trained on the proper storage of Tepezza™; and
8. The member's current weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling; and
9. Approvals will be for a maximum of 8 total infusions.

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Appendix N

Calendar Year 2019 Annual Review of Anti-Emetic Medications

Oklahoma Health Care Authority
March 2020

Current Prior Authorization Criteria

Akynzeo® (Netupitant/Palonosetron) and Akynzeo® IV (Fosnetupitant/Palonosetron) Approval Criteria:

1. An FDA approved indication for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy; and
2. For Akynzeo® oral capsules, a previously failed trial of oral aprepitant (Emend®) that resulted in an inadequate response is required, or a patient-specific, clinically significant reason why oral aprepitant cannot be used must be provided; and
3. For Akynzeo® IV, a previously failed trial of intravenous (IV) fosaprepitant (Emend® IV) that resulted in an inadequate response is required, or a patient-specific, clinically significant reason why IV fosaprepitant cannot be used must be provided; and
4. Akynzeo® IV will require a patient-specific, clinically significant reason why the oral capsule formulation cannot be used; and
5. Approval length will be based on duration of need; and
6. A quantity limit of 1 capsule or vial per chemotherapy cycle will apply; and
7. Akynzeo® oral capsules will not require prior authorization for members with cancer and claims will pay at the point of sale if the member has a reported oncology diagnosis within the past 6 months of claims history.
    a. Based on the current low net cost, Akynzeo® oral capsules will not require prior authorization for members with cancer; however, Akynzeo® oral capsules will follow the original criteria and require a previously failed trial of aprepitant if the net cost increases compared to other available products.

Bonjesta® (Doxylamine/Pyridoxine) Approval Criteria:

1. An FDA approved diagnosis of nausea and vomiting associated with pregnancy that is not responsive to conservative management; and
2. Trials with at least 2 non-pharmacological therapies that have failed to relieve nausea and vomiting; and
3. A patient-specific, clinically significant reason why member cannot use over-the-counter (OTC) doxylamine and OTC Vitamin B_6 (pyridoxine) must be provided; and
4. A patient-specific, clinically significant reason why the member cannot use Diclegis® must be provided.

Kytril® and Sancuso® (Granisetron), Anzemet® (Dolasetron), Emend® and Cinvanti® (Aprepitant), and Emend® IV (Fosaprepitant) Approval Criteria:

1. An FDA approved diagnosis; and

2. A recent trial of ondansetron (within the past 6 months) used for at least 3 days or 1 cycle that resulted in an inadequate response is required for authorization in members receiving moderately-emetogenic chemotherapy; and
3. No ondansetron trial is required for authorization of Emend® (aprepitant) in members receiving highly-emetogenic chemotherapy; and
4. For Emend® (aprepitant) oral suspension, an age restriction of 6 years and younger will apply. Members older than 6 years of age will require a patient-specific, clinically significant reason why the oral capsule formulation cannot be used; and
5. For Cinvanti™ [aprepitant intravenous (IV) emulsion], a previously failed trial of IV fosaprepitant (Emend® IV) that resulted in an inadequate response is required, or a patient-specific, clinically significant reason why IV fosaprepitant cannot be used must be provided; and
6. Approval length will be based on duration of need.

Marinol® and Syndros® (Dronabinol) and Cesamet® (Nabilone) Approval Criteria:

1. An FDA approved diagnosis; and
2. Approval length will be based on duration of need; and
3. For Marinol® (dronabinol) and Cesamet® (nabilone), a quantity limit of 60 capsules per 30 days will apply; and
4. Cesamet® (nabilone) will require a patient-specific, clinically significant reason why dronabinol oral capsules cannot be used; and
5. For Syndros® (dronabinol) oral solution, the quantity approved will be patient-specific depending on patient diagnosis, maximum recommended dosage, and manufacturer packaging; and
6. For Syndros® (dronabinol) oral solution, an age restriction of 6 years and younger will apply. Members older than 6 years of age will require a patient-specific, clinically significant reason why dronabinol oral capsules cannot be used.

Sustol® (Granisetron Subcutaneous Injection) Approval Criteria:

1. An FDA approved indication for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic chemotherapy (MEC) or anthracycline and cyclophosphamide (AC) combination chemotherapy regimens; and
2. Chemotherapy regimen must be listed on the prior authorization request; and
3. A recent trial of ondansetron (within the past 6 months) used for at least 3 days or 1 cycle that resulted in an inadequate response is required for authorization in members receiving MEC; and
4. No ondansetron trial is required for authorization of granisetron in members receiving AC combination chemotherapy regimens; and
5. A patient-specific, clinically significant reason why the member cannot use Kytril® (granisetron hydrochloride injection for intravenous use) must be provided; and
6. A quantity limit of 1 injection per chemotherapy cycle will apply.

Varubi® and Varubi® IV (Rolapitant) Approval Criteria:

1. An FDA approved indication for the prevention of delayed nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy; and
2. For oral Varubi® (rolapitant oral tablets), a previously failed trial of oral aprepitant (Emend®) that resulted in an inadequate response is required, or a patient-specific, clinically significant reason why oral aprepitant cannot be used must be provided; and
3. For Varubi® IV [rolapitant intravenous (IV) emulsion], a previously failed trial of IV fosaprepitant (Emend® IV) that resulted in an inadequate response is required, or a patient-specific, clinically significant reason why IV fosaprepitant cannot be used must be provided; and
4. Approval length will be based on duration of need; and
5. A quantity limit of 2 tablets or 2 vials per chemotherapy cycle will apply.

Zuplenz® (Ondansetron Oral Soluble Film) Approval Criteria:

1. An FDA approved diagnosis; and
2. A patient-specific, clinically significant reason why the member cannot take all other available formulations of generic ondansetron must be provided.

Utilization of Anti-Emetic Medications: Calendar Year 2019

Comparison of Calendar Years: Pharmacy Claims

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2018	73,387	99,487	$1,490,734.59	$14.98	$2.20	1,634,160	676,095
2019	74,807	101,695	$1,702,860.56	$16.74	$2.42	1,711,693	703,520
% Change	**1.9%**	**2.2%**	**14.2%**	**11.7%**	**10.0%**	**4.7%**	**4.1%**
Change	**1,420**	**2,208**	**$212,125.97**	**$1.76**	**$0.22**	**77,533**	**27,425**

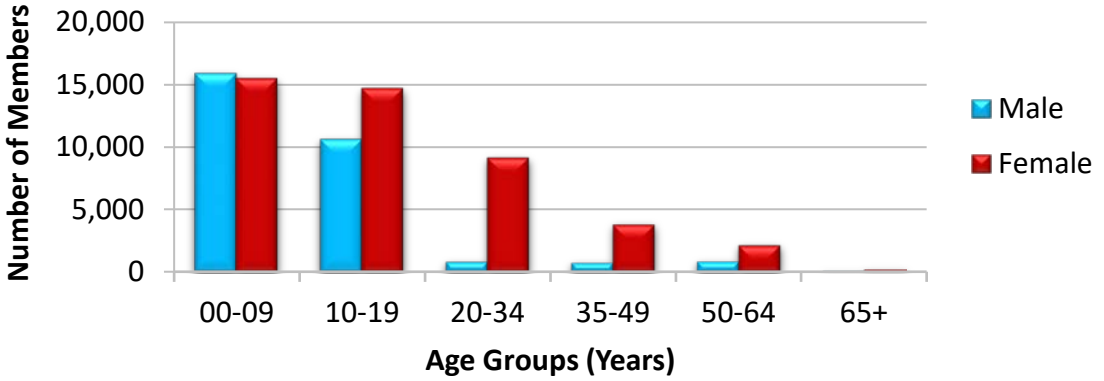
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

Calendar Year 2019 Utilization: Medical Claims

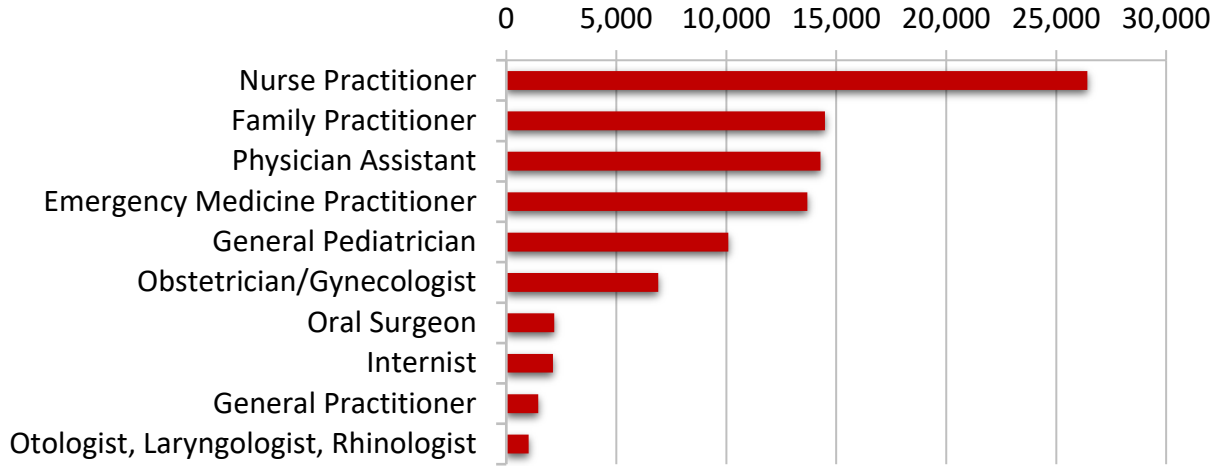
Calendar Year	*Total Members	^Total Claims	Total Cost	Cost/ Claim	Claims/ Member
2019	614	3,046	$257,162.01	$84.43	4.96

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

Demographics of Members Utilizing Anti-Emetic Medications: Pharmacy Claims



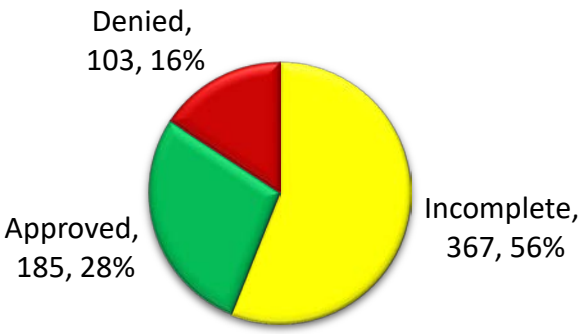
Top Prescriber Specialties of Anti-Emetic Medications by Number of Claims: Pharmacy Claims



Prior Authorization of Anti-Emetic Medications

There were 655 prior authorization requests submitted for anti-emetic medications during calendar year 2019. The following chart shows the status of the submitted petitions for calendar year 2019.

Status of Petitions



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

Anticipated Patent Expiration(s):

- Sustol® [granisetron subcutaneous (sub-Q) injection]: September 2024
- Sancuso® (granisetron transdermal patch): January 2025
- Syndros® (dronabinol oral solution): August 2028
- Varubi® (rolapitant tablet): October 2029
- Zuplenz® (ondansetron oral soluble film): July 2030
- Akynzeo® IV [fosnetupitant/palonosetron for intravenous (IV) use]: May 2032
- Bonjesta® [doxylamine/pyridoxine extended-release (ER) tablet]: February 2033
- Akynzeo® (netupitant/palonosetron capsule): September 2035
- Cinvanti® (aprepitant IV emulsion): September 2035

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

- **February 2019:** The FDA has expanded the approval of Cinvanti® (aprepitant IV emulsion) to include use as a 2-minute IV push for the prevention of acute and delayed chemotherapy-induced nausea and vomiting (CINV). Cinvanti® is a polysorbate 80-free, IV formulation of an NK1 receptor antagonist. The FDA previously approved Cinvanti® as a 30-minute IV infusion in November 2017. The expanded approval is based on results of a 2-part, Phase 1 study that demonstrated bioequivalence and a similar safety profile for patients who received Cinvanti® as a standard 30-minute IV infusion compared with a 2-minute IV push.

News:

- **June 2019:** Teva introduced an AB-rated generic version and Analog Pharma launched an authorized generic version of Duchesnay's Diclegis® (doxylamine/pyridoxine) 10mg/10mg delayed-release tablet. Diclegis® is indicated for the treatment of nausea and vomiting of pregnancy in women who do not respond to conservative management. Currently, brand name Diclegis® has a lower net cost for SoonerCare, so is preferred over the available generic products.

Pipeline:

- **Barhemsys™ (amisulpride):** Acacia Pharma announced on September 26, 2019 that the FDA has accepted its resubmitted New Drug Application (NDA) for Barhemsys™ (amisulpride injection) for post-operative nausea and vomiting (PONV). The FDA has classified the NDA resubmission as Class 2 and has assigned a Prescription Drug User Fee Act (PDUFA) goal date of February 26, 2020. As part of this process, Acacia Pharma has nominated an alternative contract manufacturer, who successfully underwent and passed regular inspections by regulatory authorities for compliance with current Good Manufacturing Practices (cGMP) to supply amisulpride.
- **APD403:** Acacia Pharma is currently developing APD403 for CINV. APD403 is based on the selective dopamine antagonist amisulpride, the same active ingredient as in Barhemsys™. APD403 is being developed as an IV injection for cancer patients to be administered immediately prior to chemotherapy to prevent acute CINV and as an oral tablet to prevent delayed CINV. APD403 has successfully completed 1 proof-of-concept

and 1 Phase 2 dose-ranging clinical study demonstrating it is well tolerated and effective at preventing acute and delayed CINV. Acacia intends to advance APD403 into Phase 3 studies following completion of a further Phase 2 clinical study.

- **Bekinda® (ondansetron ER):** RedHill Biopharma is currently developing Bekinda®, a proprietary, bimodal ER (24-hour) oral tablet formulation of ondansetron, for the treatment of acute gastroenteritis and gastritis and for the treatment of irritable bowel syndrome with diarrhea (IBS-D). A positive Phase 3 clinical study with Bekinda® for the treatment of acute gastroenteritis and gastritis (the GUARD study) successfully met its primary endpoint, and a positive Phase 2 clinical study with Bekinda® for the treatment of IBS-D also successfully met its primary endpoint. RedHill is currently in discussions with the FDA on the design of a confirmatory Phase 3 clinical study with Bekinda® for acute gastroenteritis and gastritis and is planning to finalize the design of 2 pivotal Phase 3 studies with Bekinda® for IBS-D.

Recommendations

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

Utilization Details of Anti-Emetic Medications: Calendar Year 2019

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
ONDANSETRON PRODUCTS					
ONDANSETRON ODT 4MG	62,695	51,157	$886,839.48	$2.37	$14.15
ONDANSETRON TAB 4MG	15,372	11,484	$184,155.86	$1.37	$11.98
ONDANSETRON ODT 8MG	11,280	8,086	$173,607.01	$2.23	$15.39
ONDANSETRON SOL 4MG/5ML	6,674	6,096	$135,847.20	$2.50	$20.35
ONDANSETRON TAB 8MG	4,881	3,153	$59,627.67	$1.34	$12.22
ONDANSETRON INJ 4MG/2ML	13	5	$373.12	$1.67	$28.70
ONDANSETRON INJ 40MG/2ML	8	4	$171.66	$1.91	$21.46
SUBTOTAL	**100,923**	**74,543***	**$1,440,622.00**	**$2.10**	**$14.27**
DRONABINOL PRODUCTS					
DRONABINOL CAP 5MG	94	29	$18,771.54	$6.83	$199.70
DRONABINOL CAP 2.5MG	44	30	$4,342.30	$3.76	$98.69
DRONABINOL CAP 10MG	17	4	$5,269.06	$10.64	$309.94
SUBTOTAL	**155**	**57***	**$28,382.90**	**$6.45**	**$183.1**
APREPITANT PRODUCTS					
APREPITANT CAP 80MG	19	3	$5,174.50	$139.85	$272.34
APREPITANT PAK 80MG & 125MG	12	7	$5,614.67	$155.96	$467.89
EMEND SUS 125MG	11	3	$2,125.51	$106.28	$193.23
APREPITANT CAP 125MG	9	2	$2,008.08	$223.12	$223.12
SUBTOTAL	**51**	**11***	**$14,922.76**	**$146.30**	**$292.60**
GRANISETRON PRODUCTS					

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
GRANISETRON TAB 1MG	21	6	$906.93	$4.07	$43.19
SANCUSO DIS 3.1MG	5	3	$7,427.97	$65.73	$1,485.59
SUBTOTAL	**26**	**9***	**$8,334.90**	**$24.81**	**$320.57**
DOXYLAMINE/PYRIDOXINE PRODUCTS					
DICLEGIS TAB 10-10MG	520	375	$204,082.37	$16.43	$392.47
DOXYL/PYRID TAB 10-10MG	20	20	$6,515.63	$14.48	$325.78
SUBTOTAL	**540**	**388***	**$210,598.00**	**$16.37**	**$390.00**
TOTAL	**101,695**	**74,807***	**$1,702,860.56**	**$2.42**	**$16.74**

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

Medical Claims

PRODUCT UTILIZED	^TOTAL CLAIMS	*TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
PALONOSETRON INJ J2469	2,417	515	$254,053.39	$105.11	$105.11
GRANISETRON INJ J1626	629	99	$3,108.62	$4.94	$4.94
TOTAL	**3,046**	**614**	**$257,162.01**	**$84.43**	**$84.43**

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

[1] U.S. Food and Drug Administration (FDA). Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised 01/2020. Last accessed 02/01/2020.
[2] FDA Approves Aprepitant Injection for CINV. *OncLive*. Available online at: https://www.onclive.com/web-exclusives/fda-approves-aprepitant-injection-for-cinv. Issued 02/28/2019. Last accessed 02/01/2020.
[3] Teva Pharmaceuticals USA, Inc. Doxylamine Succinate and Pyridoxine Hydrochloride Delayed-Release Tablets. Available online at: https://www.tevagenerics.com/product/doxylamine-succinate-and-pyridoxine-hydrochloride-delayed-release-tablets. Last accessed 02/01/2020.
[4] Analog Pharma Inc. Doxylamine Succinate and Pyridoxine Hydrochloride. Available online at: https://www.analogpharma.com/en/products/doxylamine-succinate-and-pyridoxine-hydrochloride. Last accessed 02/01/2020.
[5] Acacia Pharma. Acacia Pharma Announces New Barhemsys™ PDUFA Target Date of 26 February 2020. Available online at: http://acaciapharma.com/news/2019/09/acacia-pharma-announces-new-barhemsys-pdufa-target-date-of-26-february-2020. Issued 09/26/2019. Last accessed 02/01/2020.
[6] Acacia Pharma. Acacia Pharma Pipeline: APD403. Available online at: http://acaciapharma.com/pipeline/apd403. Last accessed 02/01/2020.
[7] RedHill Biopharma. RedHill Biopharma Announces Publication of RHB-102 Gastroenteritis Phase 3 Study Results in JAMA. Available online at: https://www.redhillbio.com/RedHill/Templates/showpage.asp?DBID=1&LNGID=1&TMID=178&FID=1395&PID=0&IID=13237. Issued 11/12/2019. Last accessed 02/01/2020.

Appendix O

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: February 14, 2020

FDA Approves Three Drugs for Nonprescription Use Through Rx-to-OTC Switch Process

The FDA approved 3 drugs for nonprescription, or over-the-counter (OTC), use through a process called a prescription (Rx)-to-OTC switch. The FDA approved Voltaren Arthritis Pain (diclofenac sodium 1% topical gel) for the temporary relief of arthritis pain; Pataday Twice Daily Relief (olopatadine HCl 0.1% ophthalmic solution/drops) for the temporary relief of itchy and red eyes due to pollen, ragweed, grass, animal hair or dander; and Pataday Once Daily Relief (olopatadine HCl 0.2% ophthalmic solution/drops) for the temporary relief of itchy eyes due to pollen, ragweed, grass, animal hair or dander, for OTC use. Rx-to-OTC switch is usually initiated by the manufacturer of the prescription drug. For a drug to switch to OTC status, the data provided must demonstrate that the drug is safe and effective for use in self-medication as directed in proposed labeling. The manufacturer must show that consumers can understand how to use the drug safely and effectively without the supervision of a healthcare professional.

Voltaren Arthritis Pain is a nonsteroidal anti-inflammatory drug (NSAID) and works by reducing substances in the body that cause pain and inflammation. This product, previously referred to as Voltaren Gel 1%, was first approved by the FDA in 2007 as a prescription drug and was indicated for the relief of the pain of osteoarthritis (OA) of joints responsive to topical treatment, in particular, the joints of the hands, knees, and feet. It has not been shown to work for strains, sprains, bruises, or sports injuries. Voltaren Arthritis Pain is intended for the temporary relief of joint pain due to the most common type of arthritis, OA, which increases with age, affects millions of people in the United States, and can generally be self-diagnosed. Arthritis is the swelling and tenderness of 1 or more joints. Symptoms of arthritis include pain, swelling, stiffness, and difficulty moving a joint. Voltaren Arthritis Pain is not for immediate relief and may take up to 7 days to work. Consumers should stop use and seek medical attention if arthritis pain has not improved in 7 days or if the product is needed for more than 21 days. The active ingredient in Voltaren Arthritis Pain, diclofenac, may cause a severe allergic reaction, especially in people allergic to aspirin. If an allergic reaction occurs, consumers are advised to stop use and seek medical care immediately. Liver damage may occur if this product is used more or longer than directed or when using other products containing diclofenac. This product contains an NSAID, which may cause severe stomach bleeding. NSAIDs, except aspirin, increase the risk of heart attack, heart failure, and stroke. These can be fatal. The risk is higher if consumers use more than directed or for longer than directed. If pregnant or breastfeeding, consumers should talk to a health care professional about use. This product should not be used during the last 3 months of pregnancy unless the consumer is definitely directed to do so by a doctor because diclofenac may cause problems in the unborn child or complications during the delivery.

Pataday Twice Daily Relief was first approved by the FDA in 1996 under the name Patanol as a prescription drug and was indicated for the treatment of the signs and symptoms of allergic conjunctivitis (referring to ocular redness and itching due to allergies). Pataday, now Pataday Once Daily Relief, was first approved by the FDA in 2004 as a prescription drug and was indicated for the treatment of ocular itching associated with allergic conjunctivitis. These drugs are mast cell stabilizers, which work by preventing the release of histamine and therefore preventing or controlling allergic disorders. Ocular itching caused by allergens is a common ailment in the United States, affecting millions of people. Consumers are advised to stop use and talk to their health care professional if they experience eye pain, changes in vision, increased redness of the eye, worsening of itching, or itching lasting for more than 72 hours.

All 3 products will be marketed in the United States as OTC drugs and will no longer be available as prescription drugs. Consumers should read and follow the Drug Facts labels for the OTC products. Patients

who currently take prescription versions of these products and have questions about the Rx-to-OTC switch should talk to their health care professional.

FDA NEWS RELEASE

For Immediate Release: February 24, 2020

FDA approves first generic of ProAir HFA

The FDA approved the first generic of ProAir HFA (albuterol sulfate) Inhalation Aerosol for the treatment or prevention of bronchospasm in patients 4 years of age and older with reversible obstructive airway disease and the prevention of exercise-induced bronchospasm in patients 4 years of age and older. The most common side effects associated with albuterol sulfate inhalation aerosol are headache, tachycardia, pain, dizziness, pharyngitis, rhinitis, chest pain, palpitations, tremor, and nervousness.

According to the National Heart, Lung, and Blood Institute, bronchospasms occur when the muscles surrounding the airways swell and tighten, squeezing the airways and making them smaller. Exercise and other physical activity can bring on symptoms in most people who have asthma and may occur either during or right after being active. Asthma causes recurring periods of wheezing, chest tightness, shortness of breath, and coughing. The coughing often worsens at night or early in the morning. Asthma affects people of all ages, but it most often starts during childhood. In the United States, more than 26 million people are known to have asthma, about 7 million of these people are children.

The FDA regularly takes steps to help guide industry through the development process for generic drug products, including combination products, such as metered dose inhalers, that consist of a drug and a device. The development of generic combination products can be more challenging than solid oral dosage forms, like tablets. Under the Generic Drug User Fee Amendments (GDUFA), individual companies can meet with the FDA as part of its pre-Abbreviated New Drug Application (ANDA) program to support the development of such complex generic drug products. The FDA also publishes guidance documents describing the steps the FDA recommends companies take to submit complete applications for generic drug products.

In 2016, the FDA issued a revised draft product-specific guidance for proposed generic albuterol sulfate metered dose inhalers, including drug products referencing ProAir HFA. Among other things, the draft guidance provides bioequivalence recommendations. The FDA requires sponsors to submit appropriate data and information to demonstrate that complex generic drug-device combination products meet the agency's rigorous approval standards. These standards ensure that quality generic drug products are as safe and effective as their brand name counterparts. In 2020, the FDA will continue to advance additional policies to promote generic competition for complex generic drug products. Among other steps, the agency intends to publish additional guidance documents to aid in the development of specific complex generic drug products. The FDA also plans to publish a series of guidances to address regulatory and scientific challenges that make it generally more difficult to develop complex generic drug products because of their complex formulation or mode of delivery. As part of this, the FDA intends to issue draft guidance with recommendations on establishing active ingredient sameness. In addition, the FDA is going to help advance the development of new analytical tools and in vitro tests that may provide additional accurate, sensitive, and reproducible ways to support development of complex generic drugs. Better tools can reduce complex generic drug development time and cost and can inform regulatory decisions.

FDA NEWS RELEASE

For Immediate Release: February 28, 2020

FDA Approves First Generic of Daraprim

The FDA approved an application for the first generic of Daraprim (pyrimethamine) tablets for the treatment of toxoplasmosis (an infection caused by the parasite *Toxoplasma gondii*) when used with a sulfonamide (a group of medicines used to treat bacterial infections). The most common side effects for pyrimethamine include hypersensitivity reactions that can occasionally be severe, such as Stevens-Johnson syndrome and toxic epidermal necrolysis, erythema multiforme, anaphylaxis, and hyperphenylalaninemia,

particularly when pyrimethamine is administered at the same time as a sulfonamide. With doses of pyrimethamine used for the treatment of toxoplasmosis, anorexia and vomiting may occur. Doses used in toxoplasmosis may produce megaloblastic anemia, leukopenia, thrombocytopenia, pancytopenia, neutropenia, atrophic glossitis, hematuria, and disorders of cardiac rhythm. Hematologic effects, however, may also occur at low doses in certain individuals. Pulmonary eosinophilia has been reported rarely.

Pyrimethamine should not be used in patients with known hypersensitivity to pyrimethamine or with documented megaloblastic anemia due to folate deficiency. Women who are taking pyrimethamine should not become pregnant. Patients should keep pyrimethamine out of the reach of children. A small "starting" dose for toxoplasmosis is recommended in patients with convulsive disorders to avoid the potential nervous system toxicity of pyrimethamine. Pyrimethamine should be used with caution in patients with impaired renal or hepatic function or in patients with possible folate deficiency, such as individuals with malabsorption syndrome, alcoholism or pregnancy, and those receiving therapy, such as phenytoin, affecting folate levels.

Toxoplasmosis is an infection caused by a single-celled parasite called *Toxoplasma gondii* that, when severe, can cause damage to the brain, eyes, or other organs. Toxoplasmosis can occur, among other ways, by eating undercooked, contaminated meat or shellfish; drinking water contaminated with *Toxoplasma*; or by accidental swallowing of the parasite through contact with cat feces that contain *Toxoplasma.* It is considered to be the leading cause of death attributed to foodborne illness in the United States.
Severe toxoplasmosis is more likely in pregnant women and individuals who have weak immune systems, such as those with HIV or AIDS, those taking certain types of chemotherapy and those who have recently received an organ transplant. However, occasionally even persons with healthy immune systems may experience eye damage from toxoplasmosis.

One area of focus under the FDA's Drug Competition Action Plan is improving the efficiency of the generic drug development, review and approval process, as well as closing loopholes that allow brand-name drug companies to delay the generic competition. As part of these important efforts, the FDA maintains a list of off-patent, off-exclusivity drug products without an approved generic to improve transparency and encourage the development and submission of applications for drugs with limited competition. Pyrimethamine is included on this list. The FDA also prioritizes the review of submissions for generic drugs for which there are fewer than 3 approved generic versions for the reference listed drug (RLD) and for which there are no blocking patents or exclusivities on the RLD.

Current Drug Shortages Index (as of February 25, 2020):

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

Alogliptin Tablets	***Currently in Shortage***
Aminophylline Injection, USP	***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***
Bacitracin Ophthalmic Ointment	***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***
Carisoprodol Tablets, 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***
Dexamethasone Sodium Phosphate 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***
Diphenhydramine Injection	***Currently in Shortage***
Disulfiram Tablets	***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***
Echothiophate Iodide (Phospholine Iodide) Ophthalmic Solution	***Currently in Shortage***
Enalaprilat Injection, USP	***Currently in Shortage***
Epinephrine Injection, 0.1 mg/mL	***Currently in Shortage***
Epinephrine Injection, Auto-Injector	***Currently in Shortage***
Eprosartan Mesylate Tablets	***Currently in Shortage***
Erythromycin Lactobionate for Injection, USP	***Currently in Shortage***
Erythromycin Ophthalmic Ointment	***Currently in Shortage***
Fentanyl Citrate (Sublimaze) Injection	***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***
Gemifloxacin Mesylate (Factive) Tablets	***Currently in Shortage***
Guanfacine Hydrochloride Tablets	***Currently in Shortage***
Heparin Sodium and Sodium Chloride 0.9% Injection	***Currently in Shortage***
Hydromorphone Hydrochloride Injection, USP	***Currently in Shortage***
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***
Latanoprost Ophthalmic Solution 0.005%	***Currently in Shortage***
Letermovir (Prevymis) Injection	***Currently in Shortage***
Leucovorin Calcium Lyophilized Powder for 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***
Lorazepam Injection, USP	***Currently in Shortage***
Loxapine Capsules	***Currently in Shortage***
Methadone Hydrochloride Injection	***Currently in Shortage***
Methyldopa Tablets	***Currently in Shortage***
Methylphenidate Hydrochloride (QUILLIVANT XR) for Extended-Release Oral Suspension	***Currently in Shortage***
Metoprolol Tartrate Injection, USP	***Currently in Shortage***
Metronidazole 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***
Nystatin Oral Suspension	***Currently in Shortage***
Olmesartan Medoxomil Tablets	***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***
Peritoneal Dialysis Solutions	***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***
Ranitidine Injection, USP	***Currently in Shortage***
Ranitidine Tablets/Capsules	***Currently in Shortage***
Ropivacaine Hydrochloride Injection	***Currently in Shortage***
Sclerosol Intrapleural Aerosol	***Currently in Shortage***
Sincalide (Kinevac) Lyophilized Powder for Injection	***Currently in Shortage***
Sodium Acetate Injection, USP	***Currently in Shortage***

Sodium Bicarbonate Injection, USP	***Currently in Shortage***
Sodium Chloride 23.4% Injection	***Currently in Shortage***
Sodium Chloride Injection USP, 0.9% Vials and Syringes	***Currently in Shortage***
Tacrolimus Capsules	***Currently in Shortage***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***
Thiothixene Capsules	***Currently in Shortage***
Timolol Maleate Tablets	***Currently in Shortage***
Triamcinolone Acetonide (Triesence) Injection, Suspension	***Currently in Shortage***
Trifluridine Ophthalmic Solution	***Currently in Shortage***
Valsartan Tablets	***Currently in Shortage***
Vinblastine Sulfate Injection	***Currently in Shortage***