Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
June 14, 2017
4 p.m.

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

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

MEMORANDUM

TO: Drug Utilization Review Board Members

FROM: Bethany Holderread, Pharm.D.

SUBJECT: Packet Contents for Board Meeting – June 14, 2017

DATE: June 1, 2017

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

Enclosed are the following items related to the June 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/Chloroquine (Aralen®) & Hydroxychloroquine (Plaquenil®) Induced Retinopathy Mailing Update – Appendix B

Action Item – Vote to Prior Authorize Kuvan® (Sapropterin) – Appendix C

Action Item – Vote to Prior Authorize Lumizyme® (Alglucosidase Alfa Injection) – Appendix D

Action Item – Vote to Prior Authorize Alpha$_1$-Proteinase Inhibitors: Aralast NP™, Glassia®, Prolastin®-C, and Zemaira® – Appendix E

Action Item – Vote to Prior Authorize Elaprase® (Idursulfase) – Appendix F

Action Item – Vote to Prior Authorize ColPrep™ Kit (Sodium Sulfate/Potassium Sulfate/Magnesium Sulfate) – Appendix G

Action Item – Vote to Prior Authorize Impavido® (Miltefosine) – Appendix H

Action Item – Vote to Prior Authorize Xalkori® (Crizotinib), Zykadia® (Ceritinib), Alecensa® (Alectinib), Alunbrig™ (Brigatinib), Tarceva® (Erlotinib), Gilotrif® (Afatinib), Tagrisso™ (Osimertinib), Cyramza® (Ramucirumab), and Tecentriq® (Atezolizumab) – Appendix I

Annual Review of Prostate Cancer Medications – Appendix J

Annual Review of ADHD and Narcolepsy Medications and 30-Day Notice to Prior Authorize Vyvanse® (Lisdexamfetamine Chewable Tablets) and to Update the ADHD Prior Authorization Criteria and Tier Chart – Appendix K

Annual Review of Atypical Antipsychotic Medications and 30-Day Notice to Update the Atypical Antipsychotic Prior Authorization Criteria and Tier Chart – Appendix L

Annual Review of Huntington's Disease (HD) Medications and 30-Day Notice to Prior Authorize Austedo™ (Deutetrabenazine) and Xenazine® (Tetrabenazine) – Appendix M

Annual Review of Inhaled Tobramycin Products, Pulmozyme® (Dornase Alfa), and Cayston® (Aztreonam) – Appendix N

30-Day Notice to Prior Authorize Ingrezza™ (Valbenazine) – Appendix O

Annual Review of Various Special Formulations and 30-Day Notice to Prior Authorize Carac® (Fluorouracil 0.5% Cream), GoNitro™ (Nitroglycerin Sublingual Powder), Soltamox® (Tamoxifen Citrate Oral Solution), Taytulla™ (Norethindrone Acetate/Ethinyl Estradiol Capsules & Ferrous Fumarate Capsules), Tirosint®-SOL (Levothyroxine Sodium Oral Solution), Xatmep™ (Methotrexate Oral Solution), Zovirax® (Acyclovir Ointment and Suspension), Xerese® (Acyclovir/Hydrocortisone Cream), & Denavir® (Penciclovir Cream) – Appendix P

30-Day Notice to Prior Authorize Aczone® (Dapsone Gel) and Tazorac® (Tazarotene Cream and Gel) – Appendix Q

Annual Review of H.P. Acthar® Gel (Corticotropin Injection) – Appendix R

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

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – June 14, 2017 @ 4:00 p.m.

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

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

1. Call to Order

A. Roll Call – Dr. Cothran

Items to be presented by Dr. Muchmore, Chairman:

2. Public Comment Forum

A. Acknowledgement 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. May 10, 2017 DUR Minutes – Vote
B. May 10, 2017 DUR Recommendations Memorandum

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

4. Update on Medication Coverage Authorization Unit/ Chloroquine (Aralen®) & Hydroxychloroquine (Plaquenil®) Induced Retinopathy Mailing Update – See Appendix B

A. Medication Coverage Activity for May 2017
B. Pharmacy Help Desk Activity for May 2017
C. Chloroquine (Aralen®) & Hydroxychloroquine (Plaquenil®) Induced Retinopathy Mailing Update

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

5. Action Item – Vote to Prior Authorize Kuvan® (Sapropterin) – See Appendix C

A. Introduction
B. College of Pharmacy Recommendations

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

6. Action Item – Vote to Prior Authorize Lumizyme® (Alglucosidase Alfa Injection) – See Appendix D

A. Introduction
B. College of Pharmacy Recommendations

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

7. Action Item – Vote to Prior Authorize Alpha$_1$-Proteinase Inhibitors: Aralast NP™, Glassia®, Prolastin®-C, and Zemaira® – See Appendix E

A. Introduction
B. College of Pharmacy Recommendations

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

8. Action Item – Vote to Prior Authorize Elaprase® (Idursulfase) – See Appendix F

A. Introduction
B. College of Pharmacy Recommendations

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

9. Action Item – Vote to Prior Authorize ColPrep™ Kit (Sodium Sulfate/Potassium Sulfate/Magnesium Sulfate) – See Appendix G

A. Indication(s) and Dosing
B. College of Pharmacy Recommendations

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

10. Action Item – Vote to Prior Authorize Impavido® (Miltefosine) – See Appendix H

A. Introduction
B. College of Pharmacy Recommendations

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

11. Action Item – Vote to Prior Authorize Xalkori® (Crizotinib), Zykadia® (Ceritinib), Alecensa® (Alectinib), Alunbrig™ (Brigatinib), Tarceva® (Erlotinib), Gilotrif® (Afatinib), Tagrisso™ (Osimertinib), Cyramza® (Ramucirumab), and Tecentriq® (Atezolizumab) – See Appendix I

A. Introduction
B. Recommendations

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

12. Annual Review of Prostate Cancer Medications – See Appendix J

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Prostate Cancer Medications
D. Market News and Updates
E. Recommendations
F. Utilization Details of Prostate Cancer Medications

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

13. Annual Review of ADHD and Narcolepsy Medications and 30-Day Notice to Prior Authorize Vyvanse® (Lisdexamfetamine Chewable Tablets) and Update the ADHD Prior Authorization Criteria and Tier Chart – See Appendix K

A. Current Prior Authorization Criteria
B. Utilization of ADHD & Narcolepsy Medications
C. Prior Authorization of ADHD & Narcolepsy Medications
D. Market News and Updates
E. Medicaid Drug Rebate Program
F. College of Pharmacy Recommendations
G. Utilization Details of ADHD & Narcolepsy Medications

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

14. Annual Review of Atypical Antipsychotic Medications and 30-Day Notice to Update the Atypical Antipsychotic Prior Authorization Criteria and Tier Chart – See Appendix L

A. Current Prior Authorization Criteria
B. Utilization of Atypical Antipsychotic Medications
C. Prior Authorization of Atypical Antipsychotic Medications
D. Market News and Updates
E. Medicaid Drug Rebate Program
F. College of Pharmacy Recommendations
G. Utilization Details of Atypical Antipsychotic Medications

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

15. Annual Review of Huntington's Disease (HD) Medications and 30-Day Notice to Prior Authorize Austedo™ (Deutetrabenazine) and Xenazine® (Tetrabenazine) – See Appendix M

A. Introduction
B. Chorea in HD Treatment Summary
C. Xenazine® (Tetrabenazine) Off-Label Uses
D. Utilization of HD Medications
E. Market News and Updates
F. Austedo™ (Deutetrabenazine) Product Summary
G. Xenazine® (Tetrabenazine) Product Summary
H. College of Pharmacy Recommendations
I. Utilization Details of HD Medications

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

16. Annual Review of Inhaled Tobramycin Products, Pulmozyme® (Dornase Alfa), and Cayston® (Aztreonam) – See Appendix N

A. Current Prior Authorization Criteria
B. Utilization of Inhaled Tobramycin Products, Dornase Alfa, & Aztreonam Inhalation
C. Prior Authorization of Inhaled Tobramycin Products, Dornase Alfa, & Aztreonam Inhalation
D. Market News and Updates
E. Inhaled Tobramycin Treatment Comparison
F. College of Pharmacy Recommendations
G. Utilization Details of Inhaled Tobramycin Products, Dornase Alfa, & Aztreonam Inhalation

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

17. 30-Day Notice to Prior Authorize Ingrezza™ (Valbenazine) – See Appendix O

A. Tardive Dyskinesia
B. Market News and Updates
C. Ingrezza™ (Valbenazine) Product Summary
D. College of Pharmacy Recommendations

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

18. Annual Review of Various Special Formulations and 30-Day Notice to Prior Authorize Carac® (Fluorouracil 0.5% Cream), GoNitro™ (Nitroglycerin Sublingual Powder), Soltamox® (Tamoxifen Citrate Oral Solution), Taytulla™ (Norethindrone Acetate/Ethinyl Estradiol Capsules & Ferrous Fumarate Capsules), Tirosint®-SOL (Levothyroxine Sodium Oral Solution), Xatmep™ (Methotrexate Oral Solution), Zovirax® (Acyclovir Ointment and Suspension), Xerese® (Acyclovir/Hydrocortisone Cream), & Denavir® (Penciclovir Cream) – See Appendix P

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Special Formulations
D. Prior Authorization of Special Formulations
E. Product Summaries
F. College of Pharmacy Recommendations
G. Utilization Details of Special Formulations

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

19. 30-Day Notice to Prior Authorize Aczone® (Dapsone Gel) and Tazorac® (Tazarotene Cream and Gel) – See Appendix Q

A. Introduction
B. Utilization of Aczone® (Dapsone Gel)
C. Utilization of Tazorac® (Tazarotene Cream and Gel)
D. Market News and Updates
E. Aczone® (Dapsone Gel) Product Summary
F. Tazorac® (Tazarotene Cream and Gel) Product Summary
G. College of Pharmacy Recommendations

Non-Presentation; Questions Only:

20. Annual Review of H.P. Acthar® Gel (Corticotropin Injection) – See Appendix R

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of H.P. Acthar® Gel (Corticotropin Injection)
D. Prior Authorization of H.P. Acthar® Gel (Corticotropin Injection)
E. Market News and Updates
F. College of Pharmacy Recommendations

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

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

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

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

A. Opioid Analgesics
B. Antidepressant Medications
C. Fibric Acid Medications
D. Atopic Dermatitis Medications
E. Hypoparathyroidism and Hyperparathyroidism Medications
F. Ocaliva® (Obeticholic Acid)
G. Brineura™ (Cerliponase Alfa)
H. Radicava™ (Edaravone)

**Future business subject to change.*

23. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF MAY 10, 2017

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

COLLEGE OF PHARMACY STAFF:	PRESENT	ABSENT
Terry Cothran, D.Ph.; Pharmacy Director	x	
Melissa Abbott, Pharm.D.; Clinical Pharmacist	x	
Michyla Adams, Pharm.D.; Clinical Pharmacist	x	
Emily Borders, Pharm.D.; Assistant Professor	x	
Wendi Chandler, Pharm.D.; Clinical Pharmacist	x	
Karen Egesdal, D.Ph.; SMAC-ProDUR Coordinator/OHCA Liaison	x	
Erin Ford, Pharm.D.; Clinical Pharmacist		x
Bethany Holderread, Pharm.D.; Clinical Coordinator	x	
Shellie Keast, Ph.D.; Assistant Professor		x
Carol Moore, Pharm.D.; Clinical Pharmacist		x
Brandy Nawaz, Pharm.D.; Clinical Pharmacist	x	
Stephanie Nichols, Pharm.D.; Clinical Pharmacist	x	
Timothy Pham, Ph.D.; Postdoctoral Research Fellow	x	
Leslie Robinson, D.Ph.; PA Coordinator		x
Sarah Schmidt, Pharm.D.; Clinical Assistant Professor	x	
Ashley Teel, Pharm.D.; Clinical Pharmacist	x	
Jacquelyn Travers, Pharm.D.; Practice Facilitating Pharmacist		x
Graduate Students: Christina Bulkley, Pharm.D.		x
Corby Thompson, Pharm.D.	x	
Visiting Pharmacy Student(s): Tara Schultz	x	

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

OTHERS PRESENT:		
Nima Nabavi, Novo Nordisk	Melvin Nwamadi, Abbott	Mark DeClerk, Lilly
Jeff Knappen, Spark	Brian Maves, Pfizer	Toby Thompson, Pfizer
Scott Black, Daiichi Sankyo	Jim Chapman, AbbVie	Terry Lee, Gilead
Mary Stewart Crane, J&J	Gwendolyn Cadwell, PhRMA	Kent Douglas, Neurocrine
Nicole Wilkerson, Novartis	Clayton Wright, Takeda	Marla Wiedenmann, Novo Nordisk
Kari Suttee, Novartis	Mai Duong, Novartis	Jason Lurk, Novo Nordisk

PRESENT FOR PUBLIC COMMENT:	
Jason Lurk	Novo Nordisk

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

1A: ROLL CALL

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

ACTION: NONE REQUIRED

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

2A: AGENDA ITEM NO. 8 SPEAKER: JASON LURK

ACTION: NONE REQUIRED

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

3A: APRIL 12, 2017 DUR MINUTES – VOTE

3B: APRIL 12, 2017 DUR RECOMMENDATIONS MEMORANDUM

Materials included in agenda packet; presented by Dr. Cothran

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: **UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/SPRING PIPELINE UPDATE**

4A: MEDICATION COVERAGE ACTIVITY FOR APRIL 2017

4B: PHARMACY HELP DESK ACTIVITY FOR APRIL 2017

4C: 2017 SPRING PIPELINE UPDATE

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: **VOTE TO PRIOR AUTHORIZE FOSAMAX® (ALENDRONATE 40MG TABLETS)**

5A: INTRODUCTION

5B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Chandler

Dr. Preslar recommends on taking 35mg + 5mg to equal 40mg prior to a 40mg alendronate tablet

Dr. Munoz moved to approve with Dr. Preslar's changes; seconded by Dr. Hardzog-Britt

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE BYVALSON™ (NEBIVOLOL/VALSARTAN) AND QBRELIS™ (LISINOPRIL ORAL SOLUTION)**

6A: INTRODUCTION

6B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Abbott

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: **VOTE TO PRIOR AUTHORIZE GIAZO® (BALSALAZIDE DISODIUM TABLETS)**

7A: INTRODUCTION

7B: COLLEGE OF PHARMACY RECOMMENDATIONS

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

AGENDA ITEM NO. 8: VOTE TO PRIOR AUTHORIZE INVOKAMET® XR (CANAGLIFLOZIN/METFORMIN EXTENDED-RELEASE), JENTADUETO® XR (LINAGLIPTIN/METFORMIN EXTENDED-RELEASE), ADLYXIN® (LIXISENATIDE), XULTOPHY® 100/3.6 (INSULIN DEGLUDEC/ LIRAGLUTIDE), SOLIQUA™ 100/33 (INSULIN GLARGINE/LIXISENATIDE), SYNJARDY® XR (EMPAGLIFLOZIN/METFORMIN EXTENDED-RELEASE), AND QTERN® (DAPAGLIFLOZIN/ SAXAGLIPTIN)
8A: INTRODUCTION
8B: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Nawaz
Dr. Harrell moved to approve; seconded by Ms. Varalli-Claypool
ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: ANNUAL REVIEW OF LUNG CANCER MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE TARCEVA® (ERLOTINIB), GILOTRIF® (AFATINIB), TAGRISSO™ (OSIMERTINIB), XALKORI® (CRIZOTINIB), ZYKADIA® (CERITINIB), ALECENSA® (ALECTINIB), CYRAMZA® (RAMUCIRUMAB), TECENTRIQ® (ATEZOLIZUMAB), AND ALUNBRIG™ (BRIGATINIB)
9A: INTRODUCTION
9B: CURRENT PRIOR AUTHORIZATION CRITERIA
9C: UTILIZATION OF LUNG CANCER MEDICATIONS
9D: MARKET NEWS AND UPDATES
9E: LUNG CANCER MEDICATION PRODUCT SUMMARIES
9F: RECOMMENDATIONS
9G: UTILIZATION DETAILS OF LUNG CANCER MEDICATIONS
Materials included in agenda packet; presented by Dr. Schmidt, Dr. Borders
ACTION: NONE REQUIRED

AGENDA ITEM NO. 10: 30-DAY NOTICE TO PRIOR AUTHORIZE KUVAN® (SAPROPTERIN)
10A: PHENYLKETONURIA
10B: UTILIZATION OF KUVAN® (SAPROPTERIN)
10C: MARKET NEWS AND UPDATES
10D: KUVAN® (SAPROPTERIN) PRODUCT SUMMARY
10E: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Nawaz
ACTION: NONE REQUIRED

AGENDA ITEM NO. 11: 30-DAY NOTICE TO PRIOR AUTHORIZE LUMIZYME® (ALGLUCOSIDASE ALFA INJECTION)
11A: POMPE DISEASE (ACID ALPHA-GLUCOSIDASE DEFICIENCY)
11B: UTILIZATION OF LUMIZYME® (ALGLUCOSIDASE ALFA)
11C: MARKET NEWS AND UPDATES
11D: LUMIZYME® (ALGLUCOSIDASE ALFA) PRODUCT SUMMARY
11E: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Nawaz
ACTION: NONE REQUIRED

AGENDA ITEM NO. 12: 30-DAY NOTICE TO PRIOR AUTHORIZE ALPHA$_1$-PROTEINASE INHIBITORS: ARALAST NP™, GLASSIA®, PROLASTIN®-C, AND ZEMAIRA®
12A: ALPHA$_1$ ANTITRYPSIN DEFICIENCY
12B: UTILIZATION OF ALPHA$_1$-PROTEINASE INHIBITORS
12C: MARKET NEWS AND UPDATES
12D: ALPHA$_1$-PROTEINASE INHIBITORS CLASS SUMMARY

12E: COLLEGE OF PHARMACY RECOMMENDATIONS
12F: UTILIZATION DETAILS OF ALPHA$_1$-PROTEINASE INHIBITORS
Materials included in agenda packet; presented by Dr. Chandler
ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: ANNUAL REVIEW OF ANTIPARASITIC MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE IMPAVIDO® (MILTEFOSINE)
13A: CURRENT PRIOR AUTHORIZATION CRITERIA
13B: UTILIZATION OF ANTIPARASITIC MEDICATIONS
13C: PRIOR AUTHORIZATION OF ANTIPARASITIC MEDICATIONS
13D: LEISHMANIASIS BACKGROUND INFORMATION
13E: IMPAVIDO® (MILTEFOSINE) PRODUCT SUMMARY
13F: COLLEGE OF PHARMACY RECOMMENDATIONS
13G: UTILIZATION DETAILS OF ANTIPARASITIC MEDICATIONS
Materials included in agenda packet; presented by Dr. Abbott
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: ANNUAL REVIEW OF BOWEL PREPARATION MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE COLPREP™ KIT (SODIUM SULFATE/POTASSIUM SULFATE/ MAGNESIUM SULFATE)
14A: CURRENT PRIOR AUTHORIZATION CRITERIA
14B: UTILIZATION OF BOWEL PREPARATION MEDICATIONS
14C: MARKET NEWS AND UPDATES
14D: PRIOR AUTHORIZATION OF BOWEL PREPARATION MEDICATIONS
14E: COLPREP™ KIT (SODIUM SULFATE/POTASSIUM SULFATE/MAGNESIUM SULFATE) PRODUCT SUMMARY
14F: COLLEGE OF PHARMACY RECOMMENDATIONS
14G: UTILIZATION DETAILS OF BOWEL PREPARATION MEDICATIONS
Materials included in agenda packet; presented by Dr. Nichols
ACTION: NONE REQUIRED

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

AGENDA ITEM NO. 16: ANNUAL REVIEW OF BOTULINUM TOXINS
16A: CURRENT PRIOR AUTHORIZATION CRITERIA
16B: UTILIZATION OF BOTULINUM TOXIN PRODUCTS
16C: PRIOR AUTHORIZATION OF BOTULINUM TOXIN PRODUCTS
16D: MARKET NEWS AND UPDATES
16E: COLLEGE OF PHARMACY RECOMMENDATIONS
16F: UTILIZATION DETAILS OF BOTULINUM TOXIN PRODUCTS
Materials included in agenda packet; Non-presentation; Questions only
ACTION: NONE REQUIRED

AGENDA ITEM NO. 17: ANNUAL REVIEW OF GAUCHER DISEASE MEDICATIONS
17A: INTRODUCTION
17B: CURRENT PRIOR AUTHORIZATION CRITERIA
17C: UTILIZATION OF GAUCHER DISEASE MEDICATIONS
17D: PRIOR AUTHORIZATION OF GAUCHER DISEASE MEDICATIONS

17E: MARKET NEWS AND UPDATES
17F: COLLEGE OF PHARMACY RECOMMENDATIONS
17G: UTILIZATION DETAILS OF GAUCHER DISEASE MEDICATIONS
Materials included in agenda packet; Non-presentation; Questions only
ACTION: NONE REQUIRED

AGENDA ITEM NO. 18: ANNUAL REVIEW OF GONADOTROPIN-RELEASING HORMONE (GNRH) MEDICATIONS
18A: INTRODUCTION
18B: FDA APPROVED GNRH OPTIONS FOR TREATMENT OF CENTRAL PRECOCIOUS PUBERTY OR ENDOMETRIOSIS
18C: CURRENT PRIOR AUTHORIZATION CRITERIA
18D: UTILIZATION OF GNRH MEDICATIONS
18E: PRIOR AUTHORIZATION OF GNRH MEDICATIONS
18F: MARKET NEWS AND UPDATES
18G: COLLEGE OF PHARMACY RECOMMENDATIONS
18H: UTILIZATION DETAILS OF GNRH MEDICATIONS
Materials included in agenda packet; Non-presentation; Questions only
ACTION: NONE REQUIRED

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

AGENDA ITEM NO. 20: FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)
20A: VARIOUS SPECIAL FORMULATIONS
20B: ADHD AND NARCOLEPSY MEDICATIONS
20C: ATYPICAL ANTIPSYCHOTIC MEDICATIONS
20D: PROSTATE CANCER MEDICATIONS
20E: H.P. ACTHAR® GEL (CORTICOTROPIN INJECTION)
20F: INGREZZA™ (VALBENAZINE)
20G: INHALED CYSTIC FIBROSIS MEDICATIONS
20H: AUSTEDO™ (DEUTETRABENAZINE)
20I: TAZORAC® (TAZAROTENE)
Future business subject to change.
Materials included in agenda packet; presented by Dr. Holderread
ACTION: NONE REQUIRED

AGENDA ITEM NO. 21: ADJOURNMENT
The meeting was adjourned at 5:10 pm.

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

Memorandum

Date: May 11, 2017

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

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

Subject: DUR Board Recommendations from Meeting of May 10, 2017

Recommendation 1: Spring Pipeline Update

NO ACTION REQUIRED.

Recommendation 2: Vote to Prior Authorize Fosamax® (Alendronate 40mg Tablets)

MOTION CARRIED by unanimous approval.

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

1. The placement of Fosamax® (alendronate) 40mg tablets into the Special Prior Authorization (PA) Tier of the Osteoporosis Medications PBPA category due to the wholesale acquisition cost (WAC) in comparison to other alendronate strengths. The following criteria shown in red would apply:
    a. **Fosamax® (Alendronate 40mg Tablets) Approval Criteria:**
        i. A patient-specific, clinically significant reason why the member cannot use all other available Tier-1 and Tier-2 products including a 35mg alendronate

tablet in combination with a 5mg alendronate tablet to achieve a 40mg dose.

2. Placement of Reclast® (zoledronic acid) into Tier-2 of the Osteoporosis Medications PBPA category due to WAC. Current Tier-2 criteria will apply.

Osteoporosis Medications Tier-2 Approval Criteria:

1. A trial of at least one Tier-1 medication, compliantly used for at least six months concomitantly with calcium + vitamin D, that failed to prevent fracture, or improve bone mineral density (BMD) scores; or
2. Hypersensitivity to or intolerable adverse effects with all Tier-1 medications.
3. Quantity limits apply based on FDA approved maximum doses.

Atelvia® (Risedronate Delayed-Release Tablets), Binosto® (Alendronate Effervescent Tablets), and Actonel® (Risedronate 30mg Tablets) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use all other available Tier-1 and Tier-2 products.
2. Members with a diagnosis in history of Paget's disease will not require prior authorization.

Osteoporosis Medications		
Tier-1	**Tier-2**	**Special PA**
alendronate (Fosamax®)	alendronate + D (Fosamax® +D)	alendronate effervescent tablets (Binosto®)
calcium + vitamin D*	ibandronate (Boniva®)	alendronate solution (Fosamax®)
	risedronate (Actonel®)	**alendronate 40mg tablet (Fosamax®)**
	zoledronic acid (Reclast®)	denosumab (Prolia®)
		ibandronate (Boniva® IV)
		risedronate 30mg tablet (Actonel®)
		risedronate delayed-release tablets (Atelvia®)
		teriparatide (Forteo®)

*Must be used in combination with a bisphosphonate to count as a Tier-1 trial.
Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Recommendation 3: Vote to Prior Authorize Byvalson™ (Nebivolol/Valsartan) and Qbrelis™ (Lisinopril Oral Solution)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Byvalson™ (nebivolol/valsartan) and Qbrelis™ (lisinopril oral solution) with the following criteria:

Byvalson™ (Nebivolol/Valsartan) Approval Criteria:

1. A patient-specific, clinically significant reason the member cannot use the individual components, nebivolol (Bystolic®) and valsartan (Diovan®); and
2. A quantity limit of 30 tablets per 30 days will apply.

Qbrelis™ (Lisinopril Oral Solution) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use lisinopril oral tablets in place of the oral solution formulation even when the tablets are crushed.

Recommendation 4: Vote to Prior Authorize Giazo® (Balsalazide Disodium Tablets)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Giazo® (balsalazide) with the following criteria:

Giazo® (Balsalazide) Approval Criteria:

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

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

Recommendation 5: Vote to Prior Authorize Invokamet® XR (Canagliflozin/ Metformin Extended-Release), Jentadueto® XR (Linagliptin/ Metformin Extended-Release), Adlyxin® (Lixisenatide), Xultophy® 100/3.6 (Insulin Degludec/Liraglutide), Soliqua™ 100/33 (Insulin Glargine/Lixisenatide), Synjardy® XR (Empagliflozin/Metformin Extended-Release), and Qtern® (Dapagliflozin/Saxagliptin)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following:

1. The placement of Invokamet® XR (canagliflozin/metformin extended-release), Jentadueto® XR (linagliptin/metformin extended-release), and Synjardy® XR (empagliflozin/metformin extended-release) into the Special Prior Authorization (PA) Tier of the Diabetes Medications Product Based Prior Authorization (PBPA) category.
2. The placement of Adlyxin® (lixisenatide), Xultophy® 100/3.6 (insulin degludec/ liraglutide), Soliqua™ 100/33 (insulin glargine/lixisenatide), and Qtern® (dapagliflozin/saxagliptin) into Tier-3 of the Diabetes Medications PBPA category.

3. A clinical exception will apply for medications with the FDA approved diagnosis to reduce the risk of cardiovascular (CV) death in adult patients with type 2 diabetes mellitus (DM) and established CV disease. Tier structure rules for this indication will apply.

Diabetes Medications*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
Alpha-Glucosidase Inhibitors acarbose (Precose®)	**DPP-4 Inhibitors** linagliptin (Tradjenta®) linagliptin/metformin (Jentadueto®) saxagliptin (Onglyza®) saxagliptin/metformin (Kombiglyze®) sitagliptin (Januvia®) sitagliptin/metformin (Janumet®) sitagliptin/metformin ER (Janumet XR®)	**Alpha-Glucosidase Inhibitors** miglitol (Glyset®)	**Amylinomimetics** pramlintide (Symlin®)
Biguanides metformin (Glucophage®) metformin SR (Glucophage XR®) metformin/glipizide (Metaglip®) metformin/glyburide (Glucovance®)	**Glinides** nateglinide (Starlix®) repaglinide/metformin (Prandimet®)	**Dopamine Agonists** bromocriptine (Cycloset®)	**Biguanides** metformin ER (Fortamet®, Glumetza®) metformin solution (Riomet®)
Glinides repaglinide (Prandin®)	**GLP-1 Agonists** exenatide (Byetta®) liraglutide (Victoza®)	**DPP-4 Inhibitors** alogliptin (Nesina®) alogliptin/metformin (Kazano®) alogliptin/pioglitazone (Oseni®)	**DPP-4 Inhibitors** **linagliptin/metformin ER (Jentadueto® XR)**
Sulfonylureas chlorpropamide glimepiride (Amaryl®) glipizide (Glucotrol®) glipizide SR (Glucotrol XL®) glyburide (Diabeta®) glyburide micronized (Micronase®) tolbutamide	**SGLT-2 Inhibitors** canagliflozin (Invokana®) canagliflozin/metformin (Invokamet®)	**GLP-1 Agonists** albiglutide (Tanzeum®) dulaglutide (Trulicity®) exenatide (Bydureon®) **lixisenatide (Adlyxin®)**	**SGLT-2 Inhibitors** **canagliflozin/metformin ER (Invokamet® XR)** **empagliflozin/metformin ER (Synjardy® XR)**
Thiazolidinediones pioglitazone (Actos®)		**GLP-1 Agonists/Insulin** **insulin degludec/ liraglutide (Xultophy® 100/3.6)** **insulin glargine/ lixisenatide (Soliqua™ 100/33)**	
		SGLT-2 Inhibitors dapagliflozin (Farxiga®) dapagliflozin/metformin ER (Xigduo® XR) empagliflozin (Jardiance®) empagliflozin/metformin (Synjardy®)	
		SGLT-2/DPP-4 Inhibitors **dapagliflozin/saxagliptin (Qtern®)** empagliflozin/linagliptin (Glyxambi®)	

Diabetes Medications*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
		Thiazolidinediones pioglitazone/glimepiride (Duetact®) pioglitazone/metformin (Actoplus Met®, Actoplus Met XR®) rosiglitazone (Avandia®) rosiglitazone/glimepiride (Avandaryl®) rosiglitazone/metformin (Avandamet®)	

*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
SR = sustained-release, ER = extended-release, DPP-4 = dipeptidyl peptidase-4, GLP-1 = glucagon-like peptide-1, SGLT-2 = sodium-glucose cotransporter-2

Recommendation 6: Annual Review of Lung Cancer Medications and 30-Day Notice to Prior Authorize Tarceva® (Erlotinib), Gilotrif® (Afatinib), Tagrisso™ (Osimertinib), Xalkori® (Crizotinib), Zykadia® (Ceritinib), Alecensa® (Alectinib), Cyramza® (Ramucirumab), Tecentriq® (Atezolizumab), and Alunbrig™ (Brigatinib)

NO ACTION REQUIRED.

Recommendation 7: 30-Day Notice to Prior Authorize Kuvan® (Sapropterin)

NO ACTION REQUIRED.

Recommendation 8: 30-Day Notice to Prior Authorize Lumizyme® (Alglucosidase Alfa Injection)

NO ACTION REQUIRED.

Recommendation 9: 30-Day Notice to Prior Authorize Alpha$_1$-Proteinase Inhibitors: Aralast NP™, Glassia®, Prolastin®-C, and Zemaira®

NO ACTION REQUIRED.

Recommendation 10: Annual Review of Antiparasitic Medications and 30-Day Notice to Prior Authorize Impavido® (Miltefosine)

NO ACTION REQUIRED.

Recommendation 11: Annual Review of Bowel Preparation Medications and 30-Day Notice to Prior Authorize ColPrep™ Kit (Sodium Sulfate/Potassium Sulfate/ Magnesium Sulfate)

NO ACTION REQUIRED.

Recommendation 12: 30-Day Notice to Prior Authorize Elaprase® (Idursulfase)

NO ACTION REQUIRED.

Recommendation 13: Annual Review of Botulinum Toxins

NO ACTION REQUIRED.

Recommendation 14: Annual Review of Gaucher Disease Medications

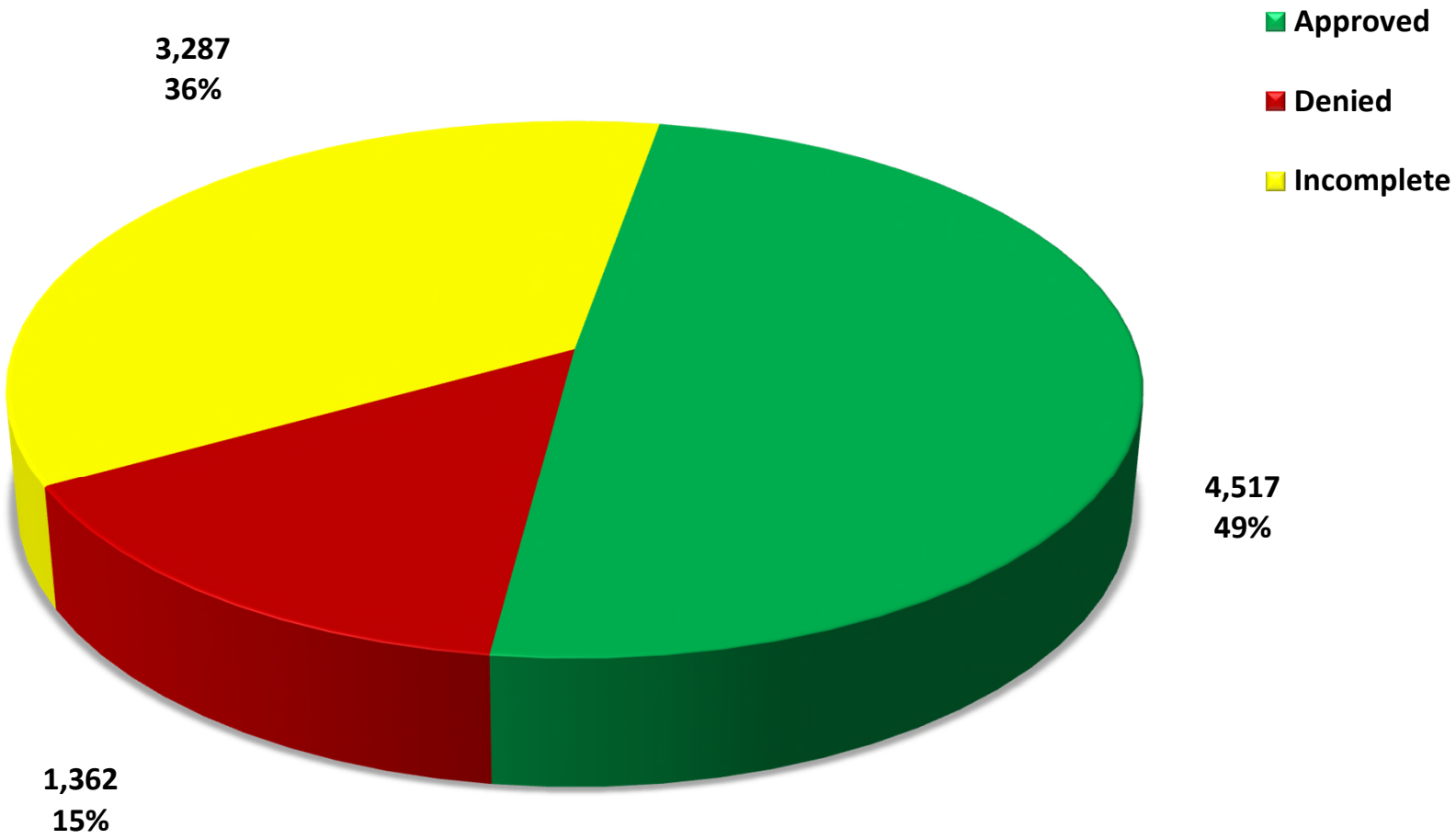
NO ACTION REQUIRED.

Recommendation 15: Annual Review of Gonadotropin-Releasing Hormone (GnRH) Medications

NO ACTION REQUIRED.

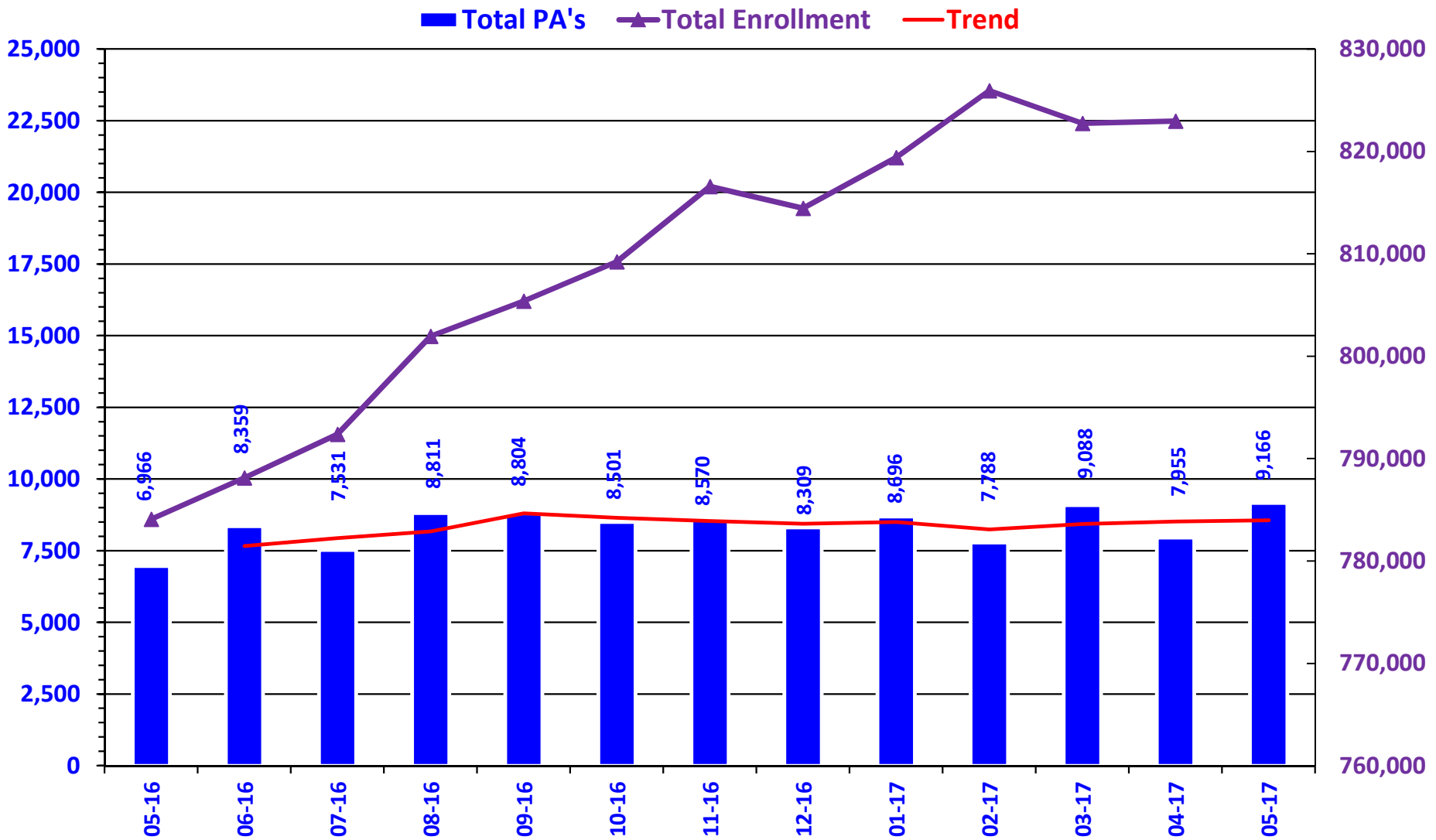
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: MAY 2017



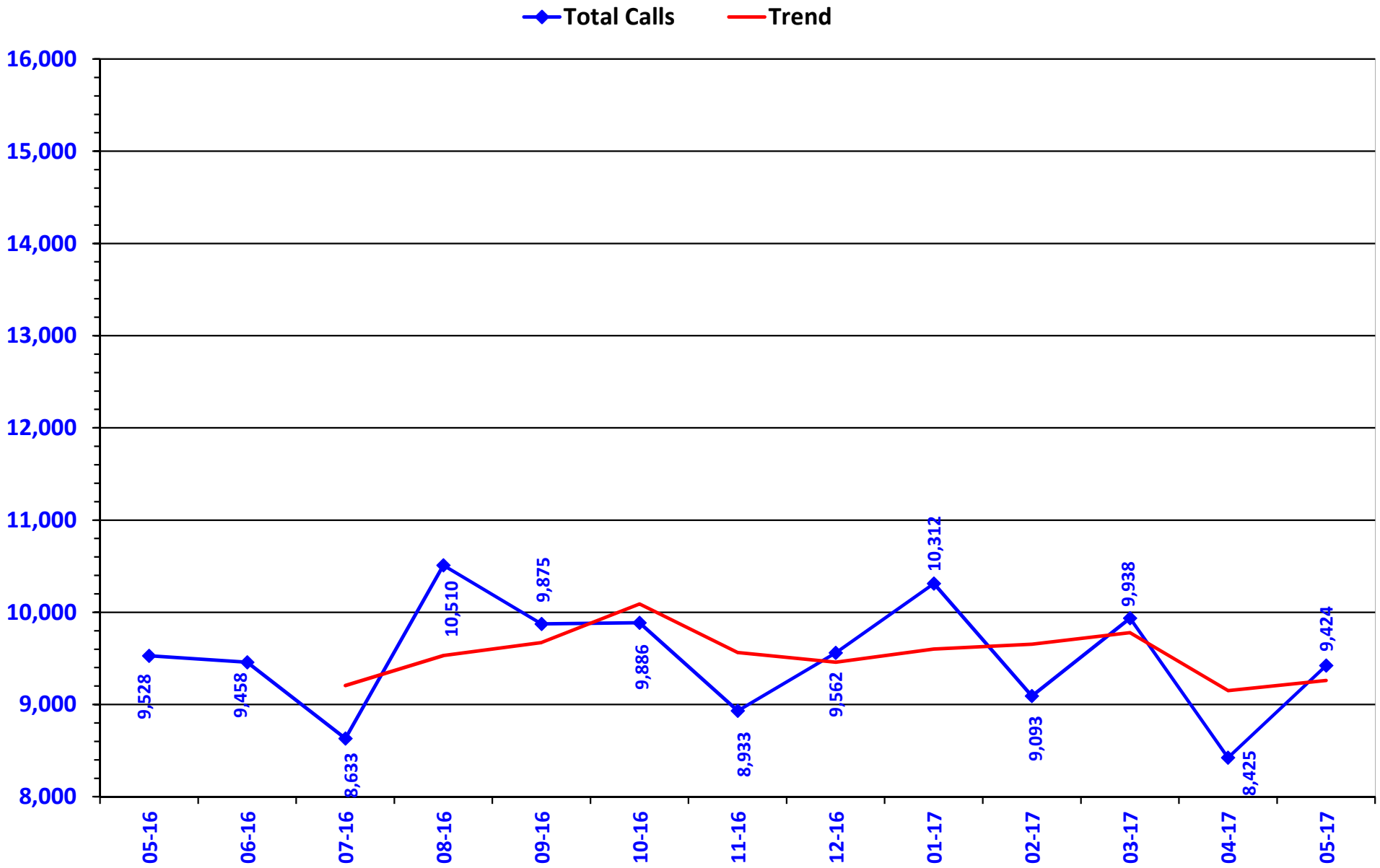
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: MAY 2016 – MAY 2017



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
MAY 2016 – MAY 2017



Prior Authorization Activity
5/1/2017 Through 5/31/2017

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	169	13	46	110	357
Analgesic - NonNarcotic	26	0	5	21	0
Analgesic - Narcotic	479	248	47	184	158
Angiotensin Receptor Antagonist	14	3	3	8	356
Antiasthma	49	17	4	28	326
Antibiotic	28	12	4	12	255
Anticonvulsant	110	39	20	51	316
Antidepressant	116	25	25	66	343
Antidiabetic	245	92	42	111	347
Antifungal	12	1	3	8	2
Antigout	12	5	0	7	357
Antihistamine	497	420	20	57	353
Antimigraine	43	8	13	22	231
Antineoplastic	36	20	2	14	156
Antiparasitic	12	1	0	11	14
Antiulcers	169	33	47	89	211
Antiviral	108	44	28	36	11
Anxiolytic	65	42	4	19	241
Atypical Antipsychotics	256	134	21	101	319
Benign Prostatic Hypertrophy	12	1	7	4	360
Biologics	97	62	11	24	335
Bladder Control	50	15	10	25	323
Blood Thinners	238	128	34	76	319
Botox	38	22	12	4	341
Buprenorphine Medications	293	215	16	62	77
Cardiovascular	131	57	21	53	297
Cephalosporins	13	5	0	8	6
Chronic Obstructive Pulmonary Disease	212	28	58	126	317
Constipation/Diarrhea Medications	149	15	63	71	175
Contraceptive	27	22	1	4	339
Dermatological	109	16	53	40	168
Diabetic Supplies	546	314	14	218	190
Endocrine & Metabolic Drugs	81	59	5	17	134
Erythropoietin Stimulating Agents	31	11	4	16	89
Fibromyalgia	225	45	106	74	326
Fish Oils	17	1	6	10	360
Gastrointestinal Agents	144	34	34	76	205
Genitourinary Agents	15	2	8	5	198
Glaucoma	15	10	1	4	187
Growth Hormones	100	73	13	14	145
Hematopoietic Agents	12	5	1	6	167
Hepatitis C	112	53	34	25	9
HFA Rescue Inhalers	90	17	25	48	342
Insomnia	45	5	15	25	194
Insulin	85	25	9	51	343
Miscellaneous Antibiotics	25	5	4	16	7
Multiple Sclerosis	63	26	16	21	223
Muscle Relaxant	60	14	17	29	52
Nasal Allergy	82	13	25	44	232
Neurological Agents	42	27	1	14	358
NSAIDs	193	33	56	104	268

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Ocular Allergy	70	12	25	33	105
Osteoporosis	21	5	7	9	356
Other*	262	53	57	152	285
Otic Antibiotic	21	2	2	17	10
Pediculicide	10	0	4	6	0
Respiratory Agents	39	24	1	14	189
Statins	62	15	15	32	357
Stimulant	1,131	721	87	323	336
Testosterone	34	9	9	16	351
Topical Antifungal	29	5	1	23	22
Topical Corticosteroids	153	4	45	104	273
Vitamin	66	24	25	17	315
Pharmacotherapy	95	79	1	15	263
Emergency PAs	1	1	0	0	
Total	**7,792**	**3,469**	**1,293**	**3,030**	
Overrides					
Brand	41	27	0	14	299
Diabetic Supplies	2	1	1	0	360
Dosage Change	379	355	4	20	11
High Dose	3	3	0	0	86
Ingredient Duplication	31	22	0	9	9
Lost/Broken Rx	71	63	2	6	11
NDC vs Age	221	145	20	56	263
Nursing Home Issue	23	17	0	6	14
Opioid Quantity	16	13	1	2	156
Other*	26	23	0	3	10
Quantity vs. Days Supply	522	353	38	131	254
STBS/STBSM	18	8	2	8	74
Stolen	14	12	1	1	11
Temporary Unlock	2	2	0	0	21
Third Brand Request	23	18	2	3	15
Overrides Total	**1,374**	**1,048**	**69**	**257**	
Total Regular PAs + Overrides	**9,166**	**4,517**	**1,362**	**3,287**	

Denial Reasons	
Unable to verify required trials.	2,503
Does not meet established criteria.	1,376
Lack required information to process request.	752

Other PA Activity	
Duplicate Requests	690
Letters	9,125
No Process	8
Changes to existing PAs	642
Helpdesk Initiated Prior Authorizations	695
PAs Missing Information	44

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

Chloroquine (Aralen®) & Hydroxychloroquine (Plaquenil®) Induced Retinopathy Mailing Update

Oklahoma Health Care Authority
June 2017

Introduction[1,2]

Retinal toxicity is a serious adverse effect of chloroquine (CQ) and hydroxychloroquine (HCQ) with long-term use. These medications are used in the treatment of several conditions including systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and related auto-immune diseases. A recent study showed that patients that used HCQ for more than 5 years had an overall prevalence of toxicity of 7.5%. This study showed that patients taking ≤ 5mg/kg of HCQ per day had less than 1% risk in the first 5 years of treatment, up to 2% risk at 10 years, then 20% after 20 years of treatment. Retinal toxicity is of serious concern because the associated damage to the retina and macula is irreversible and can cause serious vision problems, including blindness. There is no treatment for this toxicity other than cessation of therapy. Ophthalmic risk associated with these medications may be minimized with proper dosing and annual eye exams.

There are several major risk factors for toxic retinopathy with these medications, including:

- Treatment duration > 5 years
- Daily dose of HCQ > 5mg/kg real body weight or CQ > 2.3mg/kg real body weight
- Kidney impairment
- Concomitant tamoxifen use
- Underlying retinal disease

The American Academy of Ophthalmology recommends a baseline eye exam within the first year of CQ or HCQ use, then annual screenings after 5 years of use or sooner in the presence of major risk factors. The long-term use of CQ and HCQ can be safe and effective with appropriate screening.

Prescriber Mailing Summary

In June 2016, the College of Pharmacy and the Oklahoma Health Care Authority sent an educational letter to 182 prescribers of 577 unique members who had paid claims for HCQ during the analysis time frame of February 2, 2016 to May 2, 2016. There were no patients with paid claims for CQ during the time frame of the analysis.

Prescribers were notified of the ophthalmic risks associated with these medications and were encouraged to educate patients on the risks associated with these medications. Prescribers were also provided the recommendations for screening and to make referrals to eye care specialists in patients that report visual disturbances.

Retinopathy Mailing Results

The mailing was sent to 182 prescribers of 577 members with paid claims for HCQ during the analysis time frame. Of those 577 members, 150 members had a paid claim for an eye exam in the six months prior to the mailing.

The post-analysis of the mailing reviewed claims from July 1, 2016 to January 31, 2017. Results found 110 members who did not have an eye exam claim during the pre-mailing time frame had a paid claim for an eye exam in the six months post-period following the mailing.

Conclusions

Analysis of the CQ/HCQ induced retinopathy mailing revealed the total number of members with paid claims for HCQ who received an annual eye exam nearly doubled following the mailing; however, it cannot be explicitly stated that these new eye exams were given based solely as a result of the educational mailing as there is no way to determine if these eye exams were previously scheduled.

[1] Marmor MF, Kellner U, Lai TYY, Melles RB, American Academy of Ophthalmology. Recommendations on Screening for Chloroquine and Hydroxychloroquine Retinopathy (2016 Revision). *Ophthalmology*. 2016; 123: 1386-94.
[2] Hydroxychloroquine (Plaquenil®) Prescribing Information. Concordia Pharmaceuticals, Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/.../009768s037s045s047lbl.pdf. Last revised 01/2017. Last accessed 05/26/2017.

Appendix C

Vote to Prior Authorize Kuvan® (Sapropterin)

Oklahoma Health Care Authority
June 2017

Introduction[1]

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

Cost:

Medication	Cost Per Month[¥]	Cost Per Year[¥]
Kuvan® (sapropterin) all strengths/formulations	**$15,825.00**	**$189,900.00**

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.
[¥]Costs based on 20mg/kg/day for a 75kg patient.

Recommendations

The College of Pharmacy recommends the prior authorization of Kuvan® (sapropterin) with the following criteria:

Kuvan® (Sapropterin) Approval Criteria:

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

[1] Kuvan® Prescribing Information. BioMarin Pharmaceutical Inc. Available online at: http://www.kuvan.com/hcp/wp-content/file/KUVAN_Prescribing_Information1.pdf. Last revised 08/2016. Last accessed 05/2017.

Appendix D

Vote to Prior Authorize Lumizyme®
(Alglucosidase Alfa Injection)

Oklahoma Health Care Authority
June 2017

Introduction[1]

Lumizyme® (alglucosidase alfa) 50mg single-use vial for intravenous injection is a hydrolytic lysosomal glycogen-specific enzyme indicated for patients with Pompe disease (acid alpha-glucosidase [GAA] deficiency).

Cost:

Medication	Cost Per Unit*	Cost Per Treatment¥	Cost Per Year¥
Lumizyme® (alglucosidase alfa) 50mg vial	**$754.00**	**$21,112.00**	**$548,912.00**

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.
¥Costs based on 70kg patient.

Recommendations

The College of Pharmacy recommends the prior authorization of Lumizyme® (alglucosidase alfa) with the following criteria:

Lumizyme® (Alglucosidase Alfa) Infantile-Onset Approval Criteria:

1. An FDA approved diagnosis of infantile-onset Pompe disease (acid alpha-glucosidase [GAA] deficiency); and
2. Documentation of diagnosis confirmation of GAA enzyme deficiency through specific genetic laboratory test(s); and
3. Lumizyme® must be prescribed by a geneticist or a physician that specializes in the treatment of Pompe disease and/or inherited genetic disorders; and
4. Member's weight must be provided and have been taken within the last four weeks to ensure accurate dosing.

Lumizyme® (Alglucosidase Alfa) Late-Onset (Non-Infantile) Approval Criteria:

1. An FDA approved diagnosis of late-onset (non-infantile) Pompe disease (acid alpha-glucosidase [GAA] deficiency); and
2. Documentation of diagnosis confirmation of GAA enzyme deficiency through specific genetic laboratory test(s); and
3. Provider must document presence of symptoms of Pompe disease; and
4. Lumizyme® must be prescribed by a geneticist or a physician that specializes in the treatment of Pompe disease and/or inherited genetic disorders; and
5. Member's weight must be provided and have been taken within the last four weeks to ensure accurate dosing.

6. Initial approval will be for the duration of six months, at that time compliance and information regarding efficacy, such as improvement or stabilization in Forced Vital Capacity (FVC) and/or 6-minute walk test (6MWT), will be required for continued approval. Additional authorizations will be for the duration of one year.

[1] Lumizyme® Prescribing Information. Genzyme, Co. Available online at: https://www.lumizyme.com/healthcare.aspx. Last revised 08/2014. Last accessed 05/2017.

Appendix E

Vote to Prior Authorize Alpha$_1$-Proteinase Inhibitors: Aralast NP™, Glassia®, Prolastin®-C, and Zemaira®

Oklahoma Health Care Authority
June 2017

Introduction[1,2]

Alpha$_1$ antitrypsin deficiency (AATD) also referred to as alpha$_1$-proteinase inhibitor deficiency, is an inherited disorder affecting the lungs, liver, and rarely, skin. AATD is inherited by autosomal co-dominant transmission, meaning that affected individuals have inherited an abnormal alpha$_1$ antitrypsin (AAT) gene from each parent. The most common form of AATD is associated with allele Z, or homozygous PiZ (ZZ). Serum levels of AAT in these patients are about 3.4 to 7µmol/L, 10% to 15% of normal serum levels. Serum levels greater than 11µmol/L appear to be protective. AAT is a protease inhibitor of the proteolytic enzyme elastase. In the lungs, AATD causes chronic obstructive pulmonary disease (COPD). This is thought to result from an imbalance between neutrophil elastase in the lung, which destroys elastin, and the elastase inhibitor AAT, which protects against proteolytic degradation of elastin.

AATD is generally considered to be rare; however, estimates that 80,000 to 100,000 individuals in the United States have severe deficiency of AAT suggest that the disease is under-recognized. The prevalence of AATD varies considerably from one country to another; however, it is estimated that more than three million people worldwide have allele combinations associated with severe deficiency of AAT.

Slowly progressive dyspnea is the primary symptom, though many patients initially have symptoms of cough, sputum production, or wheezing. Treatment involves smoking cessation, preventive vaccinations, bronchodilators, supplemental oxygen when indicated, physical rehabilitation, and intravenous (IV) augmentation therapy with AAT. The goal of AAT augmentation is to slow the progression of emphysema. There are currently four pooled human plasma AAT products available: **Aralast NP™, Glassia®, Prolastin®-C, and Zemaira®**. These products work by restoring serum and alveolar AAT concentrations to protective levels, restoring the balance between neutrophil elastase in the lung, which destroys elastin, and the elastase inhibitor AAT, which protects against proteolytic degradation of elastin.

Cost:

Medication	Cost Per mg	Cost Per Month$^{\Delta}$	Cost Per Year$^{\Delta}$
Aralast NP™	$0.52	$9,360.00	$112,320.00
Glassia®	$0.52	$9,360.00	$112,320.00
Prolastin®-C	$0.49	$8,820.00	$105,840.00
Zemaira®	$0.52	$9,360.00	$112,320.00

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.
$^{\Delta}$Cost for treatment based on dosing of 60mg/kg for 75kg patient.

Recommendations

The College of Pharmacy recommends the prior authorization of Prolastin®-C, Aralast NP™, Glassia®, and Zemaira® (alpha$_1$-proteinase inhibitor [human]) products with the following criteria based, in part, on cost after rebates:

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

1. An FDA approved indication for augmentation and maintenance therapy of patients 18 years of age or older with severe hereditary deficiency of alpha$_1$-antitrypsin (AAT) with clinical evidence of emphysema; and
2. Diagnosis confirmed by all of the following:
    a. Genetic confirmation of PiZZ, PiZ(null), or Pi(null, null) phenotype alpha$_1$-antitrypsin deficiency (AATD) or other alleles determined to increase risk of AATD; and
    b. Serum levels of AAT less than 11µmol/L; and
    c. Documented emphysema with airflow obstruction; and
3. Prescriber must document that member's forced expiratory volume in one second (FEV_1) is less than or equal to 65% predicted; and
4. Must be prescribed by a pulmonary disease specialist or advanced care practitioner specializing in pulmonary disease; and
5. The prescriber must verify the member is a non-smoker; and
6. The prescriber must verify the member does not have antibodies to IgA; and
7. 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.

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

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

8. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling.

Zemaira® (Alpha$_1$-Proteinase Inhibitor [Human]) Approval Criteria:

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

[1] Stoller, JK. Clinical manifestations, diagnosis, and natural history of alpha$_1$-antitrypsin deficiency. *Up-To-Date*. Available online at: http://www.uptodate.com/contents/clinical-manifestations-diagnosis-and-natural-history-of-alpha-1-antitrypsin-deficiency?source=search_result&search=alpha+1+antitrypsin+deficiency&selectedTitle=1%7E90. Last revised 03/17/2016. Last accessed 05/16/2017.

[2] Izaguirre-Anariba, DE. Alpha$_1$-Antitrypsin Deficiency Clinical Presentation. *Medscape*. Available online at: http://emedicine.medscape.com/article/295686-clinical#b5. Last revised 02/10/2017. Last accessed 05/16/2017.

Appendix F

Vote to Prior Authorize Elaprase® (Idursulfase)

Oklahoma Health Care Authority
June 2017

Introduction[1,2]

Elaprase® (idursulfase) was approved by the U.S. Food and Drug Administration (FDA) in 2006 as an orphan drug for long-term enzyme replacement therapy for patients with Hunter syndrome, also known as mucopolysaccharidosis type II or MPS II. Hunter syndrome is an X-linked recessive disease caused by insufficient levels of the lysosomal enzyme iduronate-2-sulfatase. Idursulfase is a recombinant form of human iduronate-2-sulfatase, produced by recombinant DNA technology in a human cell line and is intended to provide exogenous enzyme uptake into cellular lysosomes. Idursulfase has a boxed warning for the risk of life-threatening anaphylactic reactions. The recommended dosage regimen of idursulfase is 0.5mg per kilogram (kg) of body weight administered once weekly as an intravenous (IV) infusion.

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

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

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

Recommendations

The College of Pharmacy recommends the prior authorization of Elaprase® (idursulfase) with the following criteria:

Elaprase® (Idursulfase) Approval Criteria:

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

[1] Elaprase® Package Insert. MedLibrary.org. Available online at: http://medlibrary.org/lib/rx/meds/elaprase-1/. Last revised 03/10/2016. Last accessed 05/11/2017.
[2] Elaprase® Prescribing Information. Shire Human Genetic Therapies, Inc. Available online at: http://pi.shirecontent.com/PI/PDFs/Elaprase_USA_ENG.pdf. Last revised 06/2013. Last accessed 05/11/2017.

Appendix G

Vote to Prior Authorize ColPrep™ Kit (Sodium Sulfate/ Potassium Sulfate/Magnesium Sulfate)

Oklahoma Health Care Authority
June 2017

Indication(s) and Dosing[1]

- **ColPrep™ Kit (sodium sulfate/potassium sulfate/magnesium sulfate)** is an osmotic laxative indicated for cleansing of the colon in preparation for colonoscopy in adults. ColPrep™ Kit is available as a kit containing two 200mL bottles of oral solution (each containing sodium sulfate 17.5g, potassium sulfate 3.13g, and magnesium sulfate 1.6g) and one 20-ounce mixing container with a 16-ounce fill line.
- ColPrep™ Kit should be taken as a split-dose oral regimen:
  - Day prior to colonoscopy: Early in the evening prior to colonoscopy, patients should pour the contents of one bottle of ColPrep™ Kit into the mixing container provided, dilute with water to the 16-ounce fill line, and drink the entire amount. Patients should then drink two additional containers filled to the 16-ounce line with water over the next hour.
  - Day of colonoscopy: The morning of colonoscopy (10 to 12 hours after the evening dose) patients should prepare the bottle of ColPrep™ Kit, and drink the entire amount. Patients should then drink two additional containers filled to the 16-ounce line with water over the next hour.
- Information regarding the anticipated cost and launch date of ColPrep™ Kit is unknown at this time.

Recommendations

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

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

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

[1] ColPrep™ Kit Prescribing Information. Gator Pharmaceuticals, Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/204553s001lbl.pdf. Last revised 12/2016. Last accessed 05/18/2017.

Appendix H

Vote to Prior Authorize Impavido® (Miltefosine)

Oklahoma Health Care Authority
June 2017

Introduction[1]

Impavido® (miltefosine) is an antileishmanial drug indicated in adults and adolescents 12 years of age and older weighing 30kg (66lbs) or more for treatment of visceral leishmaniasis due to *Leishmania donovani;* cutaneous leishmaniasis due to *Leishmania braziliensis*, *Leishmania guyanensis*, and *Leishmania panamensis;* and mucosal leishmaniasis due to *Leishmania braziliensis.* Impavido® is available as a 50mg capsule. The recommended dosage for patients weighing 30kg to 44kg is one 50mg capsule twice daily with food. For patients weighing 45kg or greater, the recommended dosage is one 50mg capsule three times daily with food. The treatment duration is 28 consecutive days. Miltefosine may cause fetal harm and should not be administered to pregnant women. A pregnancy test should be obtained in females of reproductive potential prior to prescribing miltefosine. Furthermore, females of reproductive potential should be advised to use effective contraception during therapy and for five months after therapy. The wholesale acquisition cost of Impavido® is $577.17 per capsule, resulting in a cost per treatment of $32,321.52 to $48,482.28, depending on patient's weight.

Recommendations

The College of Pharmacy recommends the prior authorization of Impavido® (miltefosine) with the following criteria:

Impavido® (Miltefosine) Approval Criteria:

1. An FDA approved indication for treatment of:
    a. Visceral leishmaniasis due to *Leishmania donovani*; or
    b. Cutaneous leishmaniasis due to *Leishmania braziliensis*, *Leishmania guyanensis*, or *Leishmania panamensis*; or
    c. Mucosal leishmaniasis due to *Leishmania braziliensis*; and
2. Female members must not be pregnant and female members of reproductive potential must have a pregnancy test prior to therapy initiation. Female members of reproductive potential must be willing to use effective contraception while on therapy and for five months after completion of therapy; and
3. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling.
4. A quantity limit of 84 capsules per 28 days will apply.

[1] Impavido® (Miltefosine) Prescribing Information. Profounda, Inc. Available online at: http://media.wix.com/ugd/a54292_eb861bfce29a43a185892ee0a7b15edb.pdf. Last revised 10/2015. Last accessed 05/15/2017.

Appendix I

Vote to Prior Authorize Xalkori® (Crizotinib), Zykadia® (Ceritinib), Alecensa® (Alectinib), Alunbrig™ (Brigatinib), Tarceva® (Erlotinib), Gilotrif® (Afatinib), Tagrisso™ (Osimertinib), Cyramza® (Ramucirumab), and Tecentriq® (Atezolizumab)

Oklahoma Health Care Authority
June 2017

Introduction[1]

National Comprehensive Cancer Network (NCCN) guidelines for the treatment of non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC) are continually updated, but the major indications are reflected in the product summaries below.

Xalkori® (Crizotinib)

- **Therapeutic Class:** Anaplastic Lymphoma Kinase (ALK) inhibitor
- **Indication(s):** Treatment of patients with metastatic NSCLC whose tumors are ALK-positive (as detected by an approved test) or are proto-oncogene tyrosine-protein kinase ROS (ROS1)-positive
- **How Supplied:** 200mg, 250mg capsule
- **Dose:** 250mg orally twice daily
- **Cost:** 200mg (60): $17,815.04 or 250mg (60): $17,815.04

Zykadia® (Ceritinib)

- **Therapeutic Class:** ALK inhibitor
- **Indication(s):** Treatment of patients with ALK-positive, metastatic NSCLC
- **How Supplied:** 150mg capsules
- **Dose:** 750mg orally once daily
- **Cost:** 150mg (70): $8,444.58

Alecensa® (Alectinib)

- **Therapeutic Class:** ALK inhibitor
- **Indication(s):** Treatment of patients with ALK-positive, metastatic NSCLC who have progressed on or are intolerant to crizotinib
- **How Supplied:** 150mg capsules
- **Dose:** 600mg orally twice daily
- **Cost:** 150mg (240): $15,976.33

Alunbrig™ (Brigatinib)

- **Therapeutic Class:** ALK inhibitor
- **Indication(s):** Treatment of patients with ALK-positive, metastatic NSCLC who have progressed on or are intolerant to crizotinib

- **How Supplied:** 30mg, 90mg tablets
- **Dose:** 90mg orally once daily for the first 7 days then, if tolerated, increase to 180mg orally once daily
- **Cost:** $14,250 per month

Tarceva® (Erlotinib)

- **Therapeutic Class:** Epidermal Growth Factor Receptor (EGFR) inhibitor
- **Indication(s):**
    - Treatment of metastatic NSCLC in tumors with EGFR exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an approved test either as first-line, maintenance, or as second or greater line treatment after progression following at least one prior chemotherapy regimen
    - First-line treatment of locally advanced, unresectable, or metastatic pancreatic cancer (in combination with gemcitabine)
- **How Supplied:** 25mg, 100mg, 150mg tablets
- **Dose:** 150mg orally once daily
- **Cost:** 25mg (30): $3,022.66 or 100mg (30): $8,302.25 or 150mg (30): $9,390.44

Gilotrif® (Afatinib)

- **Therapeutic Class:** EGFR inhibitor
- **Indication(s):**
    - First-line treatment of metastatic NSCLC in patients whose tumors have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an approved test
    - Treatment of previously treated metastatic squamous cell NSCLC which has progressed following platinum-based chemotherapy
- **How Supplied:** 20mg, 30mg, 40mg tablets
- **Dose:** 40mg orally once daily
- **Cost:** 20mg (30): $9,060.85 or 30mg (30): $9,060.85 or 40mg (30): $9,060.85

Tagrisso™ (Osimertinib)

- **Therapeutic Class:** EGFR inhibitor
- **Indication(s):** Treatment of metastatic EGFR T790M mutation-positive NSCLC, as detected by an approved test, in patients who have progressed on or after EGFR tyrosine kinase inhibitor (TKI) therapy
- **How Supplied:** 40mg, 80mg tablets
- **Dose:** 80mg orally once daily
- **Cost:** 40mg (30): $17,028.90 or 80mg (30): $17,028.90

Cyramza® (Ramucirumab)

- **Therapeutic Class:** Vascular Endothelial Growth Factor (VEGF) inhibitor
- **Indication(s):**
    - Treatment (in combination with docetaxel) of metastatic NSCLC in patients with disease progression on or after platinum-based chemotherapy; patients with

EGFR or ALK genomic tumor aberrations should have disease progression on an FDA-approved therapy for these aberrations prior to receiving ramucirumab
    - Treatment (in combination with FOLFIRI [irinotecan, leucovorin, and fluorouracil]) of metastatic colorectal cancer (mCRC) in patients with disease progression on or after prior therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine
    - Treatment (single-agent or in combination with paclitaxel) of advanced or metastatic gastric or gastroesophageal junction adenocarcinoma in patients with disease progression on or following fluoropyrimidine- or platinum-containing chemotherapy
- **How Supplied:** 100mg/10mL (10mL), 500mg/50mL (50mL) solution for intravenous (IV) infusion
- **Dose:** 10mg/kg on day one every 21 days in combination with docetaxel; continue until disease progression or unacceptable toxicity
- **Cost:** 100mg/10mL (10mL): $1,298.96 or 500mg/50mL (50mL): $6,494.82

Tecentriq® (Atezolizumab)
- **Therapeutic Class:** Programmed death-ligand 1 (PD-L1) inhibitor
- **Indications(s):**
    - NSCLC, metastatic
    - Urothelial carcinoma, locally advanced or metastatic
- **How Supplied:** 1,200mg/20mL (20mL) solution for IV infusion
- **Dose:** 1,200mg every three weeks, continue until disease progression or unacceptable toxicity
- **Cost:** 1,200mg/20mL (20mL): $8,620.00

Recommendations

Xalkori® (Crizotinib) Approval Criteria [Non-Small Cell Lung Cancer (NSCLC) Diagnosis]:
1. A diagnosis of metastatic NSCLC (first-line or subsequent therapy); and
2. Anaplastic lymphoma kinase (ALK) or ROS1 positivity; or
3. MET amplification; and
4. Crizotinib must be used as a single-agent only.

Xalkori® (Crizotinib) Approval Criteria [Soft Tissue Sarcoma – Inflammatory Myofibroblastic Tumor (IMT) with Anaplastic Lymphoma Kinase (ALK) Translocation Diagnosis]:
1. A diagnosis of soft tissue sarcoma – IMT; and
2. Anaplastic lymphoma kinase (ALK) positivity; and
3. Crizotinib must be used as a single-agent only.

Zykadia® (Ceritinib) Approval Criteria [Non-Small Cell Lung Cancer (NSCLC) Diagnosis]:
1. A diagnosis of metastatic NSCLC; and
2. Anaplastic lymphoma kinase (ALK) positivity; and
3. Ceritinib must be used as a single-agent only.

Zykadia® (Ceritinib) Approval Criteria [Soft Tissue Sarcoma – Inflammatory Myofibroblastic Tumor (IMT) with Anaplastic Lymphoma Kinase (ALK) Translocation Diagnosis]:

1. A diagnosis of soft tissue sarcoma – IMT; and
2. Anaplastic lymphoma kinase (ALK) positivity; and
3. Ceritinib must be used as a single-agent only.

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

1. A diagnosis of recurrent or metastatic NSCLC; and
2. Anaplastic lymphoma kinase (ALK) positivity; and
3. Progressed on or intolerant to crizotinib; or
4. Member has asymptomatic disease with rapid radiologic progression on crizotinib; and
5. Alectinib must be used as a single-agent only.

Alunbrig™ (Brigatinib) Approval Criteria [Non-Small Cell Lung Cancer (NSCLC) Diagnosis]:

1. A diagnosis of metastatic NSCLC; and
2. Anaplastic lymphoma kinase (ALK) positivity; and
3. Progressed on or intolerant to crizotinib; and
4. Brigatinib must be used as a single-agent only.

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

1. A diagnosis of NSCLC; and
2. Recurrence or metastatic disease; and
3. Epidermal growth factor receptor (EGFR) mutation detected; and
4. Erlotinib must be used as a single-agent only.

Tarceva® (Erlotinib) Approval Criteria [Pancreatic Cancer Diagnosis]:

1. A diagnosis of pancreatic cancer; and
2. Locally advanced unresectable or metastatic disease; and
3. Member must have good performance status (ECOG 0 to 2); and
4. Erlotinib must be used as a first-line agent only; and
5. Erlotinib must be used in combination with gemcitabine.

Tarceva® (Erlotinib) Approval Criteria [Kidney Cancer Diagnosis]:

1. A diagnosis of kidney cancer; and
2. Non-clear cell type; and
3. Relapsed disease or for surgically unresectable stage IV disease; and
4. Erlotinib must be used as a single-agent only.

Tarceva® (Erlotinib) Approval Criteria [Bone Cancer – Chordoma Diagnosis]:

1. A diagnosis of bone cancer – chordoma; and
2. Recurrent disease; and
3. Erlotinib must be used as a single-agent only.

Tarceva® (Erlotinib) Approval Criteria [Pancreatic Adenocarcinoma Diagnosis]:

1. A diagnosis of pancreatic adenocarcinoma; and
2. Locally advanced unresectable disease or metastatic disease; and

3. Member must have good performance status (ECOG 0 to 2); and
4. Erlotinib must be used in combination with gemcitabine.

Gilotrif® (Afatinib) Approval Criteria [Non-Small Cell Lung Cancer (NSCLC) Diagnosis]:
The following criteria must be met when used in the first-line setting:
1. A diagnosis of metastatic NSCLC; and
2. Epidermal growth factor receptor (EGFR) mutation detected; and
3. Afatinib when used in the first-line setting must be used as a single-agent only.

The following criteria must be met when used in the second-line setting:
1. A diagnosis of metastatic NSCLC; and
2. Progressed following platinum-based chemotherapy; and
3. Afatinib when used in the second-line setting may be used as a single-agent or in combination with cetuximab in patients with a known sensitizing EGFR mutation who are T790M negative.

Gilotrif® (Afatinib) Approval Criteria [Head and Neck Cancer Diagnosis]:
1. A diagnosis of head and neck cancer; and
2. Disease progression on or after platinum containing chemotherapy; and
3. Non-nasopharyngeal cancer must be one of the following:
    a. Newly diagnosed T4b, any N, M0 disease, unresectable nodal disease with no metastases, or for patients who are unfit for surgery and performance status (PS) 3; or
    b. Metastatic (M1) disease at initial presentation, recurrent/persistent disease with distant metastases, or unresectable locoregional recurrence or second primary with prior radiation therapy (RT) and PS 0 to 2; or
    c. Unresectable locoregional recurrence without prior RT and PS 3; and
4. Afatinib must be used as a single-agent.

Tagrisso™ (Osimertinib) Approval Criteria [Non-Small Cell Lung Cancer (NSCLC) Diagnosis]:
1. A diagnosis of NSCLC; and
2. Epidermal growth factor receptor (EGFR) T790M mutation-positive disease; and
3. Following progression on erlotinib, afatinib, or gefitinib for asymptomatic disease, symptomatic brain lesions, or multiple symptomatic systemic lesions; and
4. Osimertinib must be used for subsequent therapy only.

Cyramza® (Ramucirumab) Approval Criteria [Non-Small Cell Lung Cancer (NSCLC) Diagnosis]:
1. A diagnosis of NSCLC; and
2. Subsequent therapy for metastatic disease after progression; and
3. Member must have an ECOG performance status of 0 to 2; and
4. Ramucirumab must be used in combination with docetaxel.

Cyramza® (Ramucirumab) Approval Criteria [Colorectal Cancer Diagnosis]:

1. A diagnosis of colorectal cancer; and
2. Subsequent therapy for metastatic disease after progression on or after prior therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine; and
3. Ramucirumab must be used in combination with an irinotecan based regimen.

Cyramza® (Ramucirumab) Approval Criteria [Esophageal Cancer Diagnosis]:

1. A diagnosis of unresectable, locally advanced, recurrent or metastatic esophageal or esophagogastic junction adenocarcinoma; and
2. Member must have a Karnofsky performance score greater than or equal to 60% or an ECOG performance score of 0 to 2; and
3. Ramucirumab must be used as a single-agent or in combination with paclitaxel.

Cyramza® (Ramucirumab) Approval Criteria [Gastric Cancer Diagnosis]:

1. A diagnosis of gastric cancer; and
2. Member is not a surgical candidate or has unresectable, locally advanced, recurrent or metastatic disease; and
3. Member has a Karnofsky performance score of greater than or equal to 60% or an ECOG performance score of 0 to 2; and
4. Ramucirumab must be used as a single-agent or in combination with paclitaxel.

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

1. A diagnosis of NSCLC; and
2. Subsequent therapy for metastatic disease; and
3. Member must have an ECOG performance score of 0 to 2; and
4. Atezolizumab must be used as a single-agent only.

Tecentriq® (Atezolizumab) Approval Criteria [Urothelial Carcinoma]:

1. A diagnosis of locally advanced or metastatic urothelial carcinoma; and
2. Progressed on or following platinum containing chemotherapy or in cisplatin ineligible patients.

[1] National Comprehensive Cancer Network. Non-small cell lung cancer and small cell lung cancer. (Version 5.2017). http://www.nccn.org/professionals/physician_gls/pdf/bone.pdf. Last revised 11/07/2016. Last accessed 04/13/2017.

Appendix J

Annual Review of Prostate Cancer Medications

Oklahoma Health Care Authority
June 2017

Introduction[1,2,3]

According to the National Cancer Institute, in 2017 an estimated 161,360 men will be diagnosed with prostate cancer, making prostate cancer 9.6% of all new cancer cases in the United States.[1] Prostate cancer is the second leading cause of cancer death in men. The incidence of prostate cancer is closely correlated with trends in screening practices. Prostate specific antigen (PSA) is a protein produced by cells of the prostate gland and elevations in its levels may indicate prostate cancer. PSA has been used as a screening marker for prostate cancer over the last three decades with its peak utilization occurring in the early 1990s and gradually declining since that time.[1] Following the same trend, the incidence rates of prostate cancer were highest in 1992 and have slowly decreased from that date. Physicians have gone away from recommending generalized PSA screening for the average risk male for several reasons. The main reason is that the mortality associated with prostate cancer is very low with an estimated 98% survival at five years. Early detection of prostate cancer can lead to over-treatment of cancers that do not impact life expectancy. This may result in unwarranted side effects, reduced quality of life, and increased cost. Prostate cancer detection and progression models estimate that 23% to 42% of all screen-detected cancers are over-treated.[2]

The most common type of prostate cancer is adenocarcinoma, which accounts for 99% of tumors in the prostate.[3] Sarcomas, transitional, small, and squamous cell carcinomas are rare. The treatment principles for prostate cancer have largely remained the same over the past 50 years with surgery, radiation, and androgen deprivation therapy (ADT) making up the main components of therapy.[3] Androgens, the most common of which is testosterone, promote the growth of prostate cancers. ADT involves medications that reduce the body's level of androgens or surgery to remove the testicles which ultimately can decrease and slow the growth of prostate cancers. Early stage (stage I and II localized) prostate cancer is typically treated with either surgery, radiation therapy, or active surveillance. Stage III cancer treatment often involves a combination of radiation therapy, with ADT and surgery. ADT is usually recommended for initial treatment of men with metastatic (stage IV) prostate cancer and it is often combined with chemotherapy. Other treatment strategies for advanced cancers include immunotherapy and radiation. Advanced prostate cancer is incurable but treatment can help to control the tumor burden for long periods of time.

Current Prior Authorization Criteria

Zytiga® (Abiraterone) Approval Criteria:

1. A diagnosis of metastatic, castration-resistant prostate cancer; and
2. Abiraterone must be used in combination with a corticosteroid; and

3. Approvals will be for the duration of three months at which time additional authorization may be granted if the prescriber documents that the member has not shown evidence of progressive disease while on abiraterone therapy.

Jevtana® (Cabazitaxel) Approval Criteria:

1. A diagnosis of metastatic, castration-resistant prostate cancer; and
2. Member must have been previously treated with a docetaxel-containing regimen; and
3. Cabazitaxel should be used in combination with prednisone; and
4. Approvals will be for the duration of three months at which time additional authorization may be granted if the prescriber documents that the member has not shown evidence of progressive disease while on cabazitaxel therapy.

Xtandi® (Enzalutamide) Approval Criteria:

1. A diagnosis of metastatic, castration-resistant prostate cancer; and
2. Approvals will be for the duration of three months at which time additional authorization may be granted if the prescriber documents that the member has not shown evidence of progressive disease while on enzalutamide therapy.

Xofigo® (Radium-223 Dichloride) Approval Criteria:

1. A diagnosis of metastatic, castration-resistant prostate cancer; and
2. Member must have symptomatic bone metastases; and
3. Member must not have known visceral metastatic disease; and
4. Prescriber must verify radium-223 dichloride is not to be used in combination with chemotherapy; and
5. Member must have an absolute neutrophil count ≥ 1.5 x 10^9/L, platelet count ≥ 100 x 10^9/L, and hemoglobin ≥ 10 g/dL; and
6. Approvals will be for the duration of three months at which time additional authorization may be granted if the prescriber documents the following:
    a. The member has not shown evidence of progressive disease while on radium-223 dichloride therapy; and
    b. Member must have an absolute neutrophil count ≥ 1 x 10^9/L, platelet count ≥ 100 x 10^9/L (radium-223 dichloride should be delayed 6 to 8 weeks otherwise).

Provenge® (Sipuleucel-T) Approval Criteria:

1. A diagnosis of metastatic, castration-resistant prostate cancer; and
2. Member must be asymptomatic or minimally symptomatic; and
3. Member must not have hepatic metastases; and
4. Member must have a life expectancy of greater than six months; and
5. Member must have good performance status (ECOG 0 to 1); and
6. Approvals will be for the duration of three months at which time additional authorization may be granted if the prescriber documents that the member has not shown evidence of progressive disease while on sipuleucel-T therapy.

Utilization of Prostate Cancer Medications: Calendar Year 2016

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

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2015	3	21	$188,748.38	$8,988.02	$299.60	2,520	630
2016	6	26	$248,383.59	$9,553.22	$318.44	3,120	780
% Change	**100.00%**	**23.80%**	**31.60%**	**6.30%**	**6.30%**	**23.80%**	**23.80%**
Change	**3**	**5**	**$59,635.21**	**$565.20**	**$18.84**	**600**	**150**

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

Calendar Year 2016: Prostate Cancer Medications (Medical Claims)

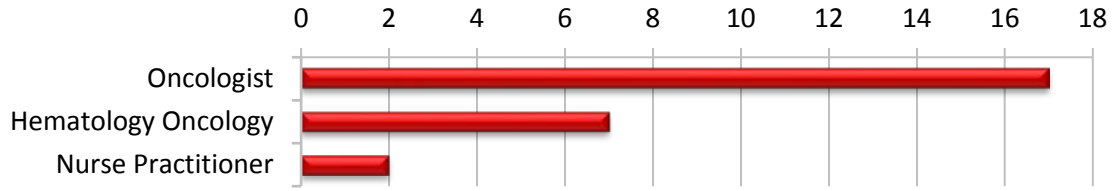
Calendar Year	*Total Members	Total Claims	Total Cost	Cost/Claim	Total Units
2016	2	4	$36,319.20	$9,079.80	240

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
There were no medical claims for prostate cancer medications during calendar year 2015 therefore a comparison cannot be provided.

Demographics of Members Utilizing Prostate Cancer Medications

- Due to the small number of members utilizing prostate cancer medications during calendar year 2016, detailed demographic information could not be provided. All members were male and age 45 years or older.

Top Prescriber Specialties of Prostate Cancer Medications By Number of Claims



Market News and Updates

The FDA Orange Book indicates the following patent expiration dates for each of the products:

- Provenge® (sipuleucel-T): 2019
- Xofigo® (radium-223 dichloride): January 2020
- Xtandi® (enzalutamide): August 2027
- Zytiga® (abiraterone): August 2027
- Jevtana® (cabazitaxel): October 2030

Recommendations

There are no recommended changes to the prostate cancer medication prior authorization criteria at this time.

Utilization Details of Prostate Cancer Medications: Calendar Year 2016

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
ABIRATERONE PRODUCTS					
ZYTIGA TAB 250MG	5	2	$45,554.00	2.5	$9,110.80
SUBTOTAL	**5**	**2**	**$45,554.00**	**2.5**	**$9,110.80**
ENZALUTAMIDE PRODUCTS					
XTANDI CAP 40MG	21	4	$202,829.59	5.25	$9,658.55
SUBTOTAL	**21**	**4**	**$202,829.59**	**5.25**	**$9,658.55**
TOTAL	**26**	**6***	**$248,383.59**	**4.33**	**$9,553.22**

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

Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM
CABAZITAXEL PRODUCTS				
JEVTANA INJECTION (J9043)	4	2	$36,319.20	$9,079.80
TOTAL	**4**	**2***	**$36,319.20**	**$9,079.80**

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

[1] National Cancer Institute. SEER Cancer Statistics. Available online at: http://www.cancer.gov/about-cancer/what-is-cancer/statistics. Last accessed 05/24/2017.
[2] Draisma G, Etzioni R, Tsodikov A, et al. Lead time and overdiagnosis in prostate-specific antigen screening: importance of methods and context. *J Natl Cancer Inst*. 2009 Mar 18;101(6):374-83.
[3] National Comprehensive Cancer Network (NCCN). *NCCN Clinical Practice Guidelines in Oncology (Prostate Cancer)*. Available online at: https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Last accessed 05/24/2017.

Appendix K

Calendar Year 2016 Annual Review of ADHD and Narcolepsy Medications and 30-Day Notice to Prior Authorize Vyvanse® (Lisdexamfetamine Chewable Tablets) and Update the ADHD Prior Authorization Criteria and Tier Chart

Oklahoma Health Care Authority
June 2017

Current Prior Authorization Criteria

ADHD Medications Tier-2 Approval Criteria:

1. A covered diagnosis; and
2. A previously failed trial with at least one long-acting Tier-1 stimulant that resulted in an inadequate response:
    a. Trials should have been within the last 180 days; and
    b. Trials should have been dosed up to maximum recommended dose or documented adverse effects at higher doses should be included; and
    c. If trials are not in member's claim history, the pharmacy profile should be submitted or detailed information regarding dates and doses should be included along with the signature from the physician; and
3. For Adzenys XR-ODT™, an age restriction of ten years and younger will apply. Members older than ten years of age will require a patient-specific, clinically significant reason why a special formulation product is needed.

ADHD Medications Tier-3 Approval Criteria:

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

b. Previously failed trials (within the last 180 days) with a long-acting Tier-1 stimulant, a long-acting Tier-2 stimulant, Intuniv®, and Strattera®, unless contraindicated, that did not yield adequate results; and
c. A patient-specific, clinically significant reason why the member cannot use clonidine immediate-release tablets.

ADHD Medications Special Prior Authorization Approval Criteria:

1. Desoxyn®, Dexedrine®, Dexedrine Spansules®, Evekeo®, and Zenzedi® Criteria:
    a. A covered diagnosis; and
    b. A patient-specific, clinically significant reason why the member cannot use all other available stimulant medications.
2. Daytrana®, Dyanavel® XR, QuilliChew ER™, Quillivant XR®, and Methylin® Chewable Tablets and Solution Criteria:
    a. An FDA approved diagnosis; and
    b. A patient-specific, clinically significant reason why the member cannot use all other available formulations of long-acting stimulant medications that can be used for members who cannot swallow capsules or tablets; and
    c. An age restriction of ten years and younger will apply. Members older than ten years of age will require a patient-specific, clinically significant reason why a special formulation product is needed.

ADHD Medications Additional Criteria:

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

Narcolepsy Medications Approval Criteria:

1. An FDA approved diagnosis; and
2. Use of Provigil® (modafinil) or Nuvigil® (armodafinil) requires a patient-specific, clinically significant reason why the member cannot use stimulant medications to improve wakefulness during the daytime; and
    a. Nuvigil® is brand name preferred due to net cost after rebates; however, brand name preferred status may be removed if the net cost changes and brand name is more costly than generic; and
3. Use of Xyrem® (sodium oxybate) requires previously failed trials (within the last 180 days) with Tier-1 and Tier-2 stimulants from different chemical categories, Provigil®, and Nuvigil®, unless contraindicated, that did not yield adequate results; and
4. The diagnosis of obstructive sleep apnea requires concurrent treatment for the obstructive sleep apnea; and
5. The diagnosis of shift work sleep disorder requires the member's work schedule to be included with the prior authorization request.

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

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

+Unique criteria applies for the diagnosis of binge eating disorder (BED).

ER = extended-release, SR = sustained-release, ODT = orally disintegrating tablet, Chew Tabs = chewable tablets, Soln = solution, Susp = suspension

Utilization of ADHD & Narcolepsy Medications: Calendar Year 2016

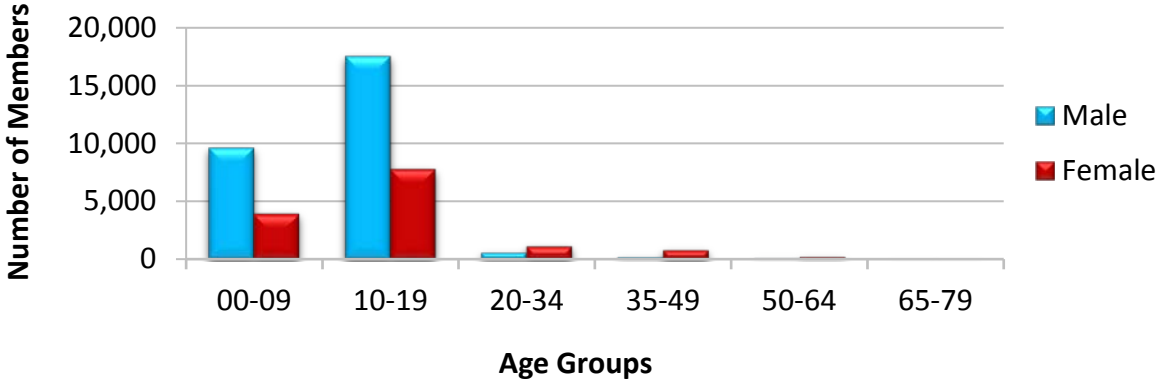
Comparison of Calendar Years: ADHD & Narcolepsy Medications

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2015	40,507	324,074	$59,311,678.79	$183.02	$6.16	11,418,465	9,631,930
2016	41,730	341,869	$62,239,990.72	$182.06	$6.13	12,090,052	10,160,259
% Change	**3.00%**	**5.50%**	**4.90%**	**-0.50%**	**-0.50%**	**5.90%**	**5.50%**
Change	**1,223**	**17,795**	**$2,928,311.93**	**-$0.96**	**-$0.03**	**671,587**	**528,329**

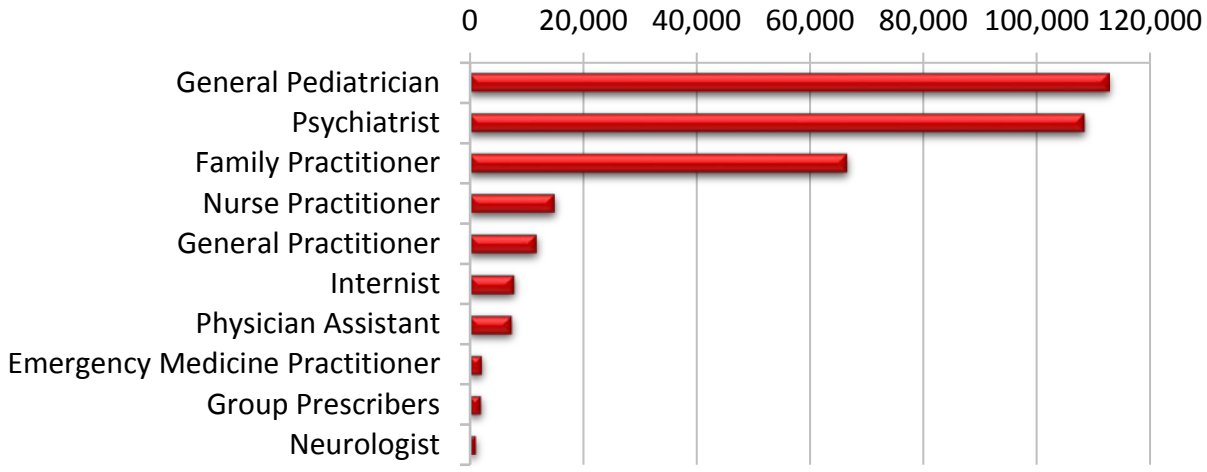
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

- Aggregate drug rebates collected during calendar year 2015 for ADHD and narcolepsy medications: $43,937,564.80[Δ]

Demographics of Members Utilizing ADHD & Narcolepsy Medications



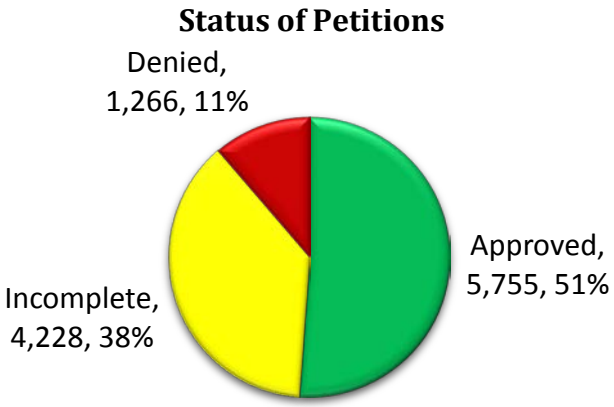
Top Prescriber Specialties of ADHD & Narcolepsy Medications by Number of Claims



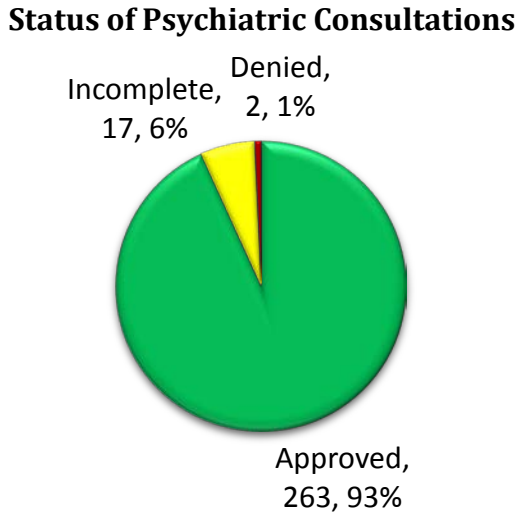
[Δ] Important considerations: Aggregate drug rebates are based on the date the claim is paid rather than the date dispensed. Claims data are based on the date dispensed. Calendar year 2015 claims data includes Indian Health Service providers; aggregated drug rebates do not.

Prior Authorization of ADHD & Narcolepsy Medications

There were 11,249 prior authorization requests submitted for ADHD and narcolepsy medications during calendar year 2016. Computer edits are in place to detect lower tiered medications in the member's recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions.



There were 282 prior authorization requests submitted for a total of 211 unique members for ADHD and narcolepsy medications during calendar year 2016 that were referred for a psychiatric consultation. Most requests were for children between 3 and 4 years of age. The following chart shows the status of the submitted petitions.



Market News and Updates[1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17]

Anticipated Patent Expiration(s):

- Focalin XR® (dexmethylphenidate extended-release [ER] capsules): November 2019
- Aptensio XR™ (methylphenidate ER capsules): December 2019
- Vyvanse® (lisdexamfetamine capsules): February 2023
- Daytrana® (methylphenidate ER patches): October 2025
- Dyanavel® XR (amphetamine ER suspension): March 2029

- Quillivant XR® (methylphenidate ER suspension): February 2031
- Adzenys XR-ODT™ (amphetamine ER orally disintegrating tablets [ODT]): June 2032
- Xyrem® (sodium oxybate solution): March 2033
- QuilliChew ER™ (methylphenidate ER chewable tablets): August 2033

New FDA Approval(s):

- **January 2017:** The U.S. Food and Drug Administration (FDA) approved Vyvanse® (lisdexamfetamine) chewable tablets for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in patients 6 years of age and older and for the treatment of moderate-to-severe binge eating disorder (BED) in adults. Vyvanse® capsules were first FDA approved in 2007 for the treatment of ADHD and then for the treatment of BED in 2015. Vyvanse® chewable tablets are available in the following strengths: 10mg, 20mg, 30mg, 40mg, 50mg, and 60mg, while Vyvanse® capsules are available in all previously listed strengths as well as 70mg. Both Vyvanse® capsules and chewable tablets are dosed once daily. Vyvanse® capsules and chewable tablets have currently provided a supplemental rebate to be placed in Tier-1; however, Vyvanse® capsules and chewable tablets will be moved to a higher tier based on net cost in comparison to other available products if the manufacturer chooses not to participate in supplemental rebates.
- **May 2017:** The FDA approved Abbreviated New Drug Applications (ANDAs) for the first generic versions of Strattera® (atomoxetine) for the treatment of ADHD in pediatric and adult patients. Four pharmaceutical companies received FDA approval to market generic atomoxetine. The anticipated release date and cost information for the new generic products are not currently available.

Other News:

- **March 2017:** Results of the Multimodal Treatment Study (MTA) showed that children with ADHD who consistently received treatment into adulthood showed no differences in symptom severity in comparison to those who took treatment holidays or who stopped treatment altogether. However, the average adult height of children who continued treatment was more than 2cm shorter than those who stopped treatment. The study is a continuation of the Multimodal Treatment Study of Children with ADHD, which was initially a 14-month trial. The trial was then transitioned into a long-term observational study, and participants were assessed eight times 2 to 16 years after baseline. Patients were classified as having a negligible, inconsistent, or consistent pattern of medication use; however, there was no significant difference in average symptom scores between the groups, indicating that ongoing medication use did not reduce symptom severity. With respect to adult height, it was determined that participants in the overall ADHD group were significantly shorter than those in the comparison group. Participants in the consistent and inconsistent groups were significantly shorter than those in the negligible group; furthermore, those in the consistent group were significantly shorter than those in the inconsistent group.
- **May 2017:** According to a large, nationwide cohort study over 10 years, male patients with ADHD had a 38% lower risk of motor vehicle crashes in months when receiving

ADHD medication compared to months when not receiving medication. Similarly, female patients had a 42% lower risk of motor vehicle crashes in months when receiving ADHD medication. Comparable reductions were found across all age groups, multiple sensitivity analyses, and when considering the long-term association between ADHD medication use and motor vehicle crashes. In the study, all patients received an ADHD diagnosis or medication from January 1, 2005 to December 31, 2014 and were followed-up for emergency department visits for motor vehicle crashes. Both male and females with ADHD had a significantly higher risk of motor vehicle crashes than their matched controls, and untreated patients with ADHD had the highest risk of a motor vehicle crash compared with both medicated patients and those in the control group. The researchers concluded that motor vehicle crashes are a prevalent and preventable cause of mortality and morbidity, and the role of medication warrants further attention.

- **May 2017:** A large review of Medicaid claims data found that black and Hispanic children were both more likely to be prescribed medication for ADHD and discontinue treatment compared to white children. Researchers examined Medicaid data from nine states on ADHD medication initiation in youth ages 6 to 12 years. Black children were also less likely to receive adequate care in both the initiation and follow-up and maintenance phases of their treatment after starting medication. The authors also argued that 7 out of 10 youth that discontinue ADHD medication do not receive psychotherapy services, meaning that minority children are more likely than white children to receive no treatment for their condition.

Pipeline:

- **November 2016:** Neos Therapeutics submitted a New Drug Application (NDA) to the FDA for NT-0201 for the treatment of ADHD. NT-0201 is a once daily, extended-release amphetamine oral suspension. The Prescription Drug User Fee Act (PDUFA) goal date for NT-0201 is September 15, 2017.
- **December 2016:** Neos Therapeutics completed the resubmission of an NDA to the FDA for Cotempla XR-ODT™ for the treatment of ADHD. Cotempla XR-ODT™ is an extended-release methylphenidate orally disintegrating tablet (ODT). In November 2015, Neos received an FDA-issued Complete Response Letter (CRL) for Cotempla XR-ODT™ requiring that the company conduct a bridging study to demonstrate bioequivalence between the clinical trial material and the to-be-marketed product, including an assessment of food effect, and to provide validation and three months of stability data. The PDUFA goal date for Cotempla XR-ODT™ is June 19, 2017. Neos Therapeutics also manufactures Adzenys XR-ODT™ (amphetamine ER ODT), which was FDA approved in January 2016.
- **January 2017:** Shire completed the resubmission of an NDA to the FDA for SHP465 for the treatment of ADHD. SHP465 is a long-acting, triple-bead, mixed amphetamine salts formulation. Shire resubmitted the NDA for SHP465 in response to the Approvable Letter from the FDA in 2007 that requested additional clinical studies and classified the response as a Class 2 resubmission. The NDA for SHP465 includes data from a database of 16 clinical studies evaluating SHP465 in more than 1,600 subjects. Positive top-line results from the SHP465-305 study in pediatric patients and from the SHP465-306 in

adult patients were reported in April 2016 and June 2016, respectively. The PDUFA goal date for SHP465 is June 20, 2017.

- **January 2017:** Alcobra reported that the Phase 3 clinical trial of metadoxine ER in adults with ADHD did not meet the primary endpoint of demonstrating a statistically significant difference from placebo in the change from baseline of the investigator rating of the Conners' Adult ADHD Rating Scales (CAARS). Therefore, Alcobra terminated the development of metadoxine ER for adults with ADHD. However, Alcobra will continue assessing the efficacy of metadoxine ER in the treatment of other conditions, including Fragile X syndrome, a rare disease which is the most common single-gene cause of autism and inherited cause of intellectual disability among boys.
- **March 2017:** Jazz Pharmaceuticals announced positive efficacy results from the Phase 3 TONES 3 and TONES 4 studies of JZP-110 in patients with obstructive sleep apnea (OSA). The Treatment of OSA and Narcolepsy Excessive Sleepiness (TONES) Phase 3 program is comprised of four studies, two in OSA, one in narcolepsy, and one open-label, long-term safety and maintenance of efficacy study. The two Phase 3 OSA studies enrolled 652 total patients. Subject to final data analysis and regulatory discussions with the FDA, Jazz Pharmaceuticals continues to target NDA submission in late 2017.
- **April 2017:** Sunovion announced positive results from a pivotal Phase 3 study evaluating the efficacy and safety of novel drug candidate dasotraline, a dopamine and norepinephrine reuptake inhibitor (DNRI), in children 6 to 12 years of age with ADHD. In a laboratory classroom setting, dasotraline showed persistent, statistically significant improvement in ADHD symptoms compared to placebo through the day, demonstrating a duration of effect of up to 24 hours, and was generally well tolerated. Sunovion plans to submit an NDA to the FDA for dasotraline in fiscal year 2017 (April 2017 to March 2018) for the treatment of ADHD. Dasotraline is also being investigated for the treatment of BED in adults.
- **May 2017:** In a post-hoc analysis of a secondary outcome from a Phase 3 trial, those on Benjorna™ (formally referred to as HLD-200) for the treatment of ADHD had statistically significant reductions in mean scores on the Before School Functioning Questionnaire (BSFQ), a measure of early morning functional impairment, over 3 weeks compared with those on placebo. Benjorna™ is a novel formulation of long-acting methylphenidate that relies on Delexis® drug delivery technology for controlled release of the drug, which is to be taken once daily in the evening with the objective of controlling symptoms of ADHD immediately upon awakening and throughout the day. The medication is coated with two layers of polymer that only permits release of the drug once it has reached the colon; thus, blood levels of methylphenidate do not begin to increase until 8 hours after the medication is taken. Primary results of the Phase 3 trial showed that the drug improved ADHD symptoms and reduced overall at-home functional impairment during the early morning, late afternoon, and evening compared to placebo. Highland Therapeutics submitted an NDA to the FDA in December 2016 for Benjorna™ for the treatment of ADHD, with a PDUFA goal date of July 30, 2017. Highland Therapeutics also has two novel formulations of amphetamine in the pipeline based on Delexis® drug delivery technology, HLD-900 for the treatment of BED and HLD-100 for the treatment of ADHD, both with further clinical studies planned for 2017.

Medicaid Drug Rebate Program[18,19,20]

Medicaid coverage of a drug requires the manufacturer to have a federal rebate agreement with the Secretary of Health and Human Services (HHS). Rebate amounts are based on the "best price" for each drug. Best price refers to the lowest price paid to a manufacturer for a drug by any payer. Best prices are reported to the Centers for Medicare & Medicaid Services (CMS) by the manufacturer, but are not publicly available.

If a drug's price increases more quickly than inflation, an additional rebate penalty is included based on the change in price compared with the consumer price index (CPI). The CPI penalty of the federal rebate is designed to keep Medicaid net cost relatively flat despite increases in drug prices. Until the first quarter of 2017, the CPI penalty only applied to brand medications; however, following a senate vote in October 2015, the Medicaid CPI penalty was extended to generic drugs with an effective date of January 1, 2017. Generic drugs became a concern of Congress after a letter to the Office of Inspector General noted that between July 2013 and June 2014, half of all generic drugs increased in price, 10% of which doubled in price during that time period. As average wholesale price (AWP) increases, the rebated amount per unit (RAPU) increases as well, resulting in minimal effect on Medicaid net cost.

Additionally, many states have negotiated supplemental rebate agreements with manufacturers to produce added rebates. The ADHD and Narcolepsy Medications Product Based Prior Authorization (PBPA) category is heavily influenced by supplemental rebates. The ADHD and narcolepsy brand name products that are preferred over available generic products are likely due to a lower net cost compared to generics, after taking into account supplemental rebate participation. In calendar year 2015, the Oklahoma Health Care Authority (OHCA) collected $43,937,564.80 in aggregate drug rebates for ADHD and narcolepsy medications. These rebates are collected after reimbursement for the medication and are not reflected in this report. The costs included in this report do not reflect net costs.

Recommendations

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

1. Place Vyvanse® (lisdexamfetamine chewable tablets) into Tier-1 based on net cost after rebates.
    a. Current Tier-1 criteria will apply.
    b. A quantity limit of 30 chewable tablets per 30 days will apply.
    c. Vyvanse® capsules and chewable tablets have currently provided a supplemental rebate to be placed in Tier-1; however, Vyvanse® capsules and chewable tablets will be moved to a higher tier based on net cost in comparison to other available products if the manufacturer chooses not to participate in supplemental rebates.
2. Move Aptensio XR™ (methylphenidate ER capsules), generic Metadate CD® (methylphenidate ER capsules), and generic Ritalin LA® (methylphenidate ER capsules) into Tier-1 based on net cost after rebates. Metadate CD® and Ritalin LA® will no longer be brand preferred.

    a. Current Tier-1 criteria will apply.
    b. Aptensio XR™ capsules have currently provided a supplemental rebate to be placed in Tier-1; however, Aptensio XR™ capsules will be moved to a higher tier based on net cost in comparison to other available products if the manufacturer chooses not to participate in supplemental rebates.
3. Move Quillivant XR® (methylphenidate ER suspension) and QuilliChew ER™ (methylphenidate ER chewable tablets) to Tier-2 based on net cost after rebates.
    a. Current Tier-2 criteria will apply.
    b. Quillivant XR® suspension and QuilliChew ER™ chewable tablets have currently been placed in Tier-2 based on net cost; however, if the net cost changes Quillivant XR® suspension and QuilliChew ER™ chewable tablets will be moved to a lower or higher tier based on net cost in comparison to other available products.
4. Move generic Metadate ER® (methylphenidate ER tablets), generic Methylin ER® (methylphenidate ER tablets), and generic Ritalin SR® (methylphenidate ER tablets) into Tier-3 based on net cost after rebates.
    a. Current Tier-3 criteria will apply.
5. Add a previously failed trial of Nuvigil® (armodafinil) trial for authorization of Provigil® (modafinil), due to a significantly lower net cost of Nuvigil® after rebates.

The proposed changes can be seen in red in the following criteria and tier chart:

ADHD Medications Tier-2 Approval Criteria:

1. A covered diagnosis; and
2. A previously failed trial with at least one long-acting Tier-1 stimulant that resulted in an inadequate response:
    a. Trials should have been within the last 180 days; and
    b. Trials should have been dosed up to maximum recommended dose or documented adverse effects at higher doses should be included; and
    c. If trials are not in member's claim history, the pharmacy profile should be submitted or detailed information regarding dates and doses should be included along with the signature from the physician; and
3. For Adzenys XR-ODT™, an age restriction of ten years and younger will apply. Members older than ten years of age will require a patient-specific, clinically significant reason why a special formulation product is needed.

ADHD Medications Tier-3 Approval Criteria:

1. A covered diagnosis; and
2. A previously failed trial with at least one long-acting Tier-1 stimulant that resulted in an inadequate response; and
3. A previously failed trial with at least one long-acting Tier-2 stimulant that resulted in an inadequate response:
    a. Trials should have been within the last 365 days; and
    b. Trials should have been dosed up to maximum recommended dose or documented adverse effects at higher doses should be included; and

c. If trials are not in member's claim history, the pharmacy profile should be submitted or detailed information regarding dates and doses should be included along with the signature from the physician.

4. A clinical exception may apply for special formulation products when there is a patient-specific, clinically significant reason why the member cannot use the available long-acting lower tiered formulations.
5. Use of Kapvay® (clonidine extended-release tablets) requires:
    a. An FDA approved diagnosis; and
    b. Previously failed trials (within the last 180 days) with a long-acting Tier-1 stimulant, a long-acting Tier-2 stimulant, Intuniv®, and Strattera®, unless contraindicated, that did not yield adequate results; and
    c. A patient-specific, clinically significant reason why the member cannot use clonidine immediate-release tablets.

ADHD Medications Special Prior Authorization Approval Criteria:

1. Desoxyn®, Dexedrine®, Dexedrine Spansules®, Evekeo®, and Zenzedi® Criteria:
    a. A covered diagnosis; and
    b. A patient-specific, clinically significant reason why the member cannot use all other available stimulant medications.
2. Daytrana®, Dyanavel® XR, ~~QuilliChew ER™, Quillivant XR®,~~ and Methylin® Chewable Tablets and Solution Criteria:
    a. An FDA approved diagnosis; and
    b. A patient-specific, clinically significant reason why the member cannot use all other available formulations of long-acting stimulant medications that can be used for members who cannot swallow capsules or tablets; and
    c. An age restriction of ten years and younger will apply. Members older than ten years of age will require a patient-specific, clinically significant reason why a special formulation product is needed.

ADHD Medications Additional Criteria:

1. Doses exceeding 1.5 times the FDA maximum are not covered.
2. Prior authorization is required for all tiers for members older than 20 years of age and for members younger than 5 years of age. All prior authorization requests for members younger than 5 years of age must be reviewed by an Oklahoma Health Care Authority (OHCA)-contracted psychiatrist.
3. Vyvanse® (Lisdexamfetamine) Approval Criteria: Binge Eating Disorder (BED)
    a. An FDA approved diagnosis of moderate-to-severe binge eating disorder (BED); and
    b. Member must be 18 years of age or older; and
    c. Vyvanse® for the diagnosis of BED must be prescribed by a psychiatrist; and
    d. Authorizations will not be granted for the purpose of weight loss without the diagnosis of BED or for the diagnosis of obesity alone. The safety and effectiveness of Vyvanse® for the treatment of obesity have not been established; and

e. A quantity limit of 30 capsules per 30 days will apply; and
f. Initial approvals will be for the duration of three months. Continued authorization will require prescriber documentation of improved response/effectiveness of Vyvanse®.

Narcolepsy Medications Approval Criteria:

1. An FDA approved diagnosis; and
2. Use of ~~Provigil® (modafinil) or~~ Nuvigil® (armodafinil) requires a patient-specific, clinically significant reason why the member cannot use stimulant medications to improve wakefulness during the daytime; and
    a. Nuvigil® is brand name preferred due to net cost after rebates; however, brand name preferred status may be removed if the net cost changes and brand name is more costly than generic; and
3. Use of Provigil® (modafinil) requires a previously failed trial (within the last 180 days) with Nuvigil® and a patient-specific, clinically significant reason why the member cannot use stimulant medications to improve wakefulness during the daytime; and
4. Use of Xyrem® (sodium oxybate) requires previously failed trials (within the last 180 days) with Tier-1 and Tier-2 stimulants from different chemical categories, Provigil®, and Nuvigil®, unless contraindicated, that did not yield adequate results; and
5. The diagnosis of obstructive sleep apnea requires concurrent treatment for the obstructive sleep apnea; and
6. The diagnosis of shift work sleep disorder requires the member's work schedule to be included with the prior authorization request.

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

*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable. **Proposed changes due to supplemental rebate participation are shown in blue. Products may be moved to a higher tier based on net cost if the manufacturer chooses not to participate in supplemental rebates.**

+Unique criteria applies for the diagnosis of binge eating disorder (BED).

ER = extended-release, SR = sustained-release, Caps = capsules, ODT = orally disintegrating tablet, Chew Tabs = Chewable tablets, Soln = solution, Susp = suspension

Utilization Details of ADHD & Narcolepsy Medications: Calendar Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
LISDEXAMFETAMINE PRODUCTS						
VYVANSE CAP 30MG	23,785	6,302	$5,895,134.16	$8.34	$247.85	9.47%
VYVANSE CAP 20MG	18,292	5,717	$4,533,859.89	$8.37	$247.86	7.28%
VYVANSE CAP 40MG	17,412	4,142	$4,358,381.63	$8.40	$250.31	7.00%
VYVANSE CAP 50MG	12,745	2,832	$3,193,688.50	$8.41	$250.58	5.13%
VYVANSE CAP 70MG	7,852	1,334	$1,966,939.59	$8.40	$250.50	3.16%
VYVANSE CAP 60MG	7,835	1,548	$1,960,735.08	$8.37	$250.25	3.15%
VYVANSE CAP 10MG	5,540	2,482	$1,357,726.18	$8.39	$245.08	2.18%
SUBTOTAL	**93,461**	**24,357**	**$23,266,465.03**	**$8.38**	**$248.94**	**37.38%**
METHYLPHENIDATE PRODUCTS						
METHYLPHENID TAB 10MG	9,847	2,329	$311,100.63	$1.06	$31.59	0.50%
METADATE CD CAP 20MG	8,618	2,758	$2,024,594.75	$7.95	$234.93	3.25%
METHYLPHENID TAB 5MG	7,846	2,292	$174,607.43	$0.75	$22.25	0.28%
METADATE CD CAP 30MG	6,712	1,918	$1,581,584.59	$7.93	$235.64	2.54%
METHYLPHENID TAB 36MG ER	6,611	1,196	$1,631,311.76	$8.25	$246.76	2.62%
METHYLPHENID TAB 54MG ER	5,990	1,019	$1,155,578.63	$6.46	$192.92	1.86%
METADATE CD CAP 40MG	4,515	1,110	$1,449,678.48	$10.79	$321.08	2.33%
METADATE CD CAP 10MG	4,240	1,786	$984,755.91	$7.90	$232.25	1.58%
METHYLPHENID TAB 20MG	4,151	828	$199,141.78	$1.61	$47.97	0.32%
METHYLPHENID TAB 54MG ER	3,688	658	$675,986.09	$6.13	$183.29	1.09%
METHYLPHENID TAB 36MG ER	3,538	691	$823,658.82	$7.78	$232.80	1.32%
METHYLPHENID TAB 27MG ER	2,235	485	$380,805.99	$5.71	$170.38	0.61%
METHYLPHENID TAB 20MG ER	2,060	600	$403,211.53	$6.59	$195.73	0.65%
METADATE CD CAP 50MG	1,757	427	$688,778.28	$13.18	$392.02	1.11%
METADATE CD CAP 60MG	1,488	304	$574,067.53	$12.91	$385.80	0.92%
METHYLPHENID TAB 18MG ER	1,471	364	$244,330.28	$5.57	$166.10	0.39%
METHYLPHENID TAB 27MG ER	1,044	261	$173,784.53	$5.57	$166.46	0.28%
METHYLPHENID TAB 10MG ER	687	233	$112,009.62	$5.38	$163.04	0.18%
METHYLPHENID TAB 18MG ER	634	166	$101,185.17	$5.34	$159.60	0.16%
METHYLPHENID SOL 5MG/5ML	437	137	$100,453.48	$7.71	$229.87	0.16%
METADATE TAB 20MG ER	407	138	$28,245.66	$2.32	$69.40	0.05%
METHYLPHENID SOL 10MG/5ML	332	73	$90,908.18	$9.06	$273.82	0.15%
QUILLIVANT SUS 25MG/5ML	309	53	$92,135.84	$10.02	$298.17	0.15%
RITALIN LA CAP 40MG	295	51	$80,263.35	$9.11	$272.08	0.13%
RITALIN LA CAP 30MG	275	67	$79,310.56	$9.70	$288.40	0.13%
RITALIN LA CAP 20MG	255	73	$64,443.62	$8.50	$252.72	0.10%
DAYTRANA DIS 30MG/9HR	217	53	$62,571.22	$9.61	$288.35	0.10%
METHYLPHENID CHW 5MG	118	49	$19,690.25	$5.55	$166.87	0.03%
METHLPHENIDA CHW 2.5MG	113	45	$10,812.08	$3.31	$95.68	0.02%
DAYTRANA DIS 20MG/9HR	113	36	$35,649.08	$10.52	$315.48	0.06%
RITALIN LA CAP 10MG	111	46	$27,092.11	$8.17	$244.07	0.04%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
DAYTRANA DIS 15MG/9HR	101	39	$39,088.22	$12.90	$387.01	0.06%
METHYLPHENID CHW 10MG	74	22	$18,509.30	$8.34	$250.13	0.03%
APTENSIO XR CAP 60MG	60	18	$11,643.05	$6.47	$194.05	0.02%
APTENSIO XR CAP 40MG	42	19	$8,230.16	$6.75	$195.96	0.01%
DAYTRANA DIS 10MG/9HR	37	23	$12,091.34	$11.09	$326.79	0.02%
METHYLIN SOL 5MG/5ML	34	19	$2,501.48	$2.53	$73.57	0.00%
APTENSIO XR CAP 30MG	28	14	$5,866.56	$6.98	$209.52	0.01%
CONCERTA TAB 54MG	24	6	$7,512.74	$10.43	$313.03	0.01%
CONCERTA TAB 36MG	24	5	$6,743.58	$9.37	$280.98	0.01%
METHYLIN SOL 10MG/5ML	21	10	$1,606.35	$2.82	$76.49	0.00%
APTENSIO XR CAP 50MG	21	11	$4,399.92	$6.98	$209.52	0.01%
METHYLPHENID CAP 40MG ER	16	3	$2,240.96	$4.67	$140.06	0.00%
APTENSIO XR CAP 10MG	12	9	$2,411.28	$6.99	$200.94	0.00%
METHYLPHENID CAP 40MG	12	2	$2,286.52	$6.35	$190.54	0.00%
RITALIN TAB 10MG	12	1	$1,250.78	$3.47	$104.23	0.00%
APTENSIO XR CAP 20MG	10	7	$1,947.64	$6.49	$194.76	0.00%
RITALIN TAB 20MG	9	1	$1,552.16	$5.75	$172.46	0.00%
METHYLPHENID CAP 30MG ER	8	4	$1,100.13	$4.78	$137.52	0.00%
METHYLPHENID TAB 20MG SR	7	3	$468.72	$2.23	$66.96	0.00%
METHYLPHENID CAP 20MG	6	2	$2,028.26	$13.43	$338.04	0.00%
METHYLPHENID CAP 20MG ER	5	3	$695.59	$4.64	$139.12	0.00%
METHYLPHENID CAP 30MG	4	3	$333.87	$2.78	$83.47	0.00%
METHYLPHENID CAP 60MG	3	1	$476.98	$5.30	$158.99	0.00%
QUILLICHEW CHW 30MG ER	3	1	$866.16	$9.62	$288.72	0.00%
QUILLICHEW CHW 40MG ER	2	1	$577.44	$9.62	$288.72	0.00%
QUILLICHEW CHW 20MG ER	2	2	$577.44	$9.62	$288.72	0.00%
METHYLPHENID CAP 50MG	1	1	$588.73	$6.54	$588.73	0.00%
APTENSIO XR CAP 15MG	1	1	$209.52	$6.98	$209.52	0.00%
SUBTOTAL	**80,693**	**20,477**	**$14,519,552.11**	**$6.05**	**$179.94**	**23.33%**
AMPHETAMINE/DEXTROAMPHETAMINE COMBINATION PRODUCTS						
AMPHET/DEXTR TAB 10MG	12,879	3,008	$429,025.82	$1.12	$33.31	0.69%
AMPHET/DEXTR TAB 20MG	8,891	1,747	$369,156.76	$1.39	$41.52	0.59%
AMPHET/DEXTR TAB 5MG	8,330	2,304	$276,916.74	$1.12	$33.24	0.44%
ADDERALL XR CAP 30MG	4,909	756	$1,096,302.79	$7.47	$223.33	1.76%
ADDERALL XR CAP 20MG	4,232	871	$994,831.13	$7.88	$235.07	1.60%
AMPHET/DEXTR TAB 30MG	4,232	739	$177,524.96	$1.41	$41.95	0.29%
AMPHET/DEXTR TAB 15MG	3,763	881	$148,465.90	$1.32	$39.45	0.24%
ADDERALL XR CAP 15MG	2,330	506	$514,164.63	$7.41	$220.67	0.83%
ADDERALL XR CAP 10MG	1,995	514	$437,469.23	$7.37	$219.28	0.70%
ADDERALL XR CAP 25MG	1,911	338	$418,759.21	$7.34	$219.13	0.67%
AMPHET/DEXTR TAB 7.5MG	861	242	$35,809.84	$1.40	$41.59	0.06%
ADDERALL XR CAP 5MG	430	122	$96,920.39	$7.56	$225.40	0.16%
AMPHET/DEXTR TAB 12.5MG	274	77	$11,792.69	$1.44	$43.04	0.02%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
AMPHET/DEXTR CAP 20MG ER	40	11	$4,160.72	$3.53	$104.02	0.01%
AMPHET/DEXTR CAP 30MG ER	25	7	$2,219.02	$2.98	$88.76	0.00%
ADDERALL TAB 20MG	15	7	$710.79	$1.58	$47.39	0.00%
AMPHET/DEXTR CAP 15MG ER	14	5	$1,595.65	$3.32	$113.98	0.00%
ADDERALL TAB 5MG	13	11	$356.52	$0.99	$27.42	0.00%
ADDERALL TAB 10MG	13	2	$376.34	$0.96	$28.95	0.00%
AMPHET/DEXTR CAP 10MG ER	12	3	$1,234.09	$3.43	$102.84	0.00%
AMPHET/DEXTR CAP 25MG ER	12	3	$1,307.95	$3.63	$109.00	0.00%
ADDERALL TAB 30MG	1	1	$169.81	$5.66	$169.81	0.00%
AMPHET/DEXTR CAP 5MG ER	1	1	$127.63	$4.25	$127.63	0.00%
SUBTOTAL	**55,183**	**12,156**	**$5,019,398.61**	**$3.05**	**$90.96**	**8.06%**
GUANFACINE PRODUCTS						
GUANFACINE TAB 2MG ER	14,967	3,451	$377,944.87	$0.85	$25.25	0.61%
GUANFACINE TAB 3MG ER	10,318	1,977	$259,257.02	$0.84	$25.13	0.42%
GUANFACINE TAB 1MG ER	10,248	3,500	$252,340.91	$0.85	$24.62	0.41%
GUANFACINE TAB 4MG ER	7,889	1,200	$199,612.65	$0.85	$25.30	0.32%
INTUNIV TAB 2MG	84	13	$25,209.36	$10.00	$300.11	0.04%
INTUNIV TAB 3MG	72	11	$22,416.48	$10.38	$311.34	0.04%
INTUNIV TAB 4MG	54	7	$14,040.68	$8.86	$260.01	0.02%
INTUNIV TAB 1MG	46	13	$13,365.73	$9.89	$290.56	0.02%
SUBTOTAL	**43,678**	**10,172**	**$1,164,187.70**	**$0.90**	**$26.65**	**1.87%**
DEXMETHYLPHENIDATE PRODUCTS						
DEXMETHYLPH TAB 10MG	8,373	1,632	$368,976.59	$1.48	$44.07	0.59%
DEXMETHYLPH TAB 5MG	6,418	1,512	$205,099.62	$1.08	$31.96	0.33%
DEXMETHYLPHE CAP 20MG ER	3,385	765	$641,016.86	$6.34	$189.37	1.03%
DEXMETHYLPH CAP 15MG ER	3,144	713	$396,922.77	$4.22	$126.25	0.64%
DEXMETHYLPH CAP 30MG ER	2,730	531	$360,821.28	$4.44	$132.17	0.58%
DEXMETHYLPHE CAP 10MG ER	2,107	592	$353,384.46	$5.62	$167.72	0.57%
FOCALIN XR CAP 25MG	2,013	399	$671,283.07	$11.19	$333.47	1.08%
FOCALIN XR CAP 20MG	1,345	398	$426,831.99	$10.61	$317.35	0.69%
DEXMETHYLPH TAB 2.5MG	1,143	364	$29,650.17	$0.88	$25.94	0.05%
DEXMETHYLPH CAP 40MG ER	820	148	$149,936.87	$6.14	$182.85	0.24%
FOCALIN XR CAP 10MG	773	247	$236,888.01	$10.28	$306.45	0.38%
FOCALIN XR CAP 15MG	747	222	$240,837.31	$10.81	$322.41	0.39%
DEXMETHYLPHE CAP 5MG ER	553	206	$85,250.69	$5.18	$154.16	0.14%
FOCALIN XR CAP 35MG	551	99	$186,773.15	$11.40	$338.97	0.30%
FOCALIN XR CAP 30MG	443	180	$138,313.13	$10.42	$312.22	0.22%
FOCALIN XR CAP 5MG	241	93	$73,743.48	$10.30	$305.99	0.12%
FOCALIN XR CAP 40MG	170	51	$58,788.88	$11.65	$345.82	0.09%
FOCALIN TAB 5MG	120	31	$6,522.35	$1.82	$54.35	0.01%
FOCALIN TAB 10MG	113	36	$8,754.93	$2.53	$77.48	0.01%
FOCALIN TAB 2.5MG	47	18	$1,512.03	$1.07	$32.17	0.00%
SUBTOTAL	**35,236**	**8,237**	**$4,641,307.64**	**$4.42**	**$131.72**	**7.46%**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
ATOMOXETINE PRODUCTS						
STRATTERA CAP 40MG	8,517	2,358	$3,521,224.03	$13.95	$413.43	5.66%
STRATTERA CAP 25MG	7,278	2,113	$2,888,895.90	$13.52	$396.94	4.64%
STRATTERA CAP 60MG	5,666	1,253	$2,219,978.16	$13.10	$391.81	3.57%
STRATTERA CAP 80MG	3,497	836	$1,494,968.57	$13.77	$427.50	2.40%
STRATTERA CAP 18MG	3,373	1,230	$1,351,300.48	$14.18	$400.62	2.17%
STRATTERA CAP 10MG	2,456	945	$969,975.80	$13.98	$394.94	1.56%
STRATTERA CAP 100MG	955	194	$420,866.28	$14.03	$440.70	0.68%
SUBTOTAL	**31,742**	**8,929**	**$12,867,209.22**	**$13.71**	**$405.37**	**20.67%**
CLONIDINE PRODUCTS						
CLONIDINE TAB 0.1MG ER	1,132	174	$259,218.67	$7.62	$228.99	0.42%
KAPVAY TAB 0.1 MG	20	2	$14,085.05	$23.48	$704.25	0.02%
SUBTOTAL	**1,152**	**176**	**$273,303.72**	**$7.90**	**$237.24**	**0.44%**
MODAFINIL PRODUCTS						
MODAFINIL TAB 200MG	284	38	$46,393.14	$5.44	$163.36	0.07%
MODAFINIL TAB 100MG	50	10	$6,310.42	$4.27	$126.21	0.01%
SUBTOTAL	**334**	**48**	**$52,703.56**	**$5.26**	**$157.80**	**0.08%**
ARMODAFINIL PRODUCTS						
NUVIGIL TAB 250MG	69	14	$43,267.09	$20.92	$627.06	0.07%
NUVIGIL TAB 150MG	43	8	$28,685.03	$22.24	$667.09	0.05%
ARMODAFINIL TAB 250MG	31	8	$15,032.57	$16.16	$484.92	0.02%
ARMODAFINIL TAB 150MG	19	8	$10,213.01	$17.92	$537.53	0.02%
NUVIGIL TAB 200MG	6	2	$3,845.90	$21.37	$640.98	0.01%
ARMODAFINIL TAB 200MG	3	1	$1,674.99	$18.61	$558.33	0.00%
SUBTOTAL	**171**	**41**	**$102,718.59**	**$20.03**	**$600.69**	**0.17%**
DEXTROAMPHETAMINE PRODUCTS						
DEXTROAMPHET TAB 10MG	53	11	$5,984.59	$3.76	$112.92	0.01%
DEXTROAMPHET CAP 15MG ER	41	6	$14,954.14	$12.16	$364.74	0.02%
DEXTROAMPHET CAP 10MG ER	30	5	$3,414.35	$3.79	$113.81	0.01%
DEXTROAMPHET CAP 5MG ER	17	2	$1,475.48	$2.89	$86.79	0.00%
DEXTROAMPHET TAB 5MG	13	4	$1,148.17	$2.94	$88.32	0.00%
ZENZEDI TAB 30MG	6	1	$2,219.22	$12.33	$369.87	0.00%
DEXTROAMPHET SOL 5MG/5ML	4	1	$2,378.32	$19.82	$594.58	0.00%
ZENZEDI TAB 15MG	3	1	$1,109.61	$12.33	$369.87	0.00%
SUBTOTAL	**167**	**31**	**$32,683.88**	**$6.52**	**$195.71**	**0.05%**
SODIUM OXYBATE PRODUCTS						
XYREM SOL 500MG/ML	32	3	$295,614.75	$307.93	$9,237.96	0.47%
SUBTOTAL	**32**	**3**	**$295,614.75**	**$307.93**	**$9,237.96**	**0.47%**
AMPHETAMINE PRODUCTS						
DYANAVEL XR SUS 2.5MG/ML	8	1	$2,178.22	$8.93	$272.28	0.00%
EVEKEO TAB 10MG	7	1	$1,224.09	$5.83	$174.87	0.00%
ADZENYS XR TAB 12.5MG	3	1	$866.16	$9.62	$288.72	0.00%
ADZENYS XR TAB 3.1MG	2	1	$577.44	$9.62	$288.72	0.00%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
SUBTOTAL	20	4	$4,845.91	$8.02	$242.30	0.01%
TOTAL	341,869	41,730*	$62,239,990.72	$6.13	$182.06	100 %

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

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[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 04/2017. Last accessed 05/23/2017.
[2] U.S. Food and Drug Administration (FDA). NDA Approval: Vyvanse® Chewable Tablets. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2017/208510Orig1s000ltr.pdf. Issued 01/28/2017. Last accessed 05/23/2017.
[3] Vyvanse® Prescribing Information. Shire U.S. Inc. Available online at: http://pi.shirecontent.com/PI/PDFs/Vyvanse_USA_ENG.pdf. Last revised 04/2017. Last accessed 05/23/2017.
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Appendix L

Calendar Year 2016 Annual Review of Atypical Antipsychotic Medications and 30-Day Notice to Update the Atypical Antipsychotic Prior Authorization Criteria and Tier Chart

Oklahoma Health Care Authority
June 2017

Current Prior Authorization Criteria

Tier-1 products are available without prior authorization for ages five years and older. Prior authorization requests for members younger than five years of age are reviewed by an Oklahoma Health Care Authority (OHCA)-contracted child psychiatrist.

Atypical Antipsychotic Tier-2 Approval Criteria:

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

Atypical Antipsychotic Tier-3 Approval Criteria:

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

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

- Authorization of Seroquel XR® (quetiapine extended-release), Symbyax® (olanzapine/fluoxetine), or Rexulti® (brexpiprazole) for a diagnosis of major depressive

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

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

Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
ER = extended-release
*Mandatory generic plan applies
◊ Does not count toward a Tier-1 trial
∞ In addition to tier trials, use of Invega® Trinza™ requires members to have been adequately treated with the 1-month paliperidone extended-release injection (Invega® Sustenna®) for at least four months.
¥ Aripiprazole (Abilify®) orally disintegrating tablets (ODT) are considered a special formulation and will require a patient-specific, clinically significant reason why a special formulation product is needed in place of the regular tablet formulation.

Utilization of Atypical Antipsychotic Medications: Calendar Year 2016

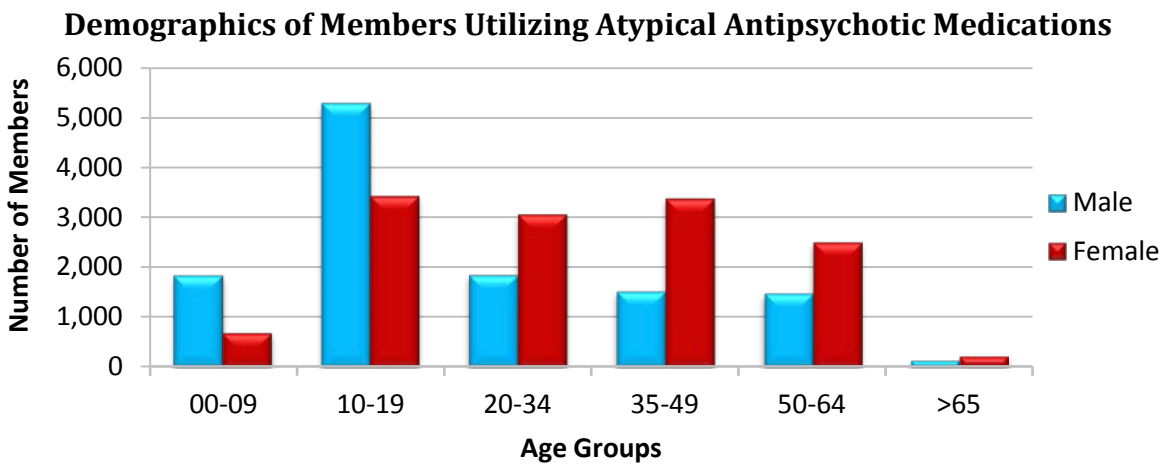
Comparison of Calendar Years

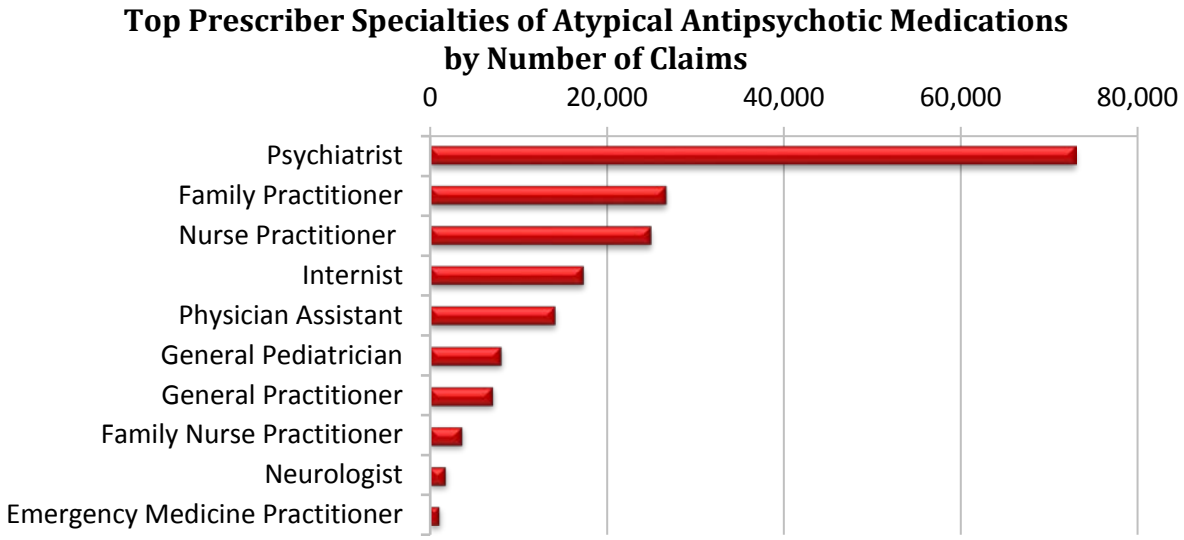
Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2015	25,230	176,550	$55,588,255.60	$314.86	$10.33	7,276,633	5,381,674
2016	25,376	181,449	$42,762,939.44	$235.67	$7.69	7,448,029	5,557,548
% Change	**0.60%**	**2.80%**	**-23.10%**	**-25.20%**	**-25.60%**	**2.40%**	**3.30%**
Change	**146**	**4,899**	**-$12,825,316.16**	**-$79.19**	**-$2.64**	**171,396**	**175,874**

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

- In 2015, aripiprazole became generically available, but due to the large federal rebate on the brand formulation, brand name Abilify® was preferred for four months of calendar year 2016.
- Aggregate drug rebates collected during calendar year 2015 for atypical antipsychotic medications: $38,220,344.65Δ

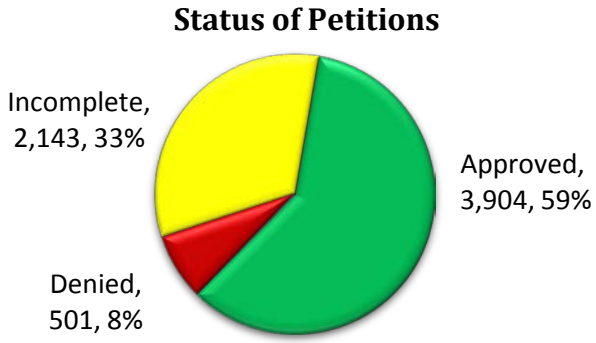
Δ Important considerations: Aggregate drug rebates are based on the date the claim is paid rather than the date dispensed. Claims data are based on the date dispensed. Calendar year 2015 claims data includes Indian Health Service providers; aggregated drug rebates do not.





Prior Authorization of Atypical Antipsychotic Medications

There were 6,548 prior authorization requests submitted for atypical antipsychotic medications during calendar year 2016. Computer edits are in place to detect lower tiered medications in a member's recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions.



There were 87 prior authorization requests submitted for a total of 69 unique members for atypical antipsychotics medications during calendar year 2016 that were referred for a psychiatric consultation. Most requests were for children between 3 and 4 years of age. The following chart shows the status of the submitted petitions.

Status of Psychiatric Consultations

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

Anticipated Patent Expiration(s):

- Saphris® (asenapine sublingual tablets): October 2026
- Rexulti® (brexpiprazole tablets): February 2027
- Vraylar™ (cariprazine capsules): December 2028
- Invega® Sustenna® (paliperidone injection): January 2031
- Latuda® (lurasidone tablets): November 2031
- Fanapt® (iloperidone tablets): December 2031
- Aristada® (aripiprazole lauroxil injection): March 2035

News:

- **November 2016:** The U.S. Food and Drug Administration (FDA) approved an Abbreviated New Drug Application (ANDA) for the first generic Seroquel® XR (quetiapine extended-release [ER]). There are currently five generic manufacturers, four of which were FDA approved in May of 2017.
- **January 2017:** The FDA approved an expanded indication for Latuda® (lurasidone) to be used for the treatment of schizophrenia in adolescents 13 to 17 years of age. This is in addition to the original U.S. indications for the treatment of adults with schizophrenia and for the treatment of adults with major depressive episodes associated with bipolar I disorder (bipolar depression) as monotherapy and as adjunctive therapy with lithium or valproate. In February 2017, topline results from a study evaluating Latuda® in children and adolescents age 10 to 17 years with bipolar depression met its primary endpoint and a supplemental New Drug Application (sNDA) is anticipated to be submitted to the FDA during 2017 pursuing this indication.
- **June 2017:** The FDA approved an additional strength and dosing schedule of Aristada® (aripiprazole lauroxil injection). Aristada® 1,064mg is recommended to be administered every two months for the treatment of schizophrenia. Aristada® was previously available in the following strengths and dosing: 441mg, 662mg, and 882mg administered once monthly and 882mg administered every six weeks.

Pipeline:

- **October 2016:** Results from the clinical development program in schizophrenia of ITI-007 60mg, an investigational atypical antipsychotic, was announced at the CNS Summit 2016 Annual Conference. ITI-007 improved symptoms of schizophrenia in three placebo-controlled trials; however, only showed statistical significance in two of the three studies, possibly in part due to an unusually high placebo response. ITI-007 is currently in Phase 3 trials for schizophrenia and in Phase 1 and 2 trials for seven other indications.

Medicaid Drug Rebate Program[8,9,10]

Medicaid coverage of a drug requires the manufacturer to have a federal rebate agreement with the Secretary of Health and Human Services (HHS). Rebate amounts are based on the "best price" for each drug. Best price refers to the lowest price paid to a manufacturer for a drug by any payer. Best prices are reported to the Centers for Medicare & Medicaid Services (CMS) by the manufacturer, but are not publicly available.

If a drug's price increases more quickly than inflation, an additional rebate penalty is included based on the change in price compared with the consumer price index (CPI). The CPI penalty of the federal rebate is designed to keep Medicaid net cost relatively flat despite increases in drug prices. Until the first quarter of 2017, the CPI penalty only applied to brand medications; however, following a senate vote in October 2015, the Medicaid CPI penalty was extended to generic drugs with an effective date of January 1, 2017. Generic drugs became a concern of Congress after a letter to the Office of Inspector General noted that between July 2013 and June 2014, half of all generic drugs increased in price, 10% of which doubled in price during that time period. As average wholesale price (AWP) increases, the rebated amount per unit (RAPU) increases as well, resulting in minimal effect on Medicaid net cost.

Additionally, many states have negotiated supplemental rebate agreements with manufacturers to produce added rebates. The Atypical Antipsychotic Medications Product Based Prior Authorization (PBPA) category is heavily influenced by supplemental rebates. In calendar year 2015, the Oklahoma Health Care Authority (OHCA) collected $38,220,344.65 in aggregate drug rebates for atypical antipsychotic medications. These rebates are collected after reimbursement for the medication and are not reflected in this report. The costs included in this report do not reflect net costs.

Recommendations

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

1. In addition to the Tier-3 criteria requirements for consideration of Symbyax® (olanzapine/fluoxetine), approval would require a patient-specific, clinically significant reason why the member could not use olanzapine and fluoxetine as individual components, both of which are available without prior authorization.

2. The movement of Seroquel® XR (quetiapine extended-release) to Tier-1 of the Atypical Antipsychotics PBPA Tier chart once the cost is comparable to other Tier-1 generic medications.
3. A trial of Seroquel® XR (*pending Tier-1 move*) will be required for approval of Latuda® (lurasidone) for a diagnosis of bipolar depression. A trial of Abilify® (aripiprazole) is not required for this diagnosis.

Atypical Antipsychotics*		
Tier-1	**Tier-2**	**Tier-3**
aripiprazole (Abilify®)¥	aripiprazole (Abilify Maintena®)	brexpiprazole (Rexulti®)
clozapine (Clozaril®)◊	aripiprazole lauroxil (Aristada®)	cariprazine (Vraylar™)
olanzapine (Zyprexa®)	asenapine (Saphris®)	clozapine (Fazaclo®)
quetiapine (Seroquel®)		clozapine oral suspension (Versacloz™)
quetiapine ER (Seroquel XR®)**	**lurasidone (Latuda®)±**	iloperidone (Fanapt®)
risperidone (Risperdal®)	paliperidone (Invega® Sustenna®)	**olanzapine/fluoxetine (Symbyax®)α**
risperidone (Risperdal Consta®)	paliperidone (Invega® Trinza™)∞	paliperidone (Invega®)
ziprasidone (Geodon®)		

Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
ER = extended-release
*Mandatory generic plan applies
◊ Does not count toward a Tier-1 trial
∞ In addition to tier trials, use of Invega® Trinza™ requires members to have been adequately treated with the 1-month paliperidone extended-release injection (Invega® Sustenna®) for at least four months.
¥ Aripiprazole (Abilify®) orally disintegrating tablets (ODT) are considered a special formulation and will require a patient-specific, clinically significant reason why a special formulation product is needed in place of the regular tablet formulation.
** Seroquel® XR (quetiapine ER) move to Tier-1 dependent on generic cost.
± Latuda® (lurasidone) requires a trial of Seroquel® XR (quetiapine ER) (*pending Tier-1 move*) for a diagnosis of bipolar depression. A trial of Abilify® (aripiprazole) is not required for this diagnosis.
α In addition to the Tier-3 criteria requirements, approval requires a patient-specific, clinically significant reason why the member cannot use olanzapine and fluoxetine as individual components.

Utilization Details of Atypical Antipsychotic Medications: Calendar Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
TIER-1 PRODUCTS						
RISPERIDONE ORAL PRODUCTS						
RISPERIDONE TAB 1MG	14,544	3,447	$135,191.75	$0.30	$9.30	0.32%
RISPERIDONE TAB 0.5MG	11,941	3,010	$98,652.36	$0.27	$8.26	0.23%
RISPERIDONE TAB 2MG	7,719	1,753	$72,530.80	$0.30	$9.40	0.17%
RISPERIDONE TAB 0.25MG	5,991	1,496	$56,441.27	$0.31	$9.42	0.13%
RISPERIDONE TAB 3MG	3,940	759	$41,169.36	$0.33	$10.45	0.10%
RISPERIDONE TAB 4MG	2,030	371	$21,636.55	$0.34	$10.66	0.05%
RISPERIDONE SOL 1MG/ML	906	177	$34,133.11	$1.14	$37.67	0.08%
RISPERIDONE TAB 0.5MG	326	91	$16,188.18	$1.70	$49.66	0.04%
RISPERIDONE TAB 2MG	145	38	$14,245.66	$2.81	$98.25	0.03%
RISPERIDONE TAB 1MG	120	52	$6,293.66	$1.76	$52.45	0.01%
RISPERIDONE TAB 0.25	53	15	$8,190.25	$5.29	$154.53	0.02%
RISPERIDONE TAB 3MG	38	12	$10,942.13	$9.53	$287.95	0.03%
RISPERDAL TAB 2MG	15	2	$14,399.38	$32.00	$959.96	0.03%
RISPERDAL SOL 1MG/ML	14	2	$12,424.07	$29.58	$887.43	0.03%
RISPERDAL TAB 4MG	13	1	$23,335.91	$61.74	$1,795.07	0.05%
RISPERIDONE TAB 4MG	12	5	$1,870.70	$5.23	$155.89	0.00%
RISPERDAL TAB 3MG	12	1	$13,474.56	$37.43	$1,122.88	0.03%
RISPERDAL TAB 1MG	6	1	$5,355.03	$29.75	$892.51	0.01%
RISPERDAL TAB 0.5MG	3	1	$818.22	$9.09	$272.74	0.00%
SUBTOTAL	**47,828**	**11,234**	**$587,292.95**	**$0.40**	**$12.28**	**1.36%**
QUETIAPINE PRODUCTS						
QUETIAPINE TAB 100MG	11,155	3,287	$112,695.84	$0.32	$10.10	0.26%
QUETIAPINE TAB 50MG	8,163	2,592	$76,245.78	$0.30	$9.34	0.18%
QUETIAPINE TAB 200MG	7,745	2,093	$104,599.37	$0.43	$13.51	0.24%
QUETIAPINE TAB 300MG	7,610	1,728	$143,710.83	$0.60	$18.88	0.34%
QUETIAPINE TAB 400MG	5,728	1,084	$110,180.29	$0.61	$19.24	0.26%
QUETIAPINE TAB 25MG	5,054	1,647	$40,775.05	$0.26	$8.07	0.10%
SEROQUEL TAB 400MG	12	1	$14,730.96	$40.92	$1,227.58	0.03%
SEROQUEL TAB 300MG	10	1	$14,833.83	$52.23	$1,483.38	0.03%
SUBTOTAL	**45,477**	**12,433**	**$617,771.95**	**$0.43**	**$13.58**	**1.44%**
CLOZAPINE PRODUCTS						
CLOZAPINE TAB 100MG	6,070	455	$382,491.89	$3.27	$63.01	0.89%
CLOZAPINE TAB 200MG	1,661	145	$133,527.77	$4.63	$80.39	0.31%
CLOZAPINE TAB 50MG	1,445	130	$56,062.66	$2.32	$38.80	0.13%
CLOZAPINE TAB 25MG	1,237	113	$32,303.94	$1.50	$26.11	0.08%
CLOZARIL TAB 100MG	58	6	$93,423.23	$55.21	$1,610.75	0.22%
SUBTOTAL	**10,471**	**849**	**$697,809.49**	**$3.61**	**$66.64**	**1.63%**
OLANZAPINE PRODUCTS						
OLANZAPINE TAB 10MG	5,733	1,655	$61,576.03	$0.34	$10.74	0.14%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
OLANZAPINE TAB 20MG	5,481	1,045	$89,614.66	$0.51	$16.35	0.21%
OLANZAPINE TAB 5MG	4,340	1,499	$39,957.29	$0.30	$9.21	0.09%
OLANZAPINE TAB 15MG	2,570	635	$35,224.18	$0.44	$13.71	0.08%
OLANZAPINE TAB 2.5MG	1,215	439	$10,240.84	$0.27	$8.43	0.02%
OLANZAPINE TAB 20MG	555	181	$104,958.65	$3.66	$189.11	0.25%
OLANZAPINE TAB 7.5MG	537	178	$6,180.62	$0.37	$11.51	0.01%
OLANZAPINE TAB 10MG	454	183	$41,879.71	$2.24	$92.25	0.10%
OLANZAPINE TAB 15MG	244	100	$33,864.18	$3.01	$138.79	0.08%
OLANZAPINE TAB 5MG	160	86	$7,419.38	$1.46	$46.37	0.02%
ZYPREXA TAB 20MG	26	2	$30,366.96	$38.93	$1,167.96	0.07%
ZYPREXA TAB 15MG	12	1	$10,510.44	$29.20	$875.87	0.02%
ZYPREXA TAB 5MG	12	1	$4,026.96	$12.91	$335.58	0.01%
ZYPREXA TAB 10MG	11	1	$6,421.58	$19.46	$583.78	0.02%
SUBTOTAL	**21,350**	**6,006**	**$482,241.48**	**$0.70**	**$22.59**	**1.12%**
ZIPRASIDONE PRODUCTS						
ZIPRASIDONE CAP 40MG	2,789	944	$122,938.60	$1.45	$44.08	0.29%
ZIPRASIDONE CAP 80MG	2,709	501	$144,005.85	$1.70	$53.16	0.34%
ZIPRASIDONE CAP 20MG	2,525	923	$109,283.43	$1.44	$43.28	0.26%
ZIPRASIDONE CAP 60MG	1,817	485	$94,112.99	$1.70	$51.80	0.22%
GEODON CAP 80MG	12	1	$6,512.49	$18.09	$542.71	0.02%
GEODON CAP 40MG	8	1	$7,115.99	$29.65	$889.50	0.02%
GEODON INJ 20MG	6	6	$1,257.46	$48.36	$209.58	0.00%
SUBTOTAL	**9,866**	**2,861**	**$485,226.81**	**$1.61**	**$49.18**	**1.15%**
RISPERIDONE INJECTABLE PRODUCTS						
RISPERDAL INJ 50MG	426	55	$620,854.33	$54.41	$1,457.40	1.45%
RISPERDAL INJ 25MG	232	49	$130,267.33	$26.19	$561.50	0.30%
RISPERDAL INJ 37.5MG	181	32	$191,672.07	$41.45	$1,058.96	0.45%
RISPERDAL INJ 12.5MG	63	11	$21,033.77	$13.03	$333.87	0.05%
SUBTOTAL	**902**	**147**	**$963,827.50**	**$42.60**	**$1,068.54**	**2.25%**
ARIPIPRAZOLE ORAL PRODUCTS						
ARIPIPRAZOLE TAB 10MG	5,062	1,350	$690,264.41	$4.30	$136.36	1.61%
ARIPIPRAZOLE TAB 5MG	4,637	1,390	$834,453.45	$5.78	$179.96	1.95%
ARIPIPRAZOLE TAB 15MG	3,484	895	$452,801.26	$4.10	$129.97	1.06%
ARIPIPRAZOLE TAB 20MG	2,411	595	$483,664.99	$6.33	$200.61	1.13%
ARIPIPRAZOLE TAB 30MG	1,645	339	$358,026.51	$6.42	$217.65	0.84%
ARIPIPRAZOLE TAB 2MG	1,305	397	$181,098.15	$4.46	$138.77	0.42%
ABILIFY TAB 10MG	1,206	694	$1,180,769.86	$30.70	$979.08	2.76%
ABILIFY TAB 5MG	1,069	604	$1,027,501.98	$30.66	$961.18	2.40%
ABILIFY TAB 15MG	860	486	$791,267.16	$29.00	$920.08	1.85%
ABILIFY TAB 20MG	606	340	$870,372.18	$44.23	$1,436.26	2.04%
ABILIFY TAB 30MG	486	252	$689,956.75	$43.05	$1,419.66	1.61%
ABILIFY TAB 2MG	345	192	$317,338.20	$30.23	$919.82	0.74%
ARIPIPRAZOLE SOL 1MG/ML	74	11	$97,735.40	$45.21	$1,320.75	0.23%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
ARIPIPRAZOLE TAB 10MG	1	1	$974.12	$32.47	$974.12	0.00%
SUBTOTAL	**23,191**	**7,546**	**$7,976,224.42**	**$10.84**	**$10.84**	**18.64%**
TIER-1 SUBTOTAL	**159,085**	**41,076**	**$11,810,394.60**	**$2.44**	**$74.24**	**27.59%**
TIER-2 PRODUCTS						
PALIPERIDONE INJECTABLE PRODUCTS						
INVEGA SUST INJ 234/1.5ML	3,218	564	$7,248,769.36	$78.78	$2,252.57	16.95%
INVEGA SUST INJ 156MG/ML	1,435	373	$2,164,997.73	$52.60	$1,508.71	5.06%
INVEGA SUST INJ 117/0.75ML	408	90	$462,328.08	$39.60	$1,133.16	1.08%
INVEGA TRINZ INJ 819MG	329	127	$2,207,810.67	$75.92	$6,710.67	5.16%
INVEGA TRINZ INJ 546MG	191	67	$863,232.60	$51.42	$4,519.54	2.02%
INVEGA TRINZ INJ 410MG	43	18	$144,523.62	$38.42	$3,361.01	0.34%
INVEGA SUST INJ 78/0.5ML	37	15	$27,398.36	$26.09	$740.50	0.06%
INVEGA TRINZ INJ 273MG	17	6	$38,686.91	$25.69	$2,275.70	0.09%
INVEGA SUST INJ 39/0.25ML	15	5	$5,598.16	$13.27	$373.21	0.01%
SUBTOTAL	**5,693**	**1,265**	**$13,163,345.49**	**$66.66**	**$2,312.20**	**30.77%**
LURASIDONE PRODUCTS						
LATUDA TAB 40MG	2,022	603	$2,263,357.11	$33.17	$1,119.37	5.29%
LATUDA TAB 80MG	1,705	377	$2,146,691.37	$37.92	$1,259.06	5.02%
LATUDA TAB 20MG	1,050	336	$1,078,117.14	$32.45	$1,026.78	2.52%
LATUDA TAB 120MG	880	183	$1,436,801.76	$49.04	$1,632.73	3.36%
LATUDA TAB 60MG	800	251	$824,974.58	$32.56	$1,031.22	1.93%
SUBTOTAL	**6,457**	**1,750**	**$7,749,941.96**	**$36.44**	**$1,200.24**	**18.12%**
QUETIAPINE EXTENDED-RELEASE PRODUCTS						
SEROQUEL XR TAB	841	146	$787,950.72	$29.70	$936.92	1.84%
SEROQUEL XR TAB	837	135	$985,992.46	$36.15	$1,178.01	2.31%
SEROQUEL XR TAB	294	65	$167,349.87	$17.53	$569.22	0.39%
SEROQUEL XR TAB	292	68	$151,048.87	$15.96	$517.29	0.35%
SEROQUEL XR TAB 50MG	230	54	$85,261.12	$12.30	$370.70	0.20%
QUETIAPINE TAB 400MG	66	50	$71,829.86	$31.57	$1,088.33	0.17%
QUETIAPINE TAB 300MG	56	46	$42,914.54	$24.14	$766.33	0.10%
QUETIAPINE TAB 200MG	12	9	$5,114.43	$11.37	$426.20	0.01%
QUETIAPINE TAB 150MG	11	8	$4,529.17	$13.64	$411.74	0.01%
QUETIAPINE TAB 50MG	11	8	$3,358.63	$10.18	$305.33	0.01%
SUBTOTAL	**2,650**	**589**	**$2,305,349.67**	**$27.15**	**$869.94**	**5.39%**
ARIPIPRAZOLE LAROXIL INJECTABLE PRODUCTS						
ARISTADA INJ 882MG/3.2ML	86	20	$193,754.44	$77.01	$2,252.96	0.45%
ARISTADA INJ 662MG/2.4ML	42	11	$71,479.62	$55.93	$1,701.90	0.17%
ARISTADA INJ 441MG/1.6ML	16	8	$18,234.57	$39.13	$1,139.66	0.04%
SUBTOTAL	**144**	**39**	**$283,468.63**	**$66.54**	**$1,968.53**	**0.66%**
ASENAPINE PRODUCTS						
SAPHRIS SUB 10MG	695	156	$596,384.52	$28.52	$858.11	1.39%
SAPHRIS SUB 5MG	492	131	$379,583.06	$25.45	$771.51	0.89%
SAPHRIS SUB 2.5MG	107	44	$88,572.68	$26.81	$827.78	0.21%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
SUBTOTAL	**1,294**	**331**	**$1,064,540.26**	**$27.20**	**$822.67**	**2.49%**
ARIPIPRAZOLE INJECTABLE PRODUCTS						
ABILIFY MAIN INJ 400MG	1,092	176	$2,018,585.20	$64.53	$1,848.52	4.72%
ABILIFY MAIN INJ 300MG	151	36	$209,528.60	$48.23	$1,387.61	0.49%
SUBTOTAL	**1,243**	**212**	**$2,228,113.80**	**$62.55**	**$1,792.53**	**5.21%**
TIER-2 SUBTOTAL	**17,481**	**4,186**	**$26,794,759.81**	**$46.67**	**$1,532.79**	**62.64%**
TIER-3 PRODUCTS						
PALIPERIDONE ORAL PRODUCTS						
PALIPERIDONE TAB ER	1,321	280	$947,300.81	$23.62	$717.11	2.22%
PALIPERIDONE TAB ER	750	139	$625,795.06	$25.93	$834.39	1.46%
PALIPERIDONE TAB ER	642	153	$333,558.03	$16.78	$519.56	0.78%
PALIPERIDONE TAB ER	107	21	$51,252.26	$17.34	$478.99	0.12%
INVEGA TAB 6MG	6	3	$9,683.26	$53.80	$1,613.88	0.02%
SUBTOTAL	**2,826**	**596**	**$1,967,589.42**	**$22.55**	**$696.25**	**4.60%**
ILOPERIDONE PRODUCTS						
FANAPT TAB 8MG	241	33	$230,225.78	$34.31	$955.29	0.54%
FANAPT TAB 6MG	219	41	$226,695.90	$35.85	$1,035.14	0.53%
FANAPT TAB 12MG	218	30	$381,878.16	$59.08	$1,751.73	0.89%
FANAPT TAB 4MG	132	23	$100,998.81	$25.71	$765.14	0.24%
FANAPT TAB 2MG	67	12	$62,815.27	$31.19	$937.54	0.15%
FANAPT TAB 10MG	65	13	$117,889.26	$61.69	$1,813.68	0.28%
FANAPT TAB 1MG	2	2	$1,017.49	$32.82	$508.75	0.00%
SUBTOTAL	**944**	**154**	**$1,121,520.67**	**$40.96**	**$1,188.05**	**2.63%**
CLOZAPINE ORALLY DISINTEGRATING PRODUCTS						
CLOZAPINE TAB 100/ODT	288	29	$222,357.01	$27.11	$772.07	0.52%
FAZACLO TAB 100 ODT	104	13	$149,397.52	$54.97	$1,436.51	0.35%
FAZACLO TAB 150 ODT	52	7	$76,856.37	$49.17	$1,478.01	0.18%
CLOZAPINE TAB 200/ODT	52	5	$77,314.75	$50.66	$1,486.82	0.18%
FAZACLO TAB 200 ODT	48	3	$63,480.69	$65.78	$1,322.51	0.15%
CLOZAPINE TAB 150/ODT	47	6	$30,939.74	$32.36	$658.29	0.07%
CLOZAPINE TAB 25MG ODT	43	6	$7,683.68	$6.61	$178.69	0.02%
SUBTOTAL	**660**	**73**	**$643,577.91**	**$36.06**	**$975.12**	**1.51%**
OLANZAPINE/FLUOXETINE COMBINATION PRODUCTS						
OLANZA/FLUOX CAP 12-50MG	26	5	$23,483.45	$21.16	$903.21	0.05%
OLANZA/FLUOX CAP 3-25MG	16	2	$2,063.58	$4.30	$128.97	0.00%
OLANZA/FLUOX CAP 6-25MG	13	5	$5,633.83	$9.39	$433.37	0.01%
OLANZA/FLUOX CAP 6-50MG	12	2	$3,985.24	$11.07	$332.10	0.01%
OLANZA/FLUOX CAP 12-25MG	9	2	$8,941.35	$17.53	$993.48	0.02%
SUBTOTAL	**76**	**16**	**$44,107.45**	**$14.41**	**$580.36**	**0.09%**
BREXPIPRAZOLE PRODUCTS						
REXULTI TAB 2MG	127	50	$124,404.58	$32.33	$979.56	0.29%
REXULTI TAB 4MG	67	19	$66,991.12	$32.52	$999.87	0.16%
REXULTI TAB 1MG	21	11	$19,728.32	$31.17	$939.44	0.05%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
REXULTI TAB 3MG	19	10	$22,446.97	$32.53	$1,181.42	0.05%
REXULTI TAB 0.5MG	8	6	$6,166.17	$30.38	$770.77	0.01%
REXULTI TAB 0.25MG	2	1	$1,973.38	$32.89	$986.69	0.00%
SUBTOTAL	**244**	**97**	**$241,710.54**	**$32.25**	**$990.62**	**0.56%**
CARIPRAZINE PRODUCTS						
VRAYLAR CAP 3MG	75	31	$80,808.26	$35.50	$1,077.44	0.19%
VRAYLAR CAP 6MG	25	9	$27,214.16	$35.48	$1,088.57	0.06%
VRAYLAR CAP 1.5MG	16	11	$13,963.30	$35.53	$872.71	0.03%
VRAYLAR CAP 4.5MG	16	7	$17,041.82	$35.50	$1,065.11	0.04%
VRAYLAR CAP 1.5-3MG	1	1	$251.50	$35.93	$251.50	0.00%
SUBTOTAL	**133**	**59**	**$139,279.04**	**$35.50**	**$1,047.21**	**0.32%**
TIER-3 SUBTOTAL	**4,883**	**995**	**$4,157,785.03**	**$28.29**	**$851.48**	**9.71%**
TOTAL	**181,449**	**25,376***	**$42,762,939.44**	**$7.69**	**$235.67**	**100%**

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

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[3] Intra-Cellular Therapies Press Release: Intra-Cellular Therapies Presents the ITI-007 Clinical Development Program in Schizophrenia at the CNS Summit 2016 Annual Conference. Available online at: http://ir.intracellulartherapies.com/releasedetail.cfm?ReleaseID=996298. Issued 10/2016. Last accessed 05/2017.

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Appendix M

Calendar Year 2016 Annual Review of Huntington's Disease (HD) Medications and 30-Day Notice to Prior Authorize Austedo™ (Deutetrabenazine) and Xenazine® (Tetrabenazine)

Oklahoma Health Care Authority
June 2017

Introduction[1,2,3,4]

Huntington's disease (HD) is a hereditary, progressive neurodegenerative disorder characterized by choreiform movements, psychiatric symptoms, and dementia. HD is caused by an excess number of cytosine-adenine-guanine (CAG) trinucleotide repeats in the huntingtin (HTT) gene on chromosome four resulting in a protein with an abnormally long polyglutamine sequence. Although the effects of the prolonged polyglutamine sequence in the huntingtin protein are not fully understood, it is thought to be toxic to brain cells. HD is inherited in an autosomal dominant fashion meaning every child of an affected parent has a 50% chance of developing the disease. The prevalence of HD in North America is estimated to be 5.7 per 100,000; other data indicate there are currently 30,000 symptomatic Americans and more than 200,000 at risk of inheriting the disease.

The diagnosis of HD is normally based on the presence of typical clinical features and a family history of the disease. HD can be confirmed via highly sensitive and specific genetic testing. Genetic testing is particularly valuable if there is an unknown or negative family history. HD genetic testing impacts the entire family due to the implications for other at risk family members. It is recommended that genetic counseling be sought before and after the testing process.

HD is characterized by a triad of motor, cognitive, and psychiatric symptoms. Motor symptoms are a key feature of HD and include chorea and the impairment of voluntary movements. Chorea is a sudden, involuntary, arrhythmic movement; chorea is more prominent in the upper extremities early in the disease but as the disease progresses chorea may include the face, trunk, and legs. Chorea typically increases in frequency and amplitude as the disease progresses with a peak approximately 10 years after disease onset. In late HD, chorea may decline and be replaced by a parkinsonian akinetic-rigid state. Cognitive symptoms of HD are progressive and are characterized by a reduction of speed and flexibility in mental processing. Psychiatric symptoms include depression, irritability, and anxiety. HD is also associated with an increased suicide risk which may be as high as 20% among HD mutation carriers and 7% among affected individuals.

HD symptoms have a wide range of age of onset, with motor symptoms most commonly arising in the fourth and fifth decade of life. Approximately 10% of HD patients will have symptoms prior to age 20 years which is considered Juvenile HD. The main determinant of age of onset is

the number of CAG repeats in the HTT gene; individuals with the earliest onset tend to have the largest expansion in the number of CAG repeats.

The average length of survival following an HD diagnosis is 10 to 20 years. The progression of HD is divided into three phases: early stage HD, middle stage HD, and late stage HD. Staging of HD is evaluated by the Total Functional Capacity Rating Scale, a tool that assesses a patient's independence by evaluating their ability to perform their occupation, finances, domestic chores, activities of daily living, and needed care level. In early stage HD, patients are frequently able to continue working; patients may have minor chorea, difficulty in solving complex problems, and depression. In middle stage HD, patients often lose their ability to work and symptoms include prominent chorea, difficulty with voluntary motor tasks, and difficulty problem solving. In late stage HD, patients require assistance in all activities of daily living and are often non-verbal. Chorea may be replaced by rigidity and bradykinesia.

Chorea in Huntington's Disease Treatment Summary[5,6,7,8]

Current guidelines for the treatment of chorea in HD recommend Xenazine® (tetrabenazine), amantadine, or riluzole. Austedo™ (deutetrabenazine) has not yet been evaluated for incorporation into the HD chorea treatment guidelines. Of the three recommended therapies, tetrabenazine is the only U.S. Food and Drug Administration (FDA) approved therapy for the treatment of chorea in HD, and the only therapy found to be likely effective in decreasing HD chorea to a very important degree. It is important to note that although the Unified Huntington's Disease Rating Scale (UHDRS) is the main outcome measure for HD studies, a "clinically important change on the UHDRS remains undefined." [5] The motor portion of the UHDRS scale measures chorea, parkinsonism, dystonia, eye movements, and other motor symptoms. Total Maximal Chorea Score (TMCS), a subscale of the UHDRS, rates chorea from 0 to 4 (with 0 representing no chorea) for seven different parts of the body. The total score ranges from 0 to 28. Since different motor features have different influences on activities of daily living, the guidelines recommend a minimal clinically important difference for UHDRS scores be studied and established. For purposes of evaluating studies, the guidelines designated a 2 to less than 3 point decrease in total motor subscore moderately important and greater than a 3 point decrease very important.

Xenazine® (Tetrabenazine) Efficacy Study:
The efficacy of tetrabenazine as a treatment for chorea of HD was established primarily in a randomized, double-blind, placebo-controlled, multi-center trial conducted in ambulatory patients with a diagnosis of HD. The diagnosis of HD was based on family history, neurological exam, and genetic testing. Treatment duration was 12 weeks, including a seven week dose titration period and a five week maintenance period. Tetrabenazine was started at a dose of 12.5mg per day, followed by upward titration at weekly intervals, in 12.5mg increments until satisfactory control of chorea was achieved, intolerable side effects occurred, or until a maximal dose of 100mg per day was reached. The primary efficacy endpoint was the TMCS. TMCS for patients in the tetrabenazine group declined by an estimated 5.0 units during maintenance therapy (average of Week 9 and Week 12 scores versus baseline), compared to an estimated 1.5 units in the placebo group. The treatment effect of -3.5 units was statistically significant

($p < 0.05$). About 7% of placebo patients had a 6-unit or greater improvement compared to 50% of tetrabenazine-treated patients. A physician-rated Clinical Global Impression (CGI) favored tetrabenazine statistically. In general, measures of functional capacity and cognition showed no difference between tetrabenazine and placebo. However, one functional measure (Part 4 of the UHDRS), a 25-item scale assessing the capacity for patients to perform certain activities of daily living, showed a decrement for patients treated with tetrabenazine compared to placebo, a difference that was nominally statistically significant. A 3-item cognitive battery specifically developed to assess cognitive function in patients with HD (Part 2 of the UHDRS) also showed a decrement for patients treated with tetrabenazine compared to placebo, but the difference was not statistically significant.

Austedo™ (Deutetrabenazine) Efficacy Study:

The efficacy of deutetrabenazine as a treatment for chorea associated with HD was evaluated in a randomized, double-blind, placebo controlled trial in 90 ambulatory patients with manifest chorea associated with HD. The diagnosis of HD was based on family history, neurological exam, and genetic testing. Treatment duration was 12 weeks, including an 8-week dose titration period and a 4-week maintenance period. Deutetrabenazine was started at 6mg per day and titrated upward, at weekly intervals, in 6mg increments until satisfactory treatment of chorea was achieved, intolerable side effects occurred, or until a maximal dose of 48mg per day was reached. The primary efficacy endpoint was the TMCS. The mean dose after titration was 40mg per day. TMCS for patients receiving deutetrabenazine improved by approximately 4.4 units from baseline to the maintenance period (average of Week 9 and Week 12), compared to approximately 1.9 units in the placebo group. The treatment effect of -2.5 units was statistically significant ($p<0.0001$). A patient-rated global impression of change assessed how patients rated their overall HD symptoms. A total of 51% of patients treated with deutetrabenazine rated their symptoms as “Much Improved” or “Very Much Improved” at the end of treatment, compared to 20% of placebo-treated patients. In a physician-rated CGI of change, 42% percent of patients treated with deutetrabenazine had their symptoms rated as “Much Improved” or “Very Much Improved” at the end of treatment compared to 13% of placebo-treated patients.

Indirect Treatment Comparison:

There are currently no head-to-head clinical studies between tetrabenazine and deutetrabenazine. The makers of deutetrabenazine, Teva Pharmaceuticals, funded an indirect tolerability comparison of the two medications. The authors compared Phase 3, 12-week, placebo-controlled clinical trials of tetrabenazine and deutetrabenazine with the purpose of evaluating tolerability and adverse events. Overall adverse events (AEs), serious AEs, specific AEs occurring in greater than or equal to 10% of patients, and discontinuations were analyzed. A placebo-adjusted risk was subtracted for both medications to estimate the risk differences of each outcome. The following table contains some of the clinically relevant results of the indirect treatment comparison study.

Parameter	Unadjusted Risk Difference	Adjusted Risk Difference
Any AE	DTB vs TBZ: -20.7 p=0.135	DTB vs TBZ: -35.3 p=0.063
Moderate-to-Severe AE	DTB vs TBZ: -39.6 p=0.005	DTB vs TBZ: -46.4 p=0.006
Mild AE	DTB vs TBZ: 18.9 p=0.194	DTB vs TBZ: 11.1 p=0.540
Discontinuation Due to AE	DTB vs TBZ: -9.3 p=0.065	DTB vs TBZ: -10.4 p=0.041
Dose Reduction Due to AE	DTB vs TBZ: -41.1 p <0.001	DTB vs TBZ: -40.5 p <0.001

AE = adverse event, DTB = deutetrabenazine, TBZ = tetrabenazine

Cost Comparison:

Medication	Maximum Daily Dose	Cost per Unit	Cost per Day	Cost per 30 Days
Austedo™ (deutetrabenazine) 12mg	48mg	$82.20	$328.80	$9,864.00
Xenazine® (tetrabenazine) 25mg	100mg	$208.46	$833.84	$25,015.20*
tetrabenazine 25mg	100mg	$126.09	$504.36	$15,130.80

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.
*Was FDA approved in 2008 and has a significant federal rebate.

Xenazine® (Tetrabenazine) Off-Label Uses[9,10,11]

The Centers for Medicare and Medicaid Services (CMS) specifies a list of compendia approved for use in determining a "medically-accepted indication" of an off-label drug. Thompson Micromedex DrugDex® is considered an approved compendia for this use. Off-label or non-FDA approved indications that DrugDex® lists as "Class I, Class IIa, or Class IIb" recommendations and/or efficacy are considered medically accepted indications for the purposes of determining coverage policies. IIb is the lowest level of accepted recommendations for off-label use, and is described as "recommended in some cases" and "the given treatment may be useful and is indicated in some, but not most cases."[9] The following table contains off-label uses of tetrabenazine with a recommendation rating of IIb or better. Other vesicular monoamine transporter-2 (VMAT2) inhibitors are pursuing these indications (see *Market News and Updates* section of this report for details).

Off-Label Uses of Tetrabenazine		
	Tardive Dyskinesia (TD)	**Tourette Syndrome**
Compendia Recommendation Level	Adult: IIb	Adult: IIb, Pediatric: IIb
Compendia Summary	"Effective in 50% or more of patients in several studies"[11] "Good efficacy in patients unresponsive to prior regimens"[11]	"Good response observed in up to one-third of patients in uncontrolled studies"[11]

Off-Label Uses of Tetrabenazine		
	Tardive Dyskinesia (TD)	**Tourette Syndrome**
Compendia Cited Studies	• Placebo-controlled study, of 6 patients: tetrabenazine 25mg 2 to 4 times daily for 1 week eliminated phenothiazine-induced facial dyskinesia in half of patients; dyskinesias returned within days of discontinuing tetrabenazine • Tetrabenazine 25mg to 200mg divided daily for a mean of 21 months in 44 TD patients: resulted in a marked reduction in abnormal movements (with excellent functional improvement) in 14% of patients; 57% demonstrated moderate reduction of abnormal movements and good functional improvement	• Tetrabenazine 37.5mg to 150mg for a mean of 14 months in an open trial of 17 patients with a mean age of 20 years (range 1 to 59 years): marked reduction in abnormal movements (with excellent functional improvement) in one patient (6%); 4 patients (23%) demonstrated moderate reduction of abnormal movements (good improvement in function); fair response in 65% of patients

Utilization of HD Medications: Calendar Year 2016

Comparison of Calendar Years

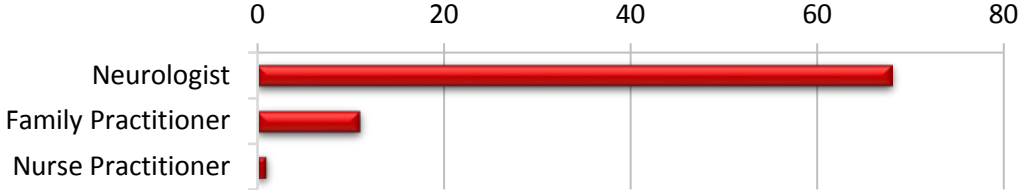
Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2015	14	88	$984,881.93	$11,191.84	$364.77	7,515	2,700
2016	13	80	$960,736.25	$12,009.20	$360.77	6,536	2,663
% Change	**-7.10%**	**-9.10%**	**-2.50%**	**7.30%**	**-1.10%**	**-13.00%**	**-1.40%**
Change	**-1**	**-8**	**-$24,145.68**	**$817.36**	**-$4.00**	**-979**	**-37**

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

Demographics of Members Utilizing HD Medications

- Due to the small number of members utilizing HD medications during calendar year 2016, detailed demographic information could not be provided.

Top Prescriber Specialties of HD Medications by Number of Claims



Market News and Updates[12,13,14,15,16,17,18,19]

Patent Expiration(s):

- Xenazine® (tetrabenazine): There are no unexpired patents for Xenazine®. A generic formulation of tetrabenazine was FDA approved in August 2015 and is currently available.
- Austedo™ (deutetrabenazine): September 2033

New Drug Approval(s):

- **April 2017:** The FDA approved Austedo™ (deutetrabenazine) for the treatment of chorea associated with HD. Deutetrabenazine is a deuterated form of tetrabenazine; deuterium reduces CYP2D6 breakdown subsequently increasing active metabolite half-lives. The increased half-life allows for less frequent daily dosing and may attenuate peak-concentration related neuropsychiatric effects (e.g., sedation) associated with tetrabenazine.
- **April 2017:** The FDA approved Ingrezza™ (valbenazine), a VMAT2 inhibitor similar to Xenazine® and Austedo™, for the treatment of adults with TD. Ingrezza™ is the first FDA approved medication for the treatment of TD.

Pipeline:

- **September 2016:** Teva Pharmaceuticals announced positive results from a placebo-controlled Phase 3 study of Austedo™ (deutetrabenazine) for the treatment of TD. The primary efficacy endpoint was change in Abnormal Involuntary Movement Scale (AIMS) score from baseline to week 12. At week 12, the AIMS rating improved from baseline by -3.3 points for 36mg (p=0.001), -3.2 points for 24mg (p=0.003), and -2.1 for 12mg (p=not significant), compared to -1.4 in placebo. Rates of neuropsychiatric adverse effects were reported to be low. The FDA has accepted a New Drug Application (NDA) for Austedo™ for the treatment of TD with a Prescription Drug User Fee Act (PDUFA) goal date of August 30, 2017. Deutetrabenazine is also in clinical development for the treatment of Tourette syndrome.
- **January 2017:** Neurocrine Biosciences announced results from their eight-week, Phase 2 study of Ingrezza™ (valbenazine) in adults with Tourette syndrome. The primary efficacy endpoint of change-from-baseline in the Yale Global Tic Severity Scale (YGTSS) at week eight was not met (p=0.18); however, results did reveal an improvement in overall symptoms of Tourette syndrome as evidenced by the Clinical Global Impression of Change (p=0.015). Adverse events were reported to be dose dependent and similar to previous clinical studies. The company plans to pursue Phase 3 development of Ingrezza™ in Tourette syndrome.

Austedo™ (Deutetrabenazine) Product Summary[20]

FDA Approval: April 2017

Indication(s): Austedo™ (deutetrabenazine) is a VMAT2 inhibitor indicated for the treatment of chorea associated with HD.

Dosing:

- Austedo™ is supplied as oral tablets in the following strengths: 6mg, 9mg, and 12mg.
- The dose of deutetrabenazine is determined individually for each patient based on tolerability and reduction of chorea.
- The recommended starting dose of deutetrabenazine in patients who are not being switched from tetrabenazine is 6mg once daily. The dose should be titrated at weekly intervals by 6mg per day to a tolerated dose that reduces chorea.
- The maximum recommended daily dose of deutetrabenazine is 48mg (24mg twice daily).
- Total daily doses of 12mg or greater should be administered in two divided doses.
- Deutetrabenazine tablets should be swallowed whole and taken with food.
- When switching patients from tetrabenazine to deutetrabenazine, tetrabenazine should be discontinued and deutetrabenazine should be initiated the following day. The following dosing regimen conversions apply.

Current Tetrabenazine Daily Dosage	Initial Regimen Of Deutetrabenazine
12.5mg	6mg once daily
25mg	6mg twice daily
37.5mg	9mg twice daily
50mg	12mg twice daily
62.5mg	15mg twice daily
75mg	18mg twice daily
87.5mg	21mg twice daily
100mg	24mg twice daily

- The total daily dose of deutetrabenazine should not exceed 36mg (maximum single-dose of 18mg) in patients receiving strong CYP2D6 inhibitors (e.g., quinidine, antidepressants such as paroxetine, fluoxetine, and bupropion).
- The total daily dose of deutetrabenazine should not exceed 36mg (maximum single-dose of 18mg) in patients who are poor CYP2D6 metabolizers.

Boxed Warning: Depression and Suicidality

- Deutetrabenazine can increase the risk of depression and suicidal thoughts and behavior (suicidality) in patients with HD.
- Anyone considering the use of deutetrabenazine must balance the risks of depression and suicidality with the clinical need for treatment of chorea.
- Patients should be closely monitored for the emergence or worsening of depression, suicidality, or unusual changes in behavior. Patients, their caregivers, and families should be informed of the risk of depression and suicidality and should be instructed to report behaviors of concern promptly to the treating prescriber.
- Particular caution should be exercised in treating patients with a history of depression or prior suicide attempts or ideation, which are increased in frequency in patients with HD. Deutetrabenazine is contraindicated in patients who are suicidal, and in patients with untreated or inadequately treated depression.

Mechanism of Action: The effects of deutetrabenazine on chorea are believed to be related to its effect as a reversible depletory of monoamines (e.g., dopamine, serotonin, norepinephrine, and histamine) from nerve terminals. The major circulating metabolites of deutetrabenazine are reversible inhibitors of VMAT2, resulting in decreased uptake of monoamines into synaptic vesicles and depletion of monoamine stores.

Contraindications:

- Patients who are suicidal, or in patients with untreated or inadequately treated depression
- Patients with hepatic impairment
- Patients taking monoamine oxidase inhibitors (MAOIs); deutetrabenazine should not be used in combination with an MAOI or within 14 days of discontinuing therapy with an MAOI
- Patients taking reserpine; at least 20 days should elapse after stopping reserpine before starting deutetrabenazine
- Patients taking tetrabenazine

Safety:

- Clinical Worsening and Adverse Events: HD is a progressive disorder characterized by changes in mood, cognition, chorea, rigidity, and functional capacity over time. VMAT2 inhibitors may cause a worsening in mood, cognition, rigidity, and functional capacity. Prescribers should periodically re-evaluate the need for deutetrabenazine in their patients by assessing the effect on chorea and possible adverse effects. It may be difficult to distinguish between adverse reactions and progression of the underlying disease; decreasing the dose or stopping the drug may help to distinguish between the two possibilities. In some patients, the underlying chorea itself may improve over time, decreasing the need for deutetrabenazine.
- Depression and Suicidality: Patients with HD are at increased risk for depression and suicidal ideation or behaviors. Deutetrabenazine may increase the risk for suicidality in patients with HD. In a 12-week, double-blind, placebo-controlled trial, suicidal ideation was reported by 2% of patients treated with deutetrabenazine, compared to no patients on placebo; depression was reported by 4% of patients treated with deutetrabenazine. All patients treated with deutetrabenazine should be observed for new or worsening depression or suicidality and if depression or suicidality does not resolve, consideration should be given to discontinuing treatment with deutetrabenazine.
- Neuroleptic Malignant Syndrome (NMS): Potentially fatal NMS has been observed in patients receiving tetrabenazine (a closely related VMAT2 inhibitor). Clinicians should be alerted to the signs and symptoms associated with NMS including hyperpyrexia, muscle rigidity, altered mental status, and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmia). The management of NMS should include immediate discontinuation of deutetrabenazine and intensive symptomatic treatment and medical monitoring. Recurrence of NMS has been reported with resumption of drug therapy.

- Akathisia, Agitation, and Restlessness: Deutetrabenazine may increase the risk of akathisia, agitation, and restlessness in patients with HD. In a 12-week, double-blind, placebo-controlled trial, akathisia, agitation, or restlessness was reported by 4% of patients treated with deutetrabenazine, compared to 2% of patients on placebo.
- Parkinsonism: Deutetrabenazine may cause parkinsonism in patients with HD. Because rigidity can develop as part of the underlying disease process, it may be difficult to distinguish between this potential drug-induced adverse reaction and progression of the underlying disease. Drug-induced parkinsonism has the potential to cause more functional disability than untreated chorea for some patients with HD.
- Sedation and Somnolence: Sedation is a common dose-limiting adverse reaction of deutetrabenazine. In a 12-week, double-blind, placebo-controlled trial, 11% of deutetrabenazine-treated patients reported somnolence compared with 4% of patients on placebo and 9% of deutetrabenazine-treated patients reported fatigue compared with 4% of placebo-treated patients.
- Corrected QT (QTc) Interval Prolongation: Tetrabenazine, a closely related VMAT2 inhibitor, causes an increase (about 8msec) in the QTc interval. A clinically relevant QT prolongation may occur in some patients treated with deutetrabenazine who are CYP2D6 poor metabolizers or are co-administered a strong CYP2D6 inhibitor. The use of deutetrabenazine should be avoided in combination with other drugs that are known to prolong QTc. Deutetrabenazine should also be avoided in patients with congenital long QT syndrome and in patients with a history of cardiac arrhythmias.
- Hyperprolactinemia: Tetrabenazine, a closely related VMAT2 inhibitor, elevates serum prolactin concentrations in humans. Tissue culture experiments indicate that approximately one-third of human breast cancers are prolactin-dependent in vitro, a factor of potential importance if deutetrabenazine is being considered for a patient with previously detected breast cancer.
- Binding to Melanin-Containing Tissues: Since deutetrabenazine binds to melanin-containing tissues, it could accumulate in these tissues over time and raise the possibility that deutetrabenazine may cause toxicity in these tissues after extended use.
- Pregnancy: There are no adequate data on the developmental risk associated with the use of deutetrabenazine in pregnant women.
- Lactation: There are no data on the presence of deutetrabenazine or its metabolites in human milk, the effects on the breastfed infant, or the effects of the drug on milk production.
- Pediatric Use: The safety and effectiveness of deutetrabenazine in pediatric patients have not been established.
- Geriatric Use: Clinical studies of deutetrabenazine did not include sufficient numbers of subjects 65 years and older to determine whether they respond differently from younger subjects.
- Hepatic Impairment: In a clinical study conducted with tetrabenazine, a closely related VMAT2 inhibitor, there was a large increase in exposure to tetrabenazine in patients with hepatic impairment. Because of concerns for a greater risk for serious adverse reactions, the use of deutetrabenazine in patients with hepatic impairment is contraindicated.

- Poor CYP2D6 Metabolizers: In patients who do not express the drug metabolizing enzyme, it is likely that the exposure to deutetrabenazine metabolites would be increased similarly to taking a strong CYP2D6 inhibitor (approximately 3-fold). In patients who are CYP2D6 poor metabolizers, the daily dose of deutetrabenazine should not exceed 36mg (maximum single dose of 18mg).

Drug Interactions:

- Strong CYP2D6 Inhibitors: Concomitant use of strong CYP2D6 inhibitors (e.g., paroxetine, fluoxetine, quinidine, bupropion) has been shown to increase the systemic exposure to the active metabolites of deutetrabenazine by approximately 3-fold. The daily dose of deutetrabenazine should not exceed 36mg per day, and a single dose of deutetrabenazine should not exceed 18mg in patients taking strong CYP2D6 inhibitors.
- Reserpine: Reserpine binds irreversibly to VMAT2 and the duration of its effect is several days. At least 20 days should elapse after stopping reserpine before starting deutetrabenazine.
- MAOIs: Deutetrabenazine should not be used in combination with an MAOI, or within 14 days of discontinuing therapy with a MAOI.
- Neuroleptic Drugs: The risk for parkinsonism, NMS, and akathisia may be increased by concomitant use of deutetrabenazine and dopamine antagonists or antipsychotics.
- Alcohol or Other Sedating Drugs: Concomitant use of alcohol or other sedating drugs may have additive effects and worsen sedation and somnolence.
- Drugs That Cause QTc Prolongation: Tetrabenazine, a closely related VMAT2 inhibitor, causes a small increase in QTc interval. The use of deutetrabenazine should be avoided in combination with other drugs that are known to prolong QTc, including antipsychotic medications (e.g., chlorpromazine, haloperidol, thioridazine, ziprasidone), antibiotics (e.g., moxifloxacin), Class 1A (e.g., quinidine, procainamide) and Class III (e.g., amiodarone, sotalol) antiarrhythmic medications, or any other medications known to prolong the QTc interval.
- Tetrabenazine: Deutetrabenazine is contraindicated in patients currently taking tetrabenazine. Deutetrabenazine may be initiated the day following discontinuation of tetrabenazine.

Adverse Reactions: The most common adverse reactions (≥4% of patients and greater than placebo) experienced during deutetrabenazine clinical studies included the following (deutetrabenazine percentage vs placebo percentage):

- Somnolence (11% vs 4%)
- Diarrhea (9% vs 0%)
- Dry mouth (9% vs 7%)
- Fatigue (9% vs 4%)
- Urinary tract infection (7% vs 2%)
- Insomnia (7% vs 4%)
- Anxiety (4% vs 2%)
- Constipation (4% vs 2%)
- Contusion (4% vs 2%)
- A total of 7% of patients reduced the dose of the study medication due to adverse events. The most common adverse reaction resulting in dose reduction was dizziness (4%). Agitation led to discontinuation in 2% of patients treated with deutetrabenazine.

Xenazine® (Tetrabenazine) Product Summary[21]

FDA Approval: August 2008

Indication(s): Xenazine® (tetrabenazine) is a VMAT2 inhibitor indicated for the treatment of chorea associated with HD.

Dosing:

- Xenazine® is supplied as oral tablets in the following strengths: 12.5mg and 25mg
- The dose of tetrabenazine is determined individually for each patient based on tolerability and reduction of chorea.
- The recommended starting dose of tetrabenazine is 12.5mg once daily in the morning. The dose should be titrated at weekly intervals by 12.5mg per day to a tolerated dose that reduces chorea.
- If a dose of 37.5mg to 50mg per day is needed, it should be given in a three times a day regimen. The maximum recommended single dose is 25mg.
- Patients who require doses of tetrabenazine greater than 50mg per day should be first tested and genotyped to determine if they are poor metabolizers (PMs), intermediate metabolizers (IMs), or extensive metabolizers (EMs) by their ability to express the drug metabolizing enzyme, CYP2D6. The dose of tetrabenazine should then be individualized accordingly to their status as PMs, IMs, or EMs.
    - Extensive and Intermediate CYP2D6 Metabolizers: The maximum recommended daily dose is 100mg and the maximum recommended single dose is 37.5mg.
    - Poor CYP2D6 Metabolizers: The recommended maximum single dose is 25mg, and the recommended daily dose should not exceed 50mg.
- The total daily dose of tetrabenazine should not exceed 50mg (maximum single-dose of 25mg) in patients receiving strong CYP2D6 inhibitors (e.g., quinidine, antidepressants such as paroxetine, fluoxetine, and bupropion).

Boxed Warning: Depression and Suicidality

- Tetrabenazine can increase the risk of depression and suicidal thoughts and behavior (suicidality) in patients with HD.
- Anyone considering the use of tetrabenazine must balance the risks of depression and suicidality with the clinical need for treatment of chorea.
- Patients should be closely monitored for the emergence or worsening of depression, suicidality, or unusual changes in behavior. Patients, their caregivers, and families should be informed of the risk of depression and suicidality and should be instructed to report behaviors of concern promptly to the treating prescriber.
- Particular caution should be exercised in treating patients with a history of depression or prior suicide attempts or ideation, which are increased in frequency in patients with HD. Tetrabenazine is contraindicated in patients who are suicidal, and in patients with untreated or inadequately treated depression.

Mechanism of Action: The effects of tetrabenazine on chorea are believed to be related to its effect as a reversible depletory of monoamines (e.g., dopamine, serotonin, norepinephrine, and

histamine) from nerve terminals. Tetrabenazine reversibly inhibits VMAT2, resulting in decreased uptake of monoamines into synaptic vesicles and depletion of monoamine stores.

Contraindications:

- Patients who are suicidal, or in patients with untreated or inadequately treated depression
- Patients with hepatic impairment
- Patients taking MAOIs; tetrabenazine should not be used in combination with an MAOI or within 14 days of discontinuing therapy with an MAOI
- Patients taking reserpine; at least 20 days should elapse after stopping reserpine before starting tetrabenazine

Safety:

- Clinical Worsening and Adverse Events: HD is a progressive disorder characterized by changes in mood, cognition, chorea, rigidity, and functional capacity over time. In a 12-week trial, tetrabenazine caused worsening in mood, cognition, rigidity, and functional capacity. Prescribers should periodically re-evaluate the need for tetrabenazine in their patients by assessing the effect on chorea and possible adverse effects. It may be difficult to distinguish between adverse reactions and progression of the underlying disease; decreasing the dose or stopping the drug may help to distinguish between the two possibilities. In some patients, the underlying chorea itself may improve over time, decreasing the need for tetrabenazine.
- Depression and Suicidality: Patients with HD are at increased risk for depression, and suicidal ideation or behaviors. Tetrabenazine may increase the risk for suicidality in patients with HD. In a 12-week, double-blind placebo-controlled study in patients with chorea associated with HD, 19% treated with tetrabenazine had an adverse event of depression or worsening depression compared to none of the placebo-treated patients. In two open-label studies, the rate of depression/worsening depression was 35%. In all of the HD chorea studies of tetrabenazine (n = 187), one patient committed suicide, one attempted suicide, and six had suicidal ideation. Clinicians should be alert to the heightened risk of suicide in patients with HD regardless of depression indices. Reported rates of completed suicide among individuals with HD ranged from 3% to 13% and over 25% of patients attempt suicide at some point in their illness.
- Laboratory Tests: Before prescribing a daily dose of tetrabenazine that is greater than 50mg per day, patients should be genotyped to determine if they express the drug metabolizing enzyme, CYP2D6. CYP2D6 testing is necessary to determine whether patients are PMs, EMs, or IMs of tetrabenazine.
- Neuroleptic Malignant Syndrome (NMS): Potentially fatal NMS has been observed in patients receiving tetrabenazine. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status, and evidence of autonomic instability. The management of NMS should include immediate discontinuation of tetrabenazine and intensive symptomatic treatment and medical monitoring. Recurrence of NMS has been reported with resumption of drug therapy.

- Akathisia, Agitation, and Restlessness: In a 12-week, double-blind, placebo-controlled study, akathisia was observed in 19% of tetrabenazine-treated patients and 0% of placebo-treated patients. Patients receiving tetrabenazine should be monitored for the presence of akathisia and for signs and symptoms of restlessness and agitation, as these may be indicators of developing akathisia. If a patient develops akathisia, the tetrabenazine dose should be reduced; however, some patients may require discontinuation of therapy.
- Parkinsonism: Tetrabenazine can cause parkinsonism. In a 12-week double-blind, placebo-controlled study, symptoms suggestive of parkinsonism (i.e., bradykinesia, hypertonia, and rigidity) were observed in 15% of tetrabenazine-treated patients compared to 0% of placebo-treated patients. Because rigidity can develop as part of the underlying disease process in HD, it may be difficult to distinguish between this drug-induced side-effect and progression of the underlying disease process. If a patient develops parkinsonism during treatment with tetrabenazine, dose reduction should be considered; in some patients, discontinuation of therapy may be necessary.
- Dysphagia: Dysphagia is a component of HD, however, drugs that reduce dopaminergic transmission have been associated with esophageal dysmotility and dysphagia. Dysphagia may be associated with aspiration pneumonia. In a 12-week, double-blind, placebo-controlled trial, dysphagia was observed in 4% of tetrabenazine-treated patients and 3% of placebo-treated patients. Some of the cases of dysphagia were associated with aspiration pneumonia.
- Sedation and Somnolence: Sedation is the most common dose-limiting adverse reaction of tetrabenazine. In a 12-week, double-blind, placebo-controlled trial, sedation occurred in 17/54 (31%) of tetrabenazine-treated patients and in 1 (3%) placebo-treated patient.
- QTc Interval Prolongation: Tetrabenazine causes an increase (about 8msec) in the QTc interval. The use of tetrabenazine should be avoided in combination with other drugs that are known to prolong the QTc interval and in patients with congenital long QT syndrome or a history of cardiac arrhythmias.
- Hypotension and Orthostatic Hypotension: Tetrabenazine induced postural dizziness in healthy volunteers receiving single doses of 25mg or 50mg. Dizziness occurred in 4% of tetrabenazine-treated patients (vs. none on placebo) in the 12-week controlled trial. Monitoring of vital signs on standing should be considered in patients who are vulnerable to hypotension.
- Hyperprolactinemia: Tetrabenazine elevates serum prolactin concentrations in humans. Following administration of tetrabenazine 25mg to healthy volunteers, peak plasma prolactin levels increased 4- to 5-fold. Tissue culture experiments indicate that approximately one third of human breast cancers are prolactin-dependent in vitro, a factor of potential importance if tetrabenazine is being considered for a patient with previously detected breast cancer.
- Tardive Dyskinesia (TD): A potentially irreversible syndrome of involuntary, dyskinetic movements may develop in patients treated with neuroleptic drugs. If signs and symptoms of TD appear in a patient treated with tetrabenazine, drug discontinuation should be considered.

- Binding to Melanin-Containing Tissues: Since tetrabenazine binds to melanin-containing tissues, it could accumulate in these tissues over time and raise the possibility that tetrabenazine may cause toxicity in these tissues after extended use.
- Pregnancy: Tetrabenazine is pregnancy category C. There are no adequate and well-controlled studies in pregnant women.
- Lactation: It is not known whether tetrabenazine or its metabolites are excreted in human milk.
- Pediatric Use: The safety and effectiveness of tetrabenazine in pediatric patients have not been established.
- Geriatric Use: The pharmacokinetics of tetrabenazine have not been formally studied in geriatric subjects.
- Hepatic Impairment: Because the safety and efficacy of the increased exposure to tetrabenazine are unknown, it is not possible to adjust the dosage of tetrabenazine in hepatic impairment to ensure safe use. The use of tetrabenazine in patients with hepatic impairment is contraindicated.
- Poor CYP2D6 Metabolizers: PMs will have higher levels of exposure to the primary metabolites. The dosage should be adjusted according to a patient's CYP2D6 metabolizer status by limiting a single dose to a maximum of 25mg and the recommended daily dose to a maximum of 50mg/day in patients who are CYP2D6 PMs.

Drug Interactions:

- Strong CYP2D6 Inhibitors: Concomitant use of strong CYP2D6 inhibitors (e.g., paroxetine, fluoxetine, quinidine) has been shown to increase the systemic exposure to the active metabolites of tetrabenazine. The daily dose of tetrabenazine should not exceed 50mg per day, and a single dose of tetrabenazine should not exceed 25mg in patients taking strong CYP2D6 inhibitors.
- Reserpine: Reserpine binds irreversibly to VMAT2 and the duration of its effect is several days. At least 20 days should elapse after stopping reserpine before starting tetrabenazine.
- MAOIs: Tetrabenazine should not be used in combination with an MAOI, or within 14 days of discontinuing therapy with an MAOI.
- Alcohol: Concomitant use of alcohol or other sedating drugs may have additive effects and worsen sedation.
- Drugs That Cause QTc Prolongation: Tetrabenazine causes a small increase in QTc interval. Tetrabenazine should be avoided in combination with other drugs that are known to prolong QTc, including antipsychotic medications (e.g., chlorpromazine, haloperidol, thioridazine, ziprasidone), antibiotics (e.g., moxifloxacin), Class 1A (e.g., quinidine, procainamide) and Class III (e.g., amiodarone, sotalol) antiarrhythmic medications, or any other medications known to prolong the QTc interval.
- Neuroleptic Drugs: The risk for parkinsonism, NMS, and akathisia may be increased by concomitant use of tetrabenazine and dopamine antagonists or antipsychotics.

Adverse Reactions: The most common adverse reactions (≥4% of patients and greater than placebo) experienced during tetrabenazine clinical studies included the following (tetrabenazine percentage vs placebo percentage):

- Sedation (31% vs 3%)
- Insomnia (22% vs 0%)
- Fatigue (22% vs 13%)
- Akathisia (19% vs 0%)
- Depression (19% vs 0%)
- Anxiety (15% vs 3%)
- Fall (15% vs 13%)
- Nausea (13% vs 7%)
- Upper respiratory tract infection (11% vs 7%)
- Balance difficulty (9% vs 0%)
- Parkinsonism/bradykinesia (9% vs 0%)
- Irritability (9% vs 3%)
- Laceration (head) (6% vs 0%)
- Ecchymosis (6% vs 0%)
- Vomiting (6% vs 3%)
- Decreased appetite (4% vs 0%)
- Obsessive reaction (4% vs 0%)
- Dizziness (4% vs 0%)
- Dysarthria (4% vs 0%)
- Unsteady gait (4% vs 0%)
- Headache (4% vs 0%)
- Shortness of breath (4% vs 0%)
- Bronchitis (4% vs 0%)
- Dysuria (4% vs 0%)
- A total of 52% of patients reduced the dose of the study medication or discontinued dose escalation due to adverse events. The most common adverse reaction resulting in dose reduction was sedation (15%).

Recommendations

The College of Pharmacy recommends the prior authorization of Xenazine® (tetrabenazine) and Austedo™ (deutetrabenazine) with the following criteria:

Xenazine® (Tetrabenazine) Approval Criteria:

1. Authorization of generic tetrabenazine (in place of brand Xenazine®) will require a patient-specific, clinically significant reason the member cannot use the brand formulation (brand formulation is preferred); and
2. A diagnosis of one of the following:
    a. Chorea associated with Huntington's disease; or
    b. Tardive dyskinesia; or
    c. Tourette syndrome; and
3. Xenazine® must be prescribed by a neurologist, or a mid-level practitioner with a supervising physician that is a neurologist; and
4. Member must not be actively suicidal or have uncontrolled depression and prescriber must verify member will be monitored for depression prior to starting Xenazine® therapy and throughout treatment; and
5. Member must not have hepatic impairment; and
6. Member must not be taking monoamine oxidase inhibitors (MAOIs) or have taken a MAOI within the last 14 days; and
7. Member must not be taking reserpine or have taken reserpine within the last 20 days; and
8. Member must not use another vesicular monoamine transporter-2 (VMAT2) inhibitor (e.g., deutetrabenazine, valbenazine) concurrently with Xenazine®; and

9. Member must not be taking medications that are known to prolong the QTc interval concomitantly with Xenazine® [antipsychotic medications (e.g., chlorpromazine, haloperidol, thioridazine, ziprasidone), antibiotics (e.g., moxifloxacin), Class 1A (e.g., quinidine, procainamide) and Class III (e.g., amiodarone, sotalol) antiarrhythmic medications, or any other medications known to prolong the QTc interval]; and
10. Patients who require doses of tetrabenazine greater than 50mg per day must be tested and genotyped to determine if they are poor metabolizers (PMs), intermediate metabolizers (IMs), or extensive metabolizers (EMs) by their ability to express the drug metabolizing enzyme, CYP2D6. The following dose limits will apply based on patient metabolizer status:
    a. Extensive and Intermediate CYP2D6 Metabolizers: 100mg divided daily; or
    b. Poor CYP2D6 Metabolizers: 50mg divided daily; and
11. The daily dose of Xenazine® must not exceed 50mg per day if the member is taking strong CYP2D6 inhibitors (e.g., paroxetine, fluoxetine, quinidine, bupropion); and
12. Approvals will be for the duration of six months at which time the prescriber must document that the signs and symptoms of chorea, tardive dyskinesia, or Tourette syndrome have decreased and the member is not showing worsening signs of depression.

Austedo™ (Deutetrabenazine) Approval Criteria:

1. An FDA approved diagnosis of chorea associated with Huntington's disease; and
2. Austedo™ must be prescribed by a neurologist, or a mid-level practitioner with a supervising physician that is a neurologist; and
3. A previous trial of Xenazine® (tetrabenazine) or a patient-specific, clinically significant reason why the member cannot use brand Xenazine® (tetrabenazine); and
4. Member must not be actively suicidal or have uncontrolled depression and prescriber must verify member will be monitored for depression prior to starting Austedo™ therapy and throughout treatment; and
5. Member must not have hepatic impairment; and
6. Member must not be taking monoamine oxidase inhibitors (MAOIs) or have taken a MAOI within the last 14 days; and
7. Member must not be taking reserpine or have taken reserpine within the last 20 days; and
8. Member must not use another vesicular monoamine transporter-2 (VMAT2) inhibitor (e.g., tetrabenazine, valbenazine) concurrently with Austedo™; and
9. Member must not be taking medications that are known to prolong the QTc interval concomitantly with Austedo™ [antipsychotic medications (e.g., chlorpromazine, haloperidol, thioridazine, ziprasidone), antibiotics (e.g., moxifloxacin), Class 1A (e.g., quinidine, procainamide) and Class III (e.g., amiodarone, sotalol) antiarrhythmic medications, or any other medications known to prolong the QTc interval]; and
10. The daily dose of Austedo™ must not exceed 36mg per day if the member is taking strong CYP2D6 inhibitors (e.g., paroxetine, fluoxetine, quinidine, bupropion) or if they are a known poor CYP2D6 metabolizer; and

11. Approvals will be for the duration of six months at which time the prescriber must document that the signs and symptoms of chorea have decreased and the member is not showing worsening signs of depression.

Utilization Details of HD Medications: Calendar Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM	PERCENT COST
XENAZINE TAB 25MG	38	4	$617,512.94	9.5	$16,250.34	64.27%
TETRABENAZIN TAB 12.5MG	16	6	$67,170.53	2.67	$4,198.16	6.99%
TETRABENAZIN TAB 25MG	13	3	$159,985.66	4.33	$12,306.59	16.65%
XENAZINE TAB 12.5MG	13	2	$116,067.12	6.5	$8,928.24	12.08%
TOTAL	**80**	**13***	**$960,736.25**	**6.15**	**$12,009.20**	**100%**

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

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Appendix N

Calendar Year 2016 Annual Review of Inhaled Tobramycin Products, Pulmozyme® (Dornase Alfa), and Cayston® (Aztreonam)

Oklahoma Health Care Authority
June 2017

Current Prior Authorization Criteria

Inhaled Tobramycin Products (Bethkis®, Tobi®, Tobi® Podhaler™, and Kitabis™ Pak), Pulmozyme® (Dornase Alfa), & Cayston® (Aztreonam) Approval Criteria:

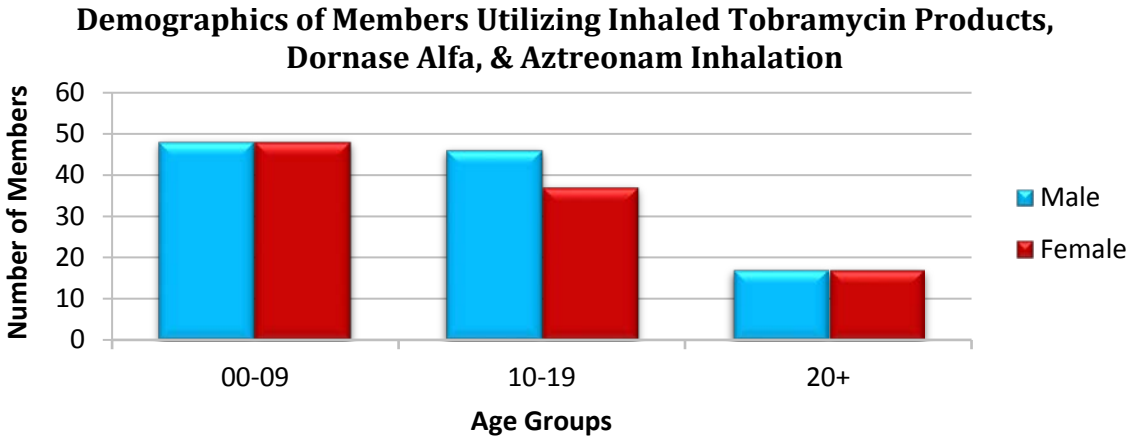
1. Use of inhaled tobramycin products, Pulmozyme® (dornase alfa), and Cayston® (aztreonam) is reserved for members who have a diagnosis of cystic fibrosis.
    a. These medications will not require a prior authorization and claims will pay at the point of sale if member has a reported diagnosis of cystic fibrosis within the past 12 months of claims history.
    b. If the member does not have a reported diagnosis, a manual prior authorization will be required for coverage consideration.
2. Use of inhaled tobramycin products and Cayston® (aztreonam) is restricted to 28 days of therapy per every 56 days to ensure cycles of 28 days on therapy followed by 28 days off therapy.
    a. Use outside of this recommended regimen may be considered for coverage via a manual prior authorization submission with a patient-specific, clinically significant reason why the member would need treatment outside of the FDA approved dosing.
    b. Pharmacies should process the prescription claim with a 56 day supply.

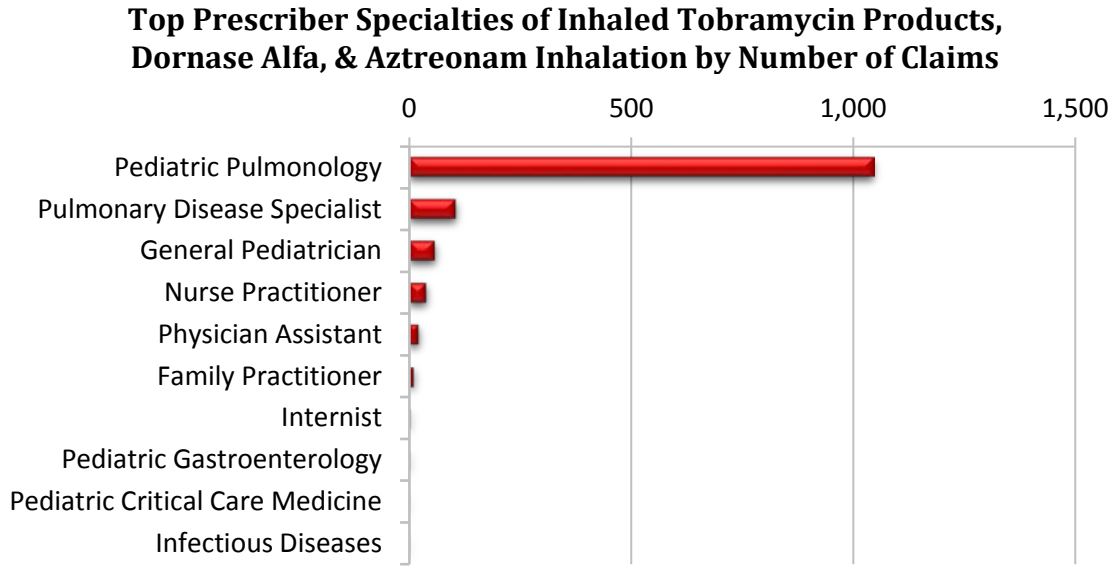
Utilization of Inhaled Tobramycin Products, Dornase Alfa, & Aztreonam Inhalation: Calendar Year 2016

Comparison of Calendar Years

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2015	208	1,187	$4,504,081.10	$3,794.51	$106.55	144,652	42,272
2016	213	1,284	$4,885,660.55	$3,805.03	$101.93	161,369	47,930
% Change	**2.40%**	**8.20%**	**8.50%**	**0.30%**	**-4.30%**	**11.60%**	**13.40%**
Change	**5**	**97**	**$381,579.45**	**$10.52**	**-$4.62**	**16,717**	**5,658**

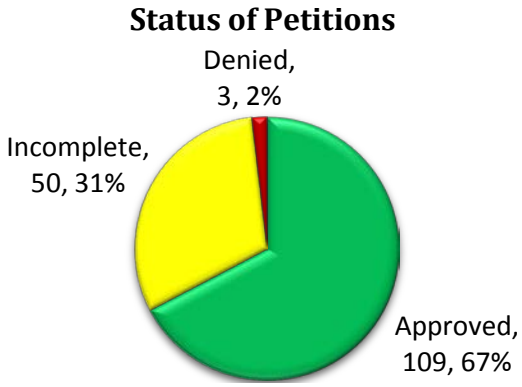
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.





Prior Authorization of Inhaled Tobramycin Products, Dornase Alfa, & Aztreonam Inhalation

There were 162 prior authorization requests submitted for inhaled tobramycin products, dornase alfa, and aztreonam inhalation during calendar year 2016. Computer edits are in place to detect a cystic fibrosis diagnosis in a member's recent diagnosis claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions.



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

Patent Expiration(s):

- Tobi® (tobramycin solution inhalation): there are no unexpired patents for the nebulized solution formulation of Tobi®. Generic nebulized tobramycin formulations are currently available.
- Cayston® (aztreonam inhalation): December 2021
- Bethkis® (tobramycin solution inhalation): March 2023
- Tobi® Podhaler™ (tobramycin powder inhalation): October 2025

Pipeline:

- **March 2016:** The U.S. Food and Drug Administration (FDA) granted Raptor Pharmaceutical's Quinsair™ (levofloxacin inhalation solution) Qualified Infectious Disease Product (QIDP) designation and Orphan Drug Designation for the treatment of chronic lung infections caused by *Pseudomonas aeruginosa (P. aeruginosa)* in patients with cystic fibrosis (CF). Quinsair™ has been approved in the European Union and Canada for the treatment of chronic lung infections caused by *P. aeruginosa;* while a Phase 3 trial in the United States has been conducted, no further clinical development is currently planned.

Other News:

- **November 2016:** According to a systematic literature review and network meta-analysis published in the journal *Clinical Therapeutics,* Cayston® (aztreonam inhalation) was found to have the greatest numeric increase in percent change from baseline in forced expiratory volume in one second (FEV_1%) predicted at four weeks among the inhaled antibiotics for the treatment of *P. aeruginosa* in patients with CF. Other antibiotics evaluated included levofloxacin inhalation solution, tobramycin inhalation solution, tobramycin inhalation powder, and colistimethate sodium. At 24 weeks, levofloxacin inhalation solution was most efficacious in improving FEV_1%.

Inhaled Tobramycin Treatment Comparison

When the Drug Utilization Review (DUR) board voted to prior authorize the inhaled tobramycin products in February 2014, access to Tobi® Podhaler™ was voted to remain similar to nebulized tobramycin with the recommendation that a study be conducted to evaluate and compare the impact of the two products on overall healthcare outcomes including hospitalizations and pharmacy costs. Faculty at the College of Pharmacy performed the study and the results of which were presented at the October 2015 DUR board meeting. Net costs were similar during fiscal year 2016 and all products were recommended to be treated with similar criteria. With the FDA approval of several generic formulations of nebulized tobramycin, net costs no longer remain similar and further review among the formulations is warranted.

Resource Evaluation of Tobramycin Formulations in a State Medicaid Program
Shellie Keast, Pharm.D., Ph.D., Assistant Professor, University of Oklahoma College of Pharmacy

Research was a longitudinal, historical cohort study designed to follow CF patients for 12 months after a switch between inhaled tobramycin formulations. The outcomes assessed

included adherence to tobramycin therapy, utilization of non-tobramycin anti-*pseudomonal* antibiotics, respiratory related hospitalizations, and pharmacy and medical costs, reported as per member per eligible month (PMPM). The switch period was defined as May 1, 2013 through April 30, 2014 and a total of 54 patients were included in the study after meeting all inclusion criteria and matching for independent variables (dry powder [DP] = podhaler formulation; solution [SOL] = nebulized formulation).

- Anti-*pseudomonal* antibiotic reimbursement PMPM was significantly different with higher reimbursement for the DP group compared to the SOL group ($1,095 vs $577, p<0.001).
- Inpatient hospitalization reimbursement PMPM for the DP group was lower than for the SOL group and was statistically significant ($503, p=0.031).
- The proportion of members considered adherent to tobramycin therapy was higher for the DP group (55.6%) compared to the SOL group (44.4%), but this was not statistically significant (p=0.457). There was no difference in odds of being adherent between groups (AOR 1.661; p=0.366).

Tobramycin Formulation	Tobramycin PMPM	Anti-*pseudomonal* Antibiotic PMPM	Inpatient PMPM	Proportion Members Adherent
Dry Powder	$3,394	$1,095*	$212*	55.6%
Solution	$2,387	$577*	$714*	44.4%

PMPM = per member per eligible month
*indicates statistically significant

Cost Comparison:

Medication	Cost per Unit	Dosing	Cost per 28 Days of Therapy
Tobi® Podhaler™ (tobramycin powder inhalation)	$42.69	4 capsules BID	$9,562.56
tobramycin nebulized solution	$11.41	300mg/5mL BID	$3,194.80
Bethkis® (tobramycin nebulized solution)	$25.33	300mg/4mL BID	$5,673.92
Kitabis™ Pak (tobramycin nebulized solution)	$16.07	300mg/5mL BID	$4,499.60

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 or milliliter; mL = milliliter; BID = twice daily

Estimated Annual Savings:

- If all members utilizing Tobi® Podhaler™ during calendar year 2016 switched to generic tobramycin nebulized solution, the estimated annual pharmacy savings would be $369,330.08. This estimation does not account for rebated prices or net costs.

Recommendations

The College of Pharmacy recommends the following changes noted in red to the inhaled tobramycin product prior authorization criteria:

Inhaled Tobramycin Products (Bethkis®, Tobi®, Tobi® Podhaler™, and Kitabis™ Pak), Pulmozyme® (Dornase Alfa), & Cayston® (Aztreonam) Approval Criteria:

1. Use of inhaled tobramycin products, Pulmozyme® (dornase alfa), and Cayston® (aztreonam) is reserved for members who have a diagnosis of cystic fibrosis.
    a. Authorization of Bethkis®, Tobi® Podhaler™, and Kitabis™ Pak requires a trial of tobramycin nebulized solution or a patient-specific, clinically significant reason why tobramycin nebulized solution is not appropriate for the member.
    b. Tobramycin nebulized solution, dornase alfa, and aztreonam inhalation will not require a prior authorization and claims will pay at the point of sale if member has a reported diagnosis of cystic fibrosis within the past 12 months of claims history.
    c. If the member does not have a reported diagnosis, a manual prior authorization will be required for coverage consideration.
2. Use of inhaled tobramycin products and Cayston® (aztreonam) is restricted to 28 days of therapy per every 56 days to ensure cycles of 28 days on therapy followed by 28 days off therapy.
    a. Use outside of this recommended regimen may be considered for coverage via a manual prior authorization submission with a patient-specific, clinically significant reason why the member would need treatment outside of the FDA approved dosing.
    b. Pharmacies should process the prescription claim with a 56 day supply.

Utilization Details of Inhaled Tobramycin Products, Dornase Alfa, & Aztreonam Inhalation: Calendar Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
DORNASE ALFA PRODUCTS					
PULMOZYME SOL 1MG/ML	892	156	$3,030,228.23	5.72	$3,397.12
SUBTOTAL	**892**	**156**	**$3,030,228.23**	**5.72**	**$3,397.12**
TOBRAMYCIN NEBULIZED PRODUCTS					
TOBRAMYCIN NEB 300/5ML	256	91	$745,799.77	2.81	$2,913.28
BETHKIS NEB 300/4ML	8	3	$47,971.20	2.67	$5,996.40
SUBTOTAL	**264**	**92**	**$793,770.97**	**2.87**	**$3,006.71**
TOBRAMYCIN POWDER PRODUCTS					
TOBI PODHALR CAP 28MG	58	23	$533,285.80	2.52	$9,194.58
SUBTOTAL	**58**	**23**	**$533,285.80**	**2.52**	**$9,194.58**
AZTREONAM PRODUCTS					
CAYSTON INH 75MG	70	26	$528,375.55	2.69	$7,548.22
SUBTOTAL	**70**	**26**	**$528,375.55**	**2.69**	**$7,548.22**
TOTAL	**1,284**	**213***	**$4,885,660.55**	**6.03**	**$3,805.03**

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

[1] U.S. Food and Drug Adminstration (FDA). Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: https://www.accessdata.fda.gov/scripts/cder/ob/. Last revised 04/2017. Last accessed 05/24/2017.
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Appendix O

30-Day Notice to Prior Authorize Ingrezza™ (Valbenazine)

Oklahoma Health Care Authority
June 2017

Tardive Dyskinesia[1,2,3,4,5,6,7]

Tardive dyskinesia (TD) is an involuntary neurological movement disorder that appears with a delayed onset after prolonged use of dopamine receptor blocking agents (DRBAs), primarily antipsychotic medications and the antiemetic drug, metoclopramide. It is estimated that at least 500,000 people in the United States have TD. The annual incidence of TD is estimated to be approximately 3 to 8 percent overall in patients treated with conventional (first-generation) antipsychotic medications; however, the incidence in patients older than 55 years of age is approximately 10 to 20 percent. The data is conflicting on whether the prevalence of TD has declined with increased use of second-generation antipsychotic medications. The risk of TD is possibly higher with high-potency conventional antipsychotics compared to most second-generation antipsychotics, but it is not certain whether most second-generation antipsychotic medications have a lower risk compared with low-potency conventional antipsychotics taken at moderate doses.

TD symptoms involve the face, mouth, tongue, trunk, or extremities. Some of the clinical features may include protruding and twisting movements of the tongue, smacking movements of the lips, chewing movements, blepharospasm, twisting finger movements, tapping foot movements, shoulder shrugging, and rocking movements. Severe TD may impact ambulation, as well as interfere with speaking, swallowing, eating, or breathing.

Prevention of TD, as well as early detection and treatment of potentially reversible cases of TD are of utmost importance. The only certain method to prevent TD is the avoidance of treatment with DRBAs. The use of antipsychotic medications requires careful evaluation of indications and should be limited to conditions where no alternative effective therapy exists. The use of metoclopramide should be limited to no longer than 12 weeks of continuous therapy. Treatment for TD should be assessed carefully as symptoms are often mild and are not bothersome enough to require therapy. Initial treatment of TD includes discontinuing the causative medication if possible. If a patient who develops signs of TD requires continued treatment, switching to a medication with less potent dopamine receptor (D2) blockade may be attempted, but all DRBAs carry a risk of TD. In April 2017, the U.S. Food and Drug Administration (FDA) approved Ingrezza™ (valbenazine), a selective vesicular monoamine transporter 2 (VMAT2) inhibitor, for the treatment of adults with TD. Valbenazine is the first medication FDA-approved for the treatment of TD. Prior to approval of valbenazine, pharmacologic treatment options for TD included VMAT2 inhibitors (e.g., tetrabenazine), amantadine, clonazepam, ginkgo biloba extract, and chemodenervation via botulinum toxin injection. The American Academy of Neurology (AAN) published treatment guidelines for TD in 2013, prior to the approval of valbenazine. The guidelines currently list two agents (ginkgo biloba in schizophrenics and clonazepam for short-term use) as level B grade for evidence for

the treatment of TD. The guidelines did not support any level A recommendations (i.e., established effectiveness) for pharmacologic or surgical treatment of TD.

Market News and Updates[8,9,10,11,12,13]

New FDA Approval(s):

- **April 2017:** The FDA approved Ingrezza™ (valbenazine) for the treatment of adults with TD. Ingrezza™ is a novel, selective vesicular monoamine transporter 2 (VMAT2) inhibitor. It is the first medication approved for the treatment of adults with TD.

Other News:

- **January 2017:** Neurocrine Biosciences, Inc. announced top-line results for a Phase 2 T-Forward study of Ingrezza™ (valbenazine) in adults with Tourette syndrome. The pre-specified primary endpoint, the change from baseline in the Yale Global Tic Severity Scale (YGTSS) at Week 8, was not met (p=0.18). However, the study showed a significant improvement in overall symptoms of Tourette syndrome as measured by the Clinical Global Impression of Change (p=0.015).
- **April 2017:** The Institute for Clinical and Economic Review (ICER) will develop a report to assess the comparative clinical effectiveness and value of drugs to treat TD. The report is expected to review evidence on valbenazine and deutetrabenazine (Austedo™), a medication currently approved for Huntington's disease and under review by the FDA for TD. An approval decision for deutetrabenazine for the TD indication is expected by August 30, 2017. The report will also include tetrabenazine (Xenazine®), a medication FDA approved for Huntington's disease and also used off-label in patients with TD. The report will be the subject of a December 2017 meeting of the New England Comparative Effectiveness Public Advisory Council.
- **May 2017:** Neurocrine Biosciences, Inc. announced that the initial Phase 2 Tourette syndrome T-Force GREEN study of Ingrezza™ (valbenazine) did not meet its primary endpoint. The pre-specified primary endpoint was the change from baseline between placebo and active groups in the YGTSS at Week 6 in the intent-to-treat population. An exposure-response analysis showed that the selected doses for this study were below the therapeutic range for adequate tic reduction for the majority of the pediatric subjects. There was a substantial reduction in tics for the subset of subjects with pharmaceutical exposure in the appropriate range; however, for subjects with sub-therapeutic exposure, tic reduction was comparable to placebo.

Pipeline:

- **Deutetrabenazine:** Teva Pharmaceuticals announced that data from a second Phase 3 registration trial studying deutetrabenazine (SD-809, Austedo™) for the treatment of TD showed statistically significant results. The results for the AIM-TD trial follow positive results from the ARM-TD trial; both were 12-week treatment studies. The primary endpoint in the AIM-TD trial was change in Abnormal Involuntary Movement Scale (AIMS) score from baseline to week 12 for three fixed doses of deutetrabenazine as compared to placebo. At week 12, the AIMS rating improved from baseline by -3.3 points for 36mg (p=0.001), -3.2 points for 24mg (p=0.003), and -2.1 points for 12mg

(p=not significant), compared to -1.4 points for placebo. The FDA is reviewing deutetrabenazine for the treatment of TD and has set a Prescription Drug User Fee Act (PDUFA) goal date of August 30, 2017. The agency granted the TD New Drug Application (NDA) priority review and it has been granted breakthrough therapy designation by the FDA for the TD indication. Austedo™ (deutetrabenazine) is currently FDA approved for the treatment of chorea associated with Huntington's disease.

Ingrezza™ (Valbenazine) Product Summary[14]

Indication(s): Ingrezza™ (valbenazine) is a VMAT2 inhibitor indicated for the treatment of adults with TD.

Dosing:

- Valbenazine is available as a 40mg oral capsule.
- The recommended initial dose is 40mg by mouth once daily. After one week, the dose should be increased to the recommended dose of 80mg once daily.
- The recommended dose for patients with moderate or severe hepatic impairment is 40mg once daily.
- Patients who are known CYP2D6 poor metabolizers may require a dose reduction based on tolerability.

Mechanism of Action: The mechanism of action of valbenazine in the treatment of TD is unknown, but is thought to be mediated through the reversible inhibition of VMAT2. VMAT2 is a transporter that regulates monoamine uptake from the cytoplasm to the synaptic vesicle for storage and release.

Contraindications:

- None

Adverse Reactions: The most common adverse reaction of valbenazine (≥5% and twice the rate of placebo) was somnolence.

Use in Specific Populations:

- Pregnancy: The limited available data on the use of valbenazine in pregnant women are insufficient to inform a drug-associated risk. No malformations were observed in animal reproductive studies when valbenazine was administered orally to rats and rabbits during the period of organogenesis at doses up to 1.8 or 24 times, respectively, the maximum recommended human dose (MRHD) of 80mg/day based on mg/m^2 body surface area. However, administration of valbenazine to pregnant rats during organogenesis through lactation produced an increase in the number of stillborn pups and postnatal pup mortalities at doses less than 1 times the MRHD based on mg/m^2. Pregnant women should be advised of the potential risk to the fetus.
- Lactation: There is no information regarding the presence of valbenazine or its metabolites in human milk, the effects on the breastfed infant, or the effects on milk production. Valbenazine and its metabolites have been detected in rat milk in concentrations higher than in plasma following oral administration of valbenazine at

doses 0.1 to 1.2 times the MRHD based on mg/m^2. Women should be advised not to breastfeed during treatment with valbenazine and for five days after the final dose based on animal findings of increased perinatal mortality in exposed fetuses and pups.

- Pediatric Use: The safety and effectiveness of valbenazine have not been established in pediatric patients.
- Geriatric Use: A dose adjustment is not required in elderly patients. In three randomized, placebo-controlled studies of valbenazine, 16% of patients were 65 years of age and older. The safety and effectiveness were similar in patients older than 65 years compared to younger patients.
- CYP2D6 Poor Metabolizers: In known CYP2D6 poor metabolizers, a dose reduction of valbenazine should be considered based on tolerability. Increased exposure to valbenazine's active metabolite is anticipated in CYP2D6 poor metabolizers and increased exposure of active metabolites may increase the risk of exposure-related adverse reactions.
- Hepatic Impairment: A dosage reduction of valbenazine is recommended for patients with moderate or severe hepatic impairment. Patients with moderate-to-severe hepatic impairment (Child-Pugh score 7 to 15) had higher exposure of valbenazine and its active metabolite compared to patients with normal hepatic function.
- Renal Impairment: A dosage adjustment is not necessary for patients with mild-to-moderate renal impairment (creatinine clearance 30 to 90mL/min). Valbenazine does not undergo primary renal clearance. In patients with severe renal impairment (creatinine clearance less than 30mL/min) valbenazine is not recommended.

Efficacy: A randomized, double-blind, placebo-controlled trial of valbenazine was conducted in patients with moderate-to-severe TD as determined by clinical observation. Patients enrolled in the study had underlying schizophrenia, schizoaffective disorder, or a mood disorder. Patients at significant risk for suicidal or violent behavior and those with unstable psychiatric symptoms were excluded. The primary efficacy measure for the assessment of TD severity was the Abnormal Involuntary Movement Scale (AIMS). The AIMS is a 12-item scale; items 1 to 7 assess the severity of involuntary movements across body regions and were used in the study. Each of the items was scored on a 0 to 4 scale with 0 = no dyskinesia; 1 = low amplitude and present during some but not most of the exam; 2 = low amplitude and present during most of the exam; 3 = moderate amplitude and present during most of the exam; or 4 = maximal amplitude and present during most of the exam. Therefore, the total AIMS dyskinesia score (sum of items 1 to 7) could range from 0 to 28, with a decrease in score indicating improvement. The AIMS was scored by central raters who interpreted the videos and were blinded to subject identification, treatment assignment, and visit number. The primary efficacy endpoint was the mean change from baseline in the AIMS dyskinesia total score at the end of Week 6. The change from baseline for two fixed doses of valbenazine (40mg or 80mg) was compared to placebo. At the end of Week 6, subjects initially assigned to placebo were re-randomized to receive either valbenazine 40mg or 80mg. Follow-up was continued through Week 48 on the assigned medication, followed by a 4-week period off-drug. A total of 234 subjects were enrolled and 29 (12%) discontinued prior to completion of the placebo-controlled period. The mean age of subjects was 56 years (range 26 to 84 years old). Of the subjects, 70% were

receiving atypical antipsychotics, 14% were receiving typical or combination antipsychotics, and 16% were not receiving antipsychotics. Valbenazine met the primary endpoint of the study with a mean change from baseline to Week 6 in the AIMS dyskinesia total score of -3.2 for the 80mg group as compared to -0.1 in the placebo group ($p<0.0001$). Among subjects remaining in the study at the end of the 48-week treatment (N=123), following discontinuation of valbenazine, the mean AIMS dyskinesia total score appeared to return toward baseline.

Cost:

Medication	Cost Per Unit	Cost Per Day	Cost Per 30 Days of Therapy
Ingrezza™ (valbenazine) 40mg	**$175.83**	**$351.66**	**$10,549.80**
Xenazine® (tetrabenazine) 25mg	$208.46	$625.38-$1,250.76*	$18,761.40-$37,522.80[+]
tetrabenazine 25mg	$126.09	$378.27-$756.54*	$11,348.10-$22,696.20

Cost does not reflect rebated price or net cost. Costs based on National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
*Cost based on off-label dosing of tetrabenazine 75mg to 150mg divided daily.
[+]Was FDA approved in 2008 and has a significant federal rebate.

Recommendations

The College of Pharmacy recommends the prior authorization of Ingrezza™ (valbenazine) with the following criteria:

Ingrezza™ (Valbenazine) Approval Criteria:

1. An FDA approved diagnosis of tardive dyskinesia meeting the following DSM-5 criteria:
    a. Involuntary athetoid or choreiform movements; and
    b. History of treatment with dopamine receptor blocking agent (DRBA); and
    c. Symptom duration lasting longer than 4 to 8 weeks; and
2. Member must be 18 years of age or older; and
3. Ingrezza™ must be prescribed by a neurologist or psychiatrist, or a mid-level practitioner with a supervising physician that is a neurologist or psychiatrist; and
4. Member must not be at significant risk for suicidal or violent behavior and must not have unstable psychiatric symptoms; and
5. The daily dose of Ingrezza™ must not exceed 40mg per day if the member is taking strong CYP3A4 inhibitors (e.g., itraconazole, ketoconazole, clarithromycin); and
6. Member must not be taking monoamine oxidase inhibitors (MAOIs); and
7. Member must not be taking other vesicular monoamine transporter 2 (VMAT2) inhibitors (e.g., tetrabenazine, deutetrabenazine); and
8. Female members must not be pregnant or breastfeeding; and
9. Prescriber must document a baseline evaluation using the Abnormal Involuntary Movement Scale (AIMS); and
10. A quantity limit of two 40mg tablets or a total dose of 80mg per day will apply; and
11. Approvals will be for the duration of six months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment as indicated by an improvement from baseline in the AIMS total score (a negative change in score indicates improvement).

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Appendix P

Fiscal Year 2016 Annual Review of Various Special Formulations and 30-Day Notice to Prior Authorize Carac® (Fluorouracil 0.5% Cream), GoNitro™ (Nitroglycerin Sublingual Powder), Soltamox® (Tamoxifen Citrate Oral Solution), Taytulla™ (Norethindrone Acetate/Ethinyl Estradiol Capsules & Ferrous Fumarate Capsules), Tirosint®-SOL (Levothyroxine Sodium Oral Solution), Xatmep™ (Methotrexate Oral Solution), Zovirax® (Acyclovir Ointment & Suspension), Xerese® (Acyclovir/Hydrocortisone Cream), & Denavir® (Penciclovir Cream)

Oklahoma Health Care Authority
June 2017

Introduction

Multiple formulations of medications are made for ease of administration, to increase bioavailability, or as new technologies are created to provide a more efficient treatment response. Some of the new formulations incur greater costs for production resulting in greater costs for the payer and consumer. Clinical review of each product and its comparative cost to other formulations are provided in the following report for reference.

Current Prior Authorization Criteria

Gralise® (Gabapentin Extended-Release Tablets) Approval Criteria:

1. An FDA-approved indication of postherpetic neuralgia; and
2. Documented treatment attempts at recommended dosing with at least one agent from two of the following drug classes that did not yield adequate relief:
    a. Tricyclic antidepressants; or
    b. Anticonvulsants; or
    c. Topical or oral analgesics; and
3. A patient-specific, clinically significant reason why the member cannot take the immediate-release formulation of gabapentin.

Horizant® (Gabapentin Enacarbil Extended-Release Tablets) Approval Criteria:

1. For the FDA-approved indication of restless leg syndrome:
    a. Member must be 18 years of age or older; and
    b. Documented treatment attempts at recommended dosing with at least two of the following that did not yield adequate relief:
        i. Carbidopa/levodopa; or
        ii. Pramipexole; or

iii. Ropinirole; and
c. A patient-specific, clinically significant reason why the member cannot take the immediate-release formulation of gabapentin.

2. For the FDA-approved indication of postherpetic neuralgia:
   a. Member must be 18 years of age or older; and
   b. Documented treatment attempts at recommended dosing with at least one agent from two of the following drug classes that did not yield adequate relief:
      i. Tricyclic antidepressants; or
      ii. Anticonvulsants; or
      iii. Topical or oral analgesics; and
   c. A patient-specific, clinically significant reason why the member cannot take the immediate-release formulation of gabapentin.

Kristalose® (Lactulose Packets for Oral Solution) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use the liquid lactulose formulation.

Metozolv® ODT [Metoclopramide Orally Disintegrating Tablets (ODT)] Approval Criteria:

1. A patient-specific, clinically significant reason why the member is unable to use the metoclopramide oral tablet formulation.

Nuvessa™ (Metronidazole Vaginal Gel 1.3%) Approval Criteria:

1. An FDA approved diagnosis of bacterial vaginosis in non-pregnant women; and
2. A patient-specific, clinically significant reason why the member cannot use MetroGel-Vaginal® 0.75% (metronidazole vaginal gel 0.75%).

Purixan® (Mercaptopurine Oral Suspension) Approval Criteria:

1. An FDA approved diagnosis of acute lymphoblastic leukemia (ALL); and
2. An age restriction on members older than 10 years of age applies. Members 10 years of age and younger do not require prior authorization for Purixan® therapy; and
3. Members older than 10 years of age require a patient-specific, clinically significant reason why the oral tablet formulation cannot be used.

Rasuvo® (Methotrexate Injection) and Otrexup™ (Methotrexate Injection) Approval Criteria:

1. An FDA approved diagnosis of one of the following:
   a. Adults with severe, active rheumatoid arthritis (RA); or
   b. Children with active polyarticular juvenile idiopathic arthritis (pJIA); or
   c. Severe, recalcitrant, disabling psoriasis confirmed by biopsy or dermatologic consultation; and
2. Members with a diagnosis of RA or pJIA must have had an adequate trial of full dose nonsteroidal anti-inflammatory drugs (NSAIDs); and
3. A patient-specific, clinically significant reason why the oral tablets or the generic injectable formulation cannot be used.

Rayos® (Prednisone Delayed-Release Tablets) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use immediate-release corticosteroid medications.

RibaPak® (Ribavirin Dose Pack), Rebetol® (Ribavirin Solution), and Ribasphere® (Ribavirin 400mg and 600mg Tablets) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use the 200mg tablets or 200mg capsules in place of the unique dosage formulations.

Sitavig® (Acyclovir Buccal Tablets) Approval Criteria:

1. An FDA approved diagnosis of recurrent herpes labialis (cold sores); and
2. A patient-specific, clinically significant reason why the member cannot use oral acyclovir or valacyclovir oral tablets.

Zyclara® (Imiquimod 2.5% and 3.75% Cream) Approval Criteria:

1. An FDA approved diagnosis of actinic keratosis (AK) of the full face or balding scalp in immunocompetent adults or topical treatment of external genital and perianal warts/condyloma acuminate (EGW) in patients 12 years and older; and
2. Member must be 12 years of age or older; and
3. Requests for a diagnosis of molluscum contagiosum in children 2 to 12 years of age will generally not be approved; and
4. A patient-specific, clinically significant reason why the member cannot use generic imiquimod 5% cream in place of Zyclara® (imiquimod) 2.5% and 3.75% cream.

Utilization of Special Formulations: Fiscal Year 2016

Comparison of Fiscal Years

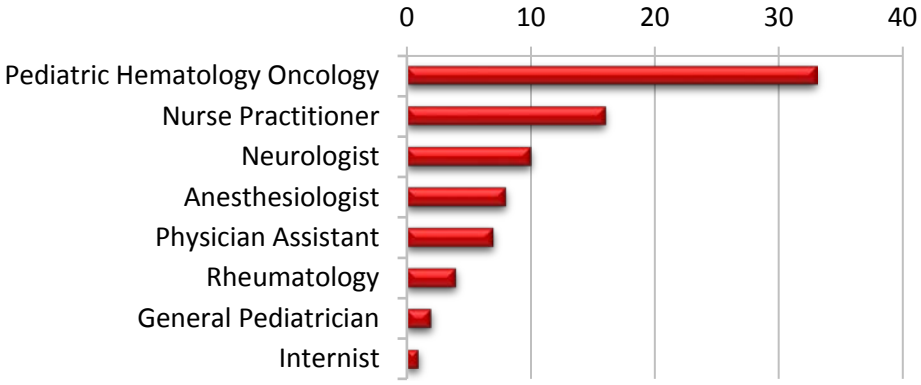
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2015	32	79	$54,956.55	$695.65	$22.02	7,311	2,496
2016	18	81	$56,356.27	$695.76	$23.88	4,791	2,360
% Change	**-43.80%**	**2.50%**	**2.50%**	**0.00%**	**8.40%**	**-34.50%**	**-5.40%**
Change	**-14**	**2**	**$1,399.72**	**$0.11**	**$1.86**	**-2,520**	**-136**

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

Demographics of Members Utilizing Special Formulations

- Due to the small number of members utilizing special formulations, detailed demographic information could not be provided.

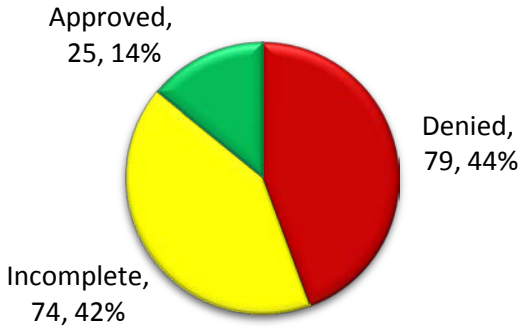
Top Prescriber Specialties of Special Formulations by Number of Claims



Prior Authorization of Special Formulations

There were 178 prior authorization requests submitted for special formulations during fiscal year 2016. The following chart shows the status of the submitted petitions.

Status of Petitions



Carac® (Fluorouracil 0.5% Cream) Product Summary[1,2,3]

Indication(s): Carac® (fluorouracil 0.5% cream) is an antineoplastic agent indicated for the topical treatment of multiple actinic or solar keratoses of the face and anterior scalp in adults.

Dosing and Administration:

- Carac® is available as a topical 0.5% fluorouracil cream, with 0.35% being incorporated into a patented porous microsphere (Microsponge®). It is supplied in a 30g tube.
- Carac® should be applied once a day to the skin where actinic keratosis lesions appear, using enough to cover the entire area with a thin film.
- Carac® should be applied up to 4 weeks as tolerated. Continued treatment up to 4 weeks results in greater lesion reduction. Treatment beyond 4 weeks was not studied in clinical trials.

Other Formulation(s) Available:

- Fluorouracil 5% Cream, 5% Solution, and 2% Solution:
  - Fluorouracil 5% cream, 5% solution, and 2% solution are recommended for the topical treatment of multiple actinic or solar keratoses. The 5% strength is also useful in the treatment of superficial basal cell carcinomas. For actinic keratosis, all the formulations are applied twice daily in an amount sufficient to cover the lesions. The usual duration of therapy is from 2 to 4 weeks.
  - Fluorouracil 5% cream is supplied in a 40g tube. Fluorouracil 5% and 2% solutions are supplied in 10mL drop dispensers.

Formulation Cost Comparison:

Product	Cost Per Gram or mL	Cost Per Treatment
Carac® (fluorouracil 0.5% cream)	**$80.16**	**$2,404.80**
fluorouracil 0.5% cream	**$48.47**	**$1,454.10**
fluorouracil cream 5%	$3.02	$120.80
fluorouracil solution 5%	$5.56	$55.60
fluorouracil solution 2%	$4.48	$44.80

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.

Fiscal Year 2016 Utilization: There were 8 claims for 5 members utilizing fluorouracil 0.5% cream brand and generic during fiscal year 2016.

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
FLUOROURACIL CRE 5%	82	76	$14,336.75	$8.20	1.08	$174.84
FLUOROURACIL CRE 0.5%	7	4	$9,842.32	$104.71	1.75	$1,406.05
FLUOROURACIL SOL 5%	4	4	$321.36	$5.54	1	$80.34
CARAC CRE 0.5%	1	1	$2,641.12	$176.07	1	$2,641.12
TOTAL	**94**	**85***	**$27,141.55**	**$14.17**	**1.11**	**$288.74**

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

GoNitro™ (Nitroglycerin Sublingual Powder) Product Summary[4,5,6]

Indication(s): GoNitro™ (nitroglycerin sublingual powder) is a nitrate vasodilator indicated for acute relief of an attack or prophylaxis of angina pectoris due to coronary artery disease.

Dosing and Administration:

- GoNitro™ is available in a packet containing 400mcg of sublingual nitroglycerin powder. The packets are supplied in boxes of 12, 36, or 96.
- GoNitro™ should be administered as one or two packets (400mcg each) under the tongue at the onset of an attack. One additional packet may be administered every 5 minutes as needed. No more than three total packets (1,200mcg) are recommended within a 15 minute period. If the chest pain persists after three packets, prompt medical

attention is advised. GoNitro™ may be used prophylactically 5 to 10 minutes prior to engaging in activities that might precipitate an acute attack.

Other Formulation(s) Available:

- Nitroglycerin Sublingual Tablets and Lingual Spray:
  - Nitroglycerin sublingual tablets and lingual spray are indicated for the acute relief of an attack or acute prophylaxis of angina pectoris due to coronary artery disease. Both dosage forms are available generically.
  - The sublingual tablets are supplied in strengths of 0.3mg, 0.4mg, and 0.6mg in bottles containing 100 tablets each, with color-coded labels, and in color-coded patient convenience packages of four bottles of 25 tablets each.
  - The lingual spray is supplied in a glass bottle. Each bottle contains 4.9g or 14.1g of nitroglycerin lingual spray which will deliver 60 or 200 metered sprays containing 400mcg of nitroglycerin per spray after priming.
  - Both dosage forms are dosed as one or two doses under the tongue (or on the tongue for the spray) at the onset of an attack. The doses may be repeated every 5 minutes as needed. No more than three doses are recommended within a 15 minute period. If the chest pain persists after three doses, prompt medical attention is advised. These products may be used prophylactically 5 to 10 minutes prior to engaging in activities that might precipitate an acute attack.

Formulation Cost Comparison:

Product	Cost Per Dose/Gram	Cost Per Package
GoNitro™ (nitroglycerin sublingual powder)	**$6.81**	**$81.72 - $653.76**
nitroglycerin sublingual tablets	$0.33 - $0.58	$33.00 - $58.00
nitroglycerin lingual spray	$19.68 - $35.20	$172.40 - $236.16

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.

Fiscal Year 2016 Utilization: There was no utilization of GoNitro™ during fiscal year 2016.

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
NITROSTAT SUB 0.4MG	2,084	1,477	$36,740.90	$0.95	1.41	$17.63
NITROGLYCRN SPR 0.4MG	91	63	$20,340.80	$7.34	1.44	$223.53
NITROSTAT SUB 0.3MG	59	45	$1,489.08	$0.83	1.31	$25.24
NITROGLYCER AER 400MCG	22	21	$4,609.02	$5.84	1.05	$209.50
NITROSTAT SUB 0.6MG	7	5	$181.96	$0.69	1.4	$25.99
NITROMIST AER 400MCG	5	4	$2,302.06	$10.96	1.25	$460.41
TOTAL	**2,268**	**1,615***	**$65,663.82**	**$1.48**	**1.40**	**$28.95**

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

Soltamox® (Tamoxifen Citrate Oral Solution) Product Summary[7,8]

Indication(s): Soltamox® (tamoxifen citrate oral solution) is a nonsteroidal selective estrogen receptor modulator (SERM), indicated for the following:

- Treatment of metastatic breast cancer in women and men
- Adjuvant treatment of node-positive breast cancer in postmenopausal women and for the adjuvant treatment of axillary node-negative breast cancer in women following total mastectomy or segmental mastectomy, axillary dissection, and breast irradiation
- The reduction in risk of invasive breast cancer in women with ductal carcinoma *in situ* (DCIS), following breast surgery and radiation
- To reduce the incidence of breast cancer in women at high risk for breast cancer

Dosing and Administration:

- Soltamox® is available as a sugar-free, clear colorless liquid, with licorice and aniseed odor and taste. It is supplied in a 150mL bottle with a dosing cup. Each 5mL of solution contains 10mg tamoxifen, equivalent to 15.2mg tamoxifen citrate. Soltamox® is bioequivalent to tamoxifen tablets.
- For patients with breast cancer, the recommended daily dose is 20mg to 40mg, given as 10mL to 20mL of solution. Dosages greater than 20mg per day should be given in divided doses (morning and evening). For DCIS and reduction in breast cancer incidence in high risk women, the recommended dose is 20mg daily for 5 years.

Other Formulation(s) Available:

- Tamoxifen Citrate 10mg and 20mg Tablets:
  - Tamoxifen citrate tablets have the same indications as Soltamox® (listed above). The dosing is the same as well, provided in a tablet formulation.
  - The tablets are available as 10mg and 20mg containing 15.2mg and 30.4mg of tamoxifen citrate, respectively. Tamoxifen citrate tablets are available generically. Procedures for proper handling of anticancer drugs should be considered, including crushing and cutting tablets.

Formulation Cost Comparison:

Product	Cost Per Tablet or mL	Cost for 30 Days
Soltamox® (tamoxifen citrate oral solution)	**$3.82**	**$1,146.00 - $2,292.00**
tamoxifen citrate 10mg tablets	$0.25	$15.00 - $30.00
tamoxifen citrate 20mg tablets	$0.53	$15.90 - $31.80

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.

Fiscal Year 2016 Utilization: There was no utilization of Soltamox® during fiscal year 2016.

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
TAMOXIFEN TAB 20MG	765	187	$23,650.62	$0.66	4.09	$30.92
TAMOXIFEN TAB 10MG	34	8	$369.06	$0.39	4.25	$10.85
TOTAL	**799**	**194***	**$24,019.68**	**$0.65**	**4.12**	**$30.06**

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

Taytulla™ (Norethindrone Acetate/Ethinyl Estradiol Capsules & Ferrous Fumarate Capsules) Product Summary[9,10]

Indication(s): Taytulla™ (norethindrone acetate/ethinyl estradiol capsules and ferrous fumarate capsules) is an estrogen/progestin combination oral contraceptive (COC) indicated for use by women to prevent pregnancy. The efficacy of Taytulla™ in women with a body mass index (BMI) of greater than 35kg/m^2 has not been evaluated.

Dosing and Administration:

- Taytulla™ consists of 28 soft gelatin capsules in a blister pack in the following order:
  - Twenty-four pink capsules (active) each containing 1mg norethindrone acetate and 20mcg ethinyl estradiol
  - Four maroon capsules (non-hormonal placebo) each containing 75mg ferrous fumarate which does not serve any therapeutic purpose
- The recommended dosing is one capsule by mouth at the same time every day. The capsules should be taken in the order directed on the blister pack without regard to meals.

Other Formulation(s) Available:

- Various Generic Formulations of Norethindrone Acetate/Ethinyl Estradiol Tablets with Ferrous Fumarate Tablets (Loestrin®24 Fe):
  - Generic formulations of Loestrin®24 Fe have the same indications as Taytulla™ (listed above). The dosing is the same as well, provided in a tablet formulation.
  - Generic formulations of Loestrin®24 Fe are available in blister card dispensers containing 28 tablets. The pack includes active and ferrous fumarate tablets in the same number and strength as the Taytulla™ capsules.

Formulation Cost Comparison:

Product	Cost Per Tablet *	Cost Per Pack *
Taytulla™ (norethindrone acetate/ethinyl estradiol capsules & ferrous fumarate capsules)	**$5.37**	**$150.36**
norethindrone acetate/ethinyl estradiol 1mg/20mcg (24) tablets & ferrous fumarate tablets	$1.26	$35.28

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.

Fiscal Year 2016 Utilization: There was no utilization of Taytulla™ during fiscal year 2016.

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
LOMEDIA 24 TAB FE	211	53	$14,160.62	$2.15	3.98	$67.11
NORETH/ETHIN TAB FE 1/20	153	59	$11,786.10	$2.03	2.59	$77.03
GILDESS 24 TAB FE 1/20	32	18	$2,936.06	$2.18	1.78	$91.75
LARIN 24 TAB FE 1/20	15	8	$1,500.38	$2.14	1.88	$100.03
MICRGSTIN 24 TAB FE 1/20	7	4	$516.05	$2.05	1.75	$73.72
BLISOVI 24 TAB FE 1/20	6	5	$413.04	$1.84	1.2	$68.84

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
JUNEL FE 24 TAB 1/20	1	1	$59.24	$2.12	1	$59.24
TOTAL	**425**	**131***	**$31,371.49**	**$2.10**	**3.24**	**$73.82**

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

Tirosint® -SOL (Levothyroxine Sodium Oral Solution) Product Summary[11,12]

Indication(s): Tirosint®-SOL (levothyroxine sodium oral solution) is L-thyroxine (T_4) indicated for the following:

- Hypothyroidism: As replacement therapy in primary (thyroidal), secondary (pituitary), and tertiary (hypothalamic) congenital or acquired hypothyroidism
- Pituitary Thyrotropin (Thyroid-Stimulating Hormone, TSH) Suppression: As an adjunct to surgery and radioiodine therapy in the management of thyrotropin-dependent well-differentiated thyroid cancer

Limitation of Use: Tirosint®-SOL is not indicated for suppression of benign thyroid nodules and nontoxic diffuse goiter in iodine-sufficient patients or for the treatment of transient hypothyroidism during the recovery phase of subacute thyroiditis.

Dosing and Administration:

- Tirosint®-SOL is a clear, colorless to slightly yellow solution supplied in a 1mL white, non-transparent, unit-dose ampule. The dosage strength is identified on the box and the pouch, and is associated with a distinct color. Each ampule bears a colored label with the dosage strength and the product name. Each box contains 30 unit-dose ampules packaged in pouches containing 5 unit-dose ampules.
- Tirosint®-SOL is available in 12 strengths ranging from 13mcg to 200mcg. The recommended dosing is once daily, on an empty stomach, one-half to one hour before breakfast. It should be administered at least four hours before or after drugs that are known to interfere with absorption.
- Tirosint®-SOL can be administered in water by squeezing the contents of one single unit-dose ampule into a glass or cup containing water. It can also be taken directly, by either squeezing it into the mouth or onto a spoon and consuming immediately.
- Tirosint®-SOL starting dose depends on a variety of factors, including age, body weight, cardiovascular status, concomitant medical conditions, concomitant medications, co-administered food, and the specific nature of the condition being treated. Peak therapeutic effect may not be attained for four to six weeks.

Other Formulation(s) Available:

- Levothyroxine Sodium Tablets:
  - Levothyroxine sodium tablets have the same indications and dosing as Tirosint®-SOL (listed above), provided in a tablet formulation. However, levothyroxine tablets do not include the limitation of use associated with Tirosint®-SOL and are also indicated for the treatment or prevention of various types of euthyroid goiters, including thyroid nodules, subacute or chronic lymphocytic thyroiditis

(Hashimoto's thyroiditis), and multinodular goiters. Levothyroxine tablets are also available in 12 different strengths which differ from Tirosint®-SOL with the exclusion of 13mcg and inclusion of 300mcg.
- Levothyroxine tablets can be crushed and mixed in a small amount (5mL to 10mL) of water for those unable to swallow tablets.

Formulation Cost Comparison:

Product	Cost Per Tablet*	Cost for 30 Days*
Tirosint®-SOL (levothyroxine sodium oral solution)	**Unknown**	**Unknown**
Synthroid® (levothyroxine sodium) tablets	$1.08 - $1.16	$32.40 - $34.80
levothyroxine sodium tablets	$0.30 - $0.76	$9.00 - $22.80

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.

Fiscal Year 2016 Utilization: There was no utilization of Tirosint®-SOL during fiscal year 2016. For other products including levothyroxine sodium tablets, Synthroid® tablets, Levoxyl® tablets, Unithroid® tablets, and Tirosint® capsules there were 50,160 claims for 14,030 members with a total cost of $975,658.45. The cost per day was $0.46 with a cost per claim of $19.28. These costs do not reflect rebated prices or net costs.

Xatmep™ (Methotrexate Oral Solution) Product Summary[13,14,15,16]

Indication(s): Xatmep™ (methotrexate oral solution) is a folate analog metabolic inhibitor indicated for the following:
- Treatment of pediatric patients with acute lymphoblastic leukemia (ALL) as a component of a combination chemotherapy maintenance regimen
- Management of pediatric patients with active polyarticular juvenile idiopathic arthritis (pJIA) who are intolerant of or had an inadequate response to first-line therapy

Dosing and Administration:
- Xatmep™ is available as a clear yellow to orange oral solution that contains 2.5mg of methotrexate per milliliter (equivalent to 2.74mg of methotrexate sodium/mL). It is supplied in a 120mL bottle.
- The recommended dosing for ALL is 20mg/m^2 one time weekly. The starting dose for pJIA is 10mg/m^2 one time weekly. Dosages should be tailored to the individual patient and adjusted gradually to achieve an optimal response.

Other Formulation(s) Available:
- Methotrexate Tablets, Methotrexate Injection Solution, and Trexall® Tablets:
  - Methotrexate tablets, methotrexate injection solution, and Trexall® tablets are indicated for the treatment neoplastic disease or maintenance therapy in combination with other chemotherapeutic agents. These products are also indicated for the symptomatic control of severe, recalcitrant, disabling psoriasis not adequately responsive to other forms of therapy. Additionally, these products are indicated in the management of selected adults with severe, active,

rheumatoid arthritis, or children with active polyarticular-course juvenile rheumatoid arthritis, who have had an insufficient therapeutic response to, or are intolerant of, an adequate trial of first-line therapy.

- Dosing varies based on the disease being treated. Methotrexate tablets are generically available in a 2.5mg strength. Methotrexate injection solution is available generically in 2mL and 10mL vials containing 25mg of methotrexate sodium per milliliter. Trexall® film-coated tablets are available as 5mg, 7.5mg, 10mg, and 15mg strengths. Procedures for proper handling of anticancer drugs should be considered when handling injection solution and tablets, including crushing and cutting tablets.

Formulation Cost Comparison:

Product	Cost Per Tablet or mL*	Cost for 30 Days*Δ
Xatmep™ (methotrexate oral solution)	**$15.80**	**$189.60**
Trexall® (methotrexate tablet) 7.5mg	$19.95	$79.80
methotrexate injection solution	$1.45	$11.60+
methotrexate tablet 2.5mg	$1.04	$12.48

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.
ΔCost for 30 days based on juvenile arthritis weekly dosing of 10mg/m² for a child weighing 18.6kg and 109.2cm tall
+Cost for 30 days of methotrexate injection solution based on use of a 2mL single-use vial for each weekly dose

Fiscal Year 2016 Utilization: There was no utilization of Xatmep™ during fiscal year 2016.

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
METHOTREXATE TAB 2.5MG	3,176	815	$144,271.88	$1.36	3.9	$45.43
METHOTREXATE INJ 25MG/ML	439	137	$8,266.97	$0.53	3.2	$18.83
METHOTREXATE INJ 50MG/2ML	324	100	$4,220.84	$0.74	3.24	$13.03
METHOTREXATE INJ 25MG/ML	49	26	$1,317.14	$0.39	1.88	$26.88
METHOTREXATE INJ 250/10ML	38	16	$474.65	$0.21	2.38	$12.49
METHOTREXATE INJ 100/4ML	16	4	$192.31	$0.53	4	$12.02
TREXALL TAB 10MG	16	4	$2,629.70	$4.16	4	$164.36
TREXALL TAB 15MG	11	3	$2,904.31	$5.46	3.67	$264.03
TREXALL TAB 7.5MG	8	4	$1,557.53	$2.97	2	$194.69
TREXALL TAB 5MG	4	3	$1,644.46	$7.34	1.33	$411.12
TOTAL	**4,081**	**1,016***	**$167,479.79**	**$1.24**	**4.02**	**$41.04**

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

Zovirax® (Acyclovir Ointment & Suspension), Xerese® (Acyclovir/Hydrocortisone Cream), and Denavir® (Penciclovir Cream) Product Summaries[17,18,19,20,21,22]

Indication(s):

- **Zovirax® (acyclovir 5% ointment)** is a synthetic nucleoside analogue indicated in the management of initial genital herpes simplex virus (HSV) and in limited non-life-threatening mucocutaneous HSV infections in immunocompromised patients.

- **Zovirax® (acyclovir suspension)** is indicated for the acute treatment of herpes zoster (shingles), initial episodes and the management of recurrent episodes of genital herpes, and chickenpox (varicella).
- **Xerese® (acyclovir/hydrocortisone 5%/1% cream)** is a combination of a nucleoside analog and a corticosteroid. It is indicated for the early treatment of recurrent HSV labialis (cold sores) to reduce the likelihood of ulcerative cold sores and to shorten the lesion healing time in adults and children (6 years of age and older).
- **Denavir® (penciclovir 1% cream)** is a nucleoside analog, indicated for the treatment of recurrent HSV labialis (cold sores) in adults and children (12 years of age and older).

Dosing and Administration:

- Zovirax® ointment is supplied in a 30g tube containing 50mg of acyclovir per gram. The recommended dosing is topical application of a sufficient quantity to adequately cover all lesions every 3 hours, 6 times per day for 7 days**.**
- Zovirax® suspension is supplied as an off-white, banana-flavored oral suspension containing 200mg of acyclovir per 5mL. Dosing varies depending on diagnosis.
- Xerese® is supplied in a 5g tube containing 5% acyclovir and 1% hydrocortisone per gram. The recommended dosing is topical application 5 times a day for 5 days.
- Denavir® is supplied in 1.5g and 5g tubes containing 10mg of penciclovir per gram. The recommended dosing is topical application every 2 hours during waking hours for a period of 4 days.

Other Formulation(s) Available:

- <u>Acyclovir Tablets and Capsules:</u>
  - Acyclovir tablets and capsules are indicated for the acute treatment of herpes zoster (shingles), initial episodes and the management of recurrent episodes of genital herpes, and chickenpox (varicella). Dosing varies depending on diagnosis. The tablets are generically available in 400mg and 800mg strengths. The capsules are generically available in a 200mg strength.
    - Per the Centers for Disease Control and Prevention (CDC) treatment guidelines for genital HSV, topical therapy with antiviral drugs offers minimal clinical benefit and is discouraged. The CDC indicates that three oral antiviral medications provide clinical benefit for genital herpes: acyclovir, valacyclovir, and famciclovir.
- <u>Zovirax® (Acyclovir 5% Cream):</u>
  - Zovirax® cream is for the treatment of recurrent herpes labialis (cold sores) in immunocompetent adults and adolescents 12 years of age and older. The recommended dosing is topical application 5 times a day for 4 days. It is supplied in a 5g tube containing 50mg of acyclovir per gram.

Formulation Cost Comparison:

Product	Cost Per Tablet/Capsule or Gram*	Cost for Treatment*+
Zovirax® (acyclovir 5% ointment)	**$8.56**	**$256.80**
Xerese® (acyclovir/hydrocortisone 5%/1% cream)	**$225.47**	**$1,127.35**
Denavir® (penciclovir 1% cream)	**$143.08**	**$715.40**
Zovirax® (acyclovir 5% cream)	$140.34	$701.70Δ
acyclovir tablets	$0.09	$2.70
acyclovir capsules	$0.11	$5.50

Costs do not reflect rebated prices or net costs.
ΔZovirax® (acyclovir 5% cream) has a significant rebate.
*Costs based on National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable. +Cost per treatment based on usual dosing regimen for HSV or one tube of topical product.

Fiscal Year 2016 Utilization:

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
ACYCLOVIR TAB 400MG	3,789	2,105	$33,414.72	$0.45	1.8	$8.82
ACYCLOVIR TAB 800MG	1,506	1,115	$17,744.36	$0.87	1.35	$11.78
ACYCLOVIR SUS 200/5ML	1,396	1,111	$188,086.21	$14.04	1.26	$134.73
ACYCLOVIR OIN 5%	849	690	$291,721.94	$27.62	1.23	$343.61
ACYCLOVIR CAP 200MG	819	513	$6,665.15	$0.50	1.6	$8.14
ZOVIRAX CRE 5%	593	451	$451,036.39	$62.17	1.31	$760.60
DENAVIR CRE 1%	95	71	$67,101.95	$23.49	1.34	$706.34
XERESE CRE 5-1%	15	10	$13,869.29	$63.33	1.5	$924.62
TOTAL	**9,062**	**6,066***	**$1,069,640.01**	**$7.50**	**1.49**	**$118.04**

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

Recommendations

The College of Pharmacy recommends the prior authorization of Carac® (fluorouracil 0.5% cream), GoNitro™ (nitroglycerin sublingual powder), Soltamox® (tamoxifen citrate oral solution), Taytulla™ (norethindrone acetate/ethinyl estradiol capsules & ferrous fumarate capsules), Tirosint®-SOL (levothyroxine sodium oral solution), Xatmep™ (methotrexate oral solution), Zovirax® (acyclovir ointment and suspension), Xerese® (acyclovir/hydrocortisone cream), and Denavir® (penciclovir cream) with the following criteria:

Carac® (Fluorouracil 0.5% Cream) Approval Criteria:

1. An FDA approved diagnosis of multiple actinic or solar keratoses of the face and anterior scalp in adults; and
2. A patient-specific, clinically significant reason why the member cannot use fluorouracil 5% cream, fluorouracil 5% solution, or fluorouracil 2% solution.

GoNitro™ (Nitroglycerin Sublingual Powder) Approval Criteria:

1. An FDA approved indication of acute relief of an attack or prophylaxis of angina pectoris due to coronary artery disease; and

2. A patient-specific, clinically significant reason why the member cannot use nitroglycerin sublingual tablets or nitroglycerin lingual spray.

Soltamox® (Tamoxifen Citrate Oral Solution) Approval Criteria:

1. An FDA approved indication of one of the following:
    a. Treatment of metastatic breast cancer in women and men; or
    b. Adjuvant treatment of node-positive breast cancer in postmenopausal women and for the adjuvant treatment of axillary node-negative breast cancer in women following total mastectomy or segmental mastectomy, axillary dissection, and breast irradiation; or
    c. The reduction in risk of invasive breast cancer in women with ductal carcinoma in situ (DCIS), following breast surgery and radiation; or
    d. To reduce the incidence of breast cancer in women at high risk for breast cancer; and
2. A patient-specific, clinically significant reason why the member cannot use tamoxifen tablets.

Taytulla™ (Norethindrone Acetate/Ethinyl Estradiol Capsules & Ferrous Fumarate Capsules) Approval Criteria:

1. An FDA approved indication to prevent pregnancy in women; and
2. A patient-specific, clinically significant reason why the member cannot use all other generic formulations of norethindrone acetate/ethinyl estradiol tablets with ferrous fumarate tablets.

Tirosint®-SOL (Levothyroxine Sodium Oral Solution) Approval Criteria:

1. An FDA approved diagnosis of one of the following:
    a. Hypothyroidism: As replacement therapy in primary (thyroidal), secondary (pituitary), and tertiary (hypothalamic) congenital or acquired hypothyroidism; or
    b. Pituitary Thyrotropin (Thyroid-Stimulating Hormone, TSH) Suppression: As an adjunct to surgery and radioiodine therapy in the management of thyrotropin-dependent well-differentiated thyroid cancer; and
2. A patient-specific, clinically significant reason why the member cannot use all other formulations of levothyroxine sodium in the place of oral solution even when tablets are crushed.

Xatmep™ (Methotrexate Oral Solution) Approval Criteria:

1. An FDA approved indication of one of the following:
    a. Treatment of pediatric patients with acute lymphoblastic leukemia (ALL) as a component of a combination chemotherapy maintenance regimen; or
    b. Management of pediatric patients with active polyarticular juvenile idiopathic arthritis (pJIA) who are intolerant of or had an inadequate response to first-line therapy; and
2. A patient-specific, clinically significant reason why the oral tablets or generic injectable formulation cannot be used.

Zovirax® (Acyclovir Ointment) Approval Criteria:

1. An FDA approved indication of management of initial genital herpes or in limited non-life-threatening mucocutaneous HSV infections in immunocompromised patients; and
2. A patient-specific, clinically significant reason why the member cannot use oral acyclovir, famciclovir, or valacyclovir tablets.

Zovirax® (Acyclovir Suspension) Approval Criteria:

1. An age restriction of seven years and younger will apply. Members older than seven years of age will require a patient-specific, clinically significant reason why a special formulation product is needed.

Sitavig® (Acyclovir Buccal Tablets), Xerese® (Acyclovir/Hydrocortisone Cream), and Denavir® (Penciclovir Cream) Approval Criteria:

1. An FDA approved diagnosis of recurrent herpes labialis (cold sores); and
2. A patient-specific, clinically significant reason why the member cannot use oral acyclovir, famciclovir, or valacyclovir tablets.

Utilization Details of Special Formulations: Fiscal Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
GABAPENTIN PRODUCTS						
HORIZANT TAB 600MG	21	5	$10,841.61	$15.71	4.2	$516.27
SUBTOTAL	**21**	**5**	**$10,841.61**	**$15.71**	**4.2**	**$516.27**
IMIQUIMOD PRODUCTS						
ZYCLARA CRE 3.75%	1	1	$1,098.87	$39.25	1	$1,098.87
SUBTOTAL	**1**	**1**	**$1,098.87**	**$39.25**	**1**	**$1,098.87**
LACTULOSE PRODUCTS						
KRISTALOSE PAK 20GM	9	1	$3,729.44	$13.81	9	$414.38
KRISTALOSE PAK 10GM	2	2	$593.22	$9.89	1	$296.61
SUBTOTAL	**11**	**3**	**$4,322.66**	**$13.10**	**3.67**	**$392.97**
MERCAPTOPURINE PRODUCTS						
PURIXAN SUS 20MG/ML	40	6	$35,222.62	$32.37	6.67	$880.57
SUBTOTAL	**40**	**6**	**$35,222.62**	**$32.37**	**6.67**	**$880.57**
METHOTREXATE PRODUCTS						
OTREXUP INJ 15MG	7	2	$4,263.60	$21.75	3.5	$609.09
OTREXUP INJ 20MG	1	1	$606.91	$21.68	1	$606.91
SUBTOTAL	**8**	**3**	**$4,870.51**	**$21.74**	**2.67**	**$608.81**
TOTAL	**81**	**18***	**$56,356.27**	**$23.88**	**4.5**	**$695.76**

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

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Appendix Q

30-Day Notice to Prior Authorize Aczone® (Dapsone Gel) and Tazorac® (Tazarotene Cream and Gel)

Oklahoma Health Care Authority
June 2017

Introduction[1,2]

Acne vulgaris is a common skin condition affecting approximately 50 million patients in the United States, including 85% of teenagers. Acne is a multifactorial inflammatory disease that effects the pilosebaceous follicles of the skin with four key pathogenic factors including follicular hyperkeratinization, microbial colonization with *Propionibacterium acnes*, sebum production, and inflammation. Neuroendocrine regulatory mechanisms, diet, and genetic factors are also factors that can play a role in acne pathogenesis. Although there is no mortality associated with acne, there is significant physical and psychological morbidity (i.e. permanent scarring, poor self-image, depression, and anxiety). To date, there is no universally agreed-upon grading system of severity; however, severity is often estimated based on a number of factors including: clinical type of lesions, presence of scarring, presence of draining lesions, lack of therapeutic response, and psychological impact of acne. Despite the lack of a universal grading system, severity is often divided into three categories: mild, moderate, and severe. The American Academy of Dermatology released updated acne vulgaris treatment guidelines in 2016, with treatment options including topical therapies, systemic antibiotics, isotretinoin, and hormonal agents. A summary of their recommendations can be seen in Table 1.

Table 1. Treatment Algorithm for Management of Acne Vulgaris*

Severity	Mild	Moderate	Severe
1st Line Treatment	Benzoyl peroxide (BP) or topical retinoid -OR- Topical combination therapy^	Topical combination therapy^ -OR- Oral antibiotic + topical retinoid + BP -OR- Oral antibiotic + topical retinoid + BP + topical antibiotic	Oral antibiotic + topical combination therapy^ -OR- Oral isotretinoin
Alternative Treatment	Add topical retinoid or BP (if not on already) -OR- Consider alternate retinoid -OR- Consider topical dapsone	Consider alternate combination therapy -OR- Consider change in oral antibiotic -OR- Add combined oral contraceptive or oral spironolactone (females) -OR- Consider oral isotretinoin	Consider change in oral antibiotic -OR- Add combined oral contraceptive or oral spironolactone (females) -OR- Consider oral isotretinoin

*Modified from American Academy of Dermatology Acne Vulgaris Treatment Guidelines
^Combinations include BP + Antibiotic, BP + Retinoid or BP + Retinoid + Antibiotic (May be prescribed as a fixed combination product or as separate components.)

Psoriasis is a chronic, inflammatory, multisystem disease with predominantly skin and joint manifestations affecting approximately 2% of the population. Approximately 80% of patients with psoriasis have mild-to-moderate disease. A majority of these patients can be treated with topical agents, which generally provide both high efficacy and safety. The severity of psoriasis is defined not only by the extent of body surface area (BSA) involvement (<5% mild, ≥5% but

<10% moderate, and ≥10% severe), but also by involvement of hands, feet, facial, or genital regions, by which despite involvement of a smaller BSA, the disease may interfere significantly with activities of daily living. Topical corticosteroids are the cornerstone of treatment for a majority of patients with psoriasis. Additional topical therapies include vitamin D analogs, tazarotene, or a combination of a topical corticosteroid with either a vitamin D analog or tazarotene.

Utilization of Aczone® (Dapsone Gel): Calendar Year 2016

Calendar Year 2016 Utilization

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	6	7	$3,847.96	$549.71	$6.28	450	613
Total	**6**	**7**	**$3,847.96**	**$549.71**	**$6.28**	**450**	**613**

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

- There was no use of Aczone® (dapsone gel) during calendar year 2015.

Demographics of Members Utilizing Aczone® (Dapsone Gel)

- Due to the small number of members utilizing Aczone® (dapsone gel) during calendar year 2016, detailed demographic information could not be provided.

Top Prescriber Specialties of Aczone® (Dapsone Gel) by Number of Claims

- The top prescriber specialties listed on paid pharmacy claims during calendar year 2016 included physician assistant, family practitioner, dermatologist, and nurse practitioner.

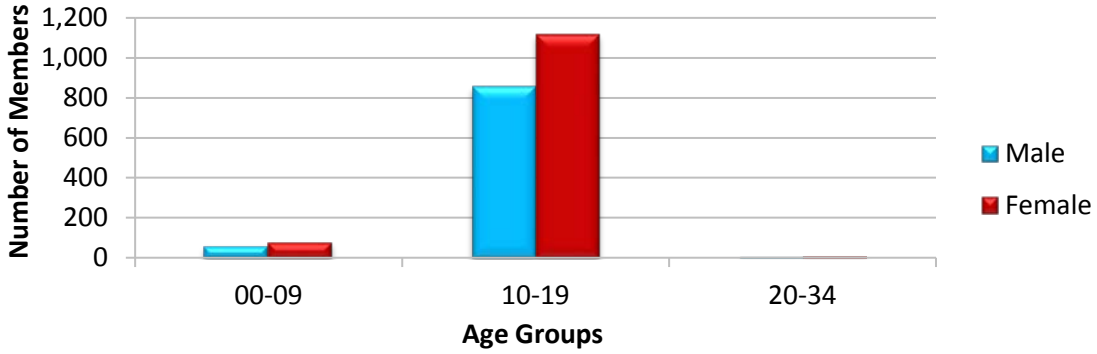
Utilization of Tazorac® (Tazarotene Cream and Gel): Calendar Year 2016

Comparison of Calendar Years

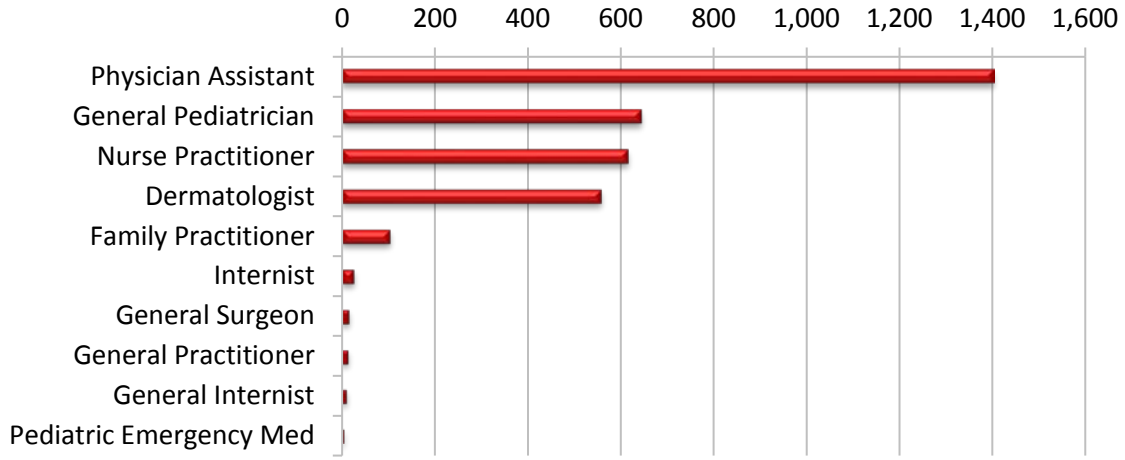
Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2015	1,744	2,737	$1,133,605.17	$414.18	$15.53	115,850	73,018
2016	2,129	3,417	$1,566,736.64	$458.51	$18.37	142,665	85,265
% Change	**22.10%**	**24.80%**	**38.20%**	**10.70%**	**18.30%**	**23.10%**	**16.80%**
Change	**385**	**680**	**$433,131.47**	**$44.33**	**$2.84**	**26,815**	**12,247**

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

Demographics of Members Utilizing Tazorac® Cream and Gel



Top Prescriber Specialties of Tazorac® Cream and Gel by Number of Claims



Market News and Updates[3,4,5]

New FDA Approval(s):

- **February 2016:** The U.S. Food and Drug Administration (FDA) approved Aczone® (dapsone) 7.5% Gel, a topical treatment for acne in patients 12 years of age and older.
- **July 2016:** The FDA approved Differin® (adapalene) 0.1% gel for the once-daily, over-the-counter (OTC) treatment of acne for use in people 12 years of age and older. Adapalene is the first retinoid to be made available OTC for treatment of acne and the first new active ingredient for acne treatment for OTC use since the 1980's.
- **April 2017:** The FDA approved Taro's AB-rated generic tazarotene 0.1% cream. This is the first generic approval of Tazorac®.

Aczone® (Dapsone Gel) Product Summary[6]

Indication(s): Aczone® (dapsone gel) is a sulfone indicated for the topical treatment of acne vulgaris in patients 12 years of age and older.

Dosing:

- Recommended dosing is to apply approximately a pea-sized amount in a thin layer to entire face once daily.
- If no improvement after 12 weeks, treatment should be reassessed.

Mechanism of Action: The mechanism of action of dapsone gel in treating acne vulgaris is not known.

Contraindications: None

Warnings and Precautions:

- Methemoglobinemia: Cases of methemoglobinemia, with resultant hospitalization, have been reported with twice daily dapsone 5% gel. Patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency, or congenital or idiopathic methemoglobinemia are more susceptible to drug-induced methemoglobinemia. Use of dapsone gel in those patients with congenital or idiopathic methemoglobinemia should be avoided. Signs and symptoms of methemoglobinemia may be delayed some hours after exposure. Patients should be advised to discontinue dapsone gel and seek immediate medical attention in the event of cyanosis.
- Hemolysis: Oral dapsone treatment produced dose-related hemolysis and hemolytic anemia. Individuals with G6PD deficiency are more prone to hemolysis with certain drugs. There was no evidence of clinically relevant hemolysis or hemolytic anemia in subjects treated with topical dapsone; however, some subjects with G6PD deficiency treated with twice daily dapsone 5% gel developed laboratory changes suggestive of hemolysis. Dapsone gel should be discontinued if signs and symptoms suggestive of hemolytic anemia occur and should be avoided in patients taking oral dapsone or antimalarial medications due to potential for hemolytic reactions. Combination of dapsone gel with trimethoprim/sulfamethoxazole may increase the likelihood of hemolysis in patients with G6PD deficiency.
- Peripheral Neuropathy: Peripheral neuropathy (motor loss and muscle weakness) has been reported with oral dapsone treatment. No events of peripheral neuropathy were observed in clinical trials with topical dapsone treatment.
- Skin Reactions: Skin reactions (i.e. toxic epidermal necrolysis, erythema multiforme, morbilliform and scarlatiniform reactions, bullous and exfoliative dermatitis, erythema nodosum, and urticaria) have been reported with oral dapsone treatment. These types of skin reactions were not observed in clinical trials with topical dapsone treatment.

Adverse Reactions: The most common adverse reactions (incidence ≥ 0.9%) were application site dryness and pruritus. Methemoglobinemia has been identified during postmarketing use of topical dapsone. Although not observed in clinical trials with topical dapsone, serious adverse reactions have been reported with oral dapsone use, including agranulocytosis, hemolytic anemia, peripheral neuropathy, and skin reactions.

Drug Interactions:

- Trimethoprim-Sulfamethoxazole (TMP-SMX): TMP-SMX increases the systemic level of dapsone and its metabolites. The systemic exposure from dapsone gel is expected to be about 1% of that from the 100mg oral dose, even when co-administered with TMP-SMX.
- Topical Benzoyl Peroxide: Topical benzoyl peroxide used at the same time as dapsone gel may result in temporary, local yellow or orange skin and facial hair discoloration.

Use in Specific Populations:

- Pregnancy: There are no adequate and well controlled studies in pregnant women. Oral dapsone has been shown to have embryocidal effects in rats and rabbits during the period of organogenesis in doses of 75mg/kg/day and 150mg/kg/day respectively. These effects may have been secondary to maternal toxicity. Dapsone gel should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
- Nursing Mothers: Although systemic absorption of dapsone following topical application of dapsone gel is minimal relative to oral dapsone, it is known that dapsone is excreted in human milk. Since there is a potential for oral dapsone to cause adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or discontinue dapsone gel, taking into account the importance of the drug to the mother.
- Pediatric Use: The safety and efficacy of dapsone gel has not been established in pediatric patients below the age of 12 years.
- Geriatric Use: Clinical trials of dapsone gel did not include sufficient numbers of subjects aged 65 years and older to determine whether they respond differently from younger subjects.
- Glucose-6-phosphate Dehydrogenase (G6PD) Deficiency: Individuals with G6PD deficiency may be more prone to methemoglobinemia and hemolysis.

Efficacy: The safety and efficacy of once daily dapsone 7.5% gel was assessed in two 12-week, multicenter, randomized, double-blinded, vehicle-controlled studies. Efficacy was assessed in a total of 4,340 subjects 12 years of age and older. Treatment response was defined at week twelve as the proportion of subjects who were rated "none" or "minimal" with at least a two-grade improvement from baseline on the Global Acne Assessment Score (GAAS), and mean absolute change from baseline in both inflammatory and non-inflammatory lesion counts. A GAAS score of "none" corresponded to no evidence of facial acne and a score of "minimal" corresponded to a few non-inflammatory lesions (comedones) being present and to a few inflammatory lesions (papules/pustules) that may be present. At twelve weeks, dapsone 7.5% gel had GAAS success of 30% compared to 21% with vehicle. Dapsone 7.5% gel had a mean percent reduction of 56% for inflammatory lesions and 45% for non-inflammatory lesions.

Cost:

Medication	Cost Per Gram or mL	Cost Per 30 Days of Therapy*
Aczone® (dapsone) 7.5% gel	$8.63	$517.96
Azelex (azelaic acid) 20% cream	$12.04	$361.22
benzoyl peroxide 10% gel	$0.20[+]	$5.49[+]
clindamycin 1% gel	$1.75	$52.55
erythromycin 2% solution	$0.56	$33.83

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 is unavailable.

*Cost per 30 days based off of smallest package size.

[+]Cost based off of Walgreens generic 28-oz tube from walgreens.com, last checked 04/24/2017.

Tazorac® (Tazarotene Cream and Gel) Product Summary[7,8]

Indication(s):

- Tazarotene 0.1% cream and gel are indicated for topical treatment of acne vulgaris.
- Tazarotene 0.05% and 0.1% cream and gel are indicated for topical treatment of plaque psoriasis.

Dosing:

- *Acne Vulgaris:* Patients should cleanse the face gently, dry skin, and then apply a thin layer on the affected area once daily in the evening.
- *Plaque Psoriasis:* Patients should apply a thin layer to the affected area once daily in the evening. If a bath or shower is taken prior to application, skin should be dry before application. If emollients are used, they should be applied at least an hour before application of tazarotene.
    - It is recommended to initiate treatment with tazarotene 0.05%, then increasing the strength to 0.1% if tolerated and medically indicated.

Mechanism of Action: Tazarotene is a retinoid prodrug that is converted to its active form, the carboxylic acid of tazarotene, by de-esterification. Tazarotenic acid binds to all three members of the retinoic acid receptor (RAR) family: RARα, RARβ, and RARγ, but shows relative selectivity for RARβ and RARγ and may modify gene expression.

Contraindications:

- Women who are pregnant or may become pregnant
- Hypersensitivity or intolerance to any components

Warnings and Precautions:

- Embryofetal Toxicity: Tazarotene is a teratogenic substance and it is not known what level of exposure is required for teratogenicity in humans. Women of child-bearing potential should be warned of potential risk and use adequate birth-control measures. A negative pregnancy test should be obtained within two weeks prior to initiation of tazarotene treatment and treatment should begin during a menstrual period.
- Local Irritation: Some individuals may experience excessive pruritus, burning, skin redness, or peeling. If these effects occur, the medication should be discontinued until the integrity of the skin is restored, or dosing should be reduced to an interval the patient can tolerate, although efficacy of reduced frequency has not been established. Tazarotene should not be used on eczematous skin. Weather extremes, such as wind or cold, may be more irritating to patients using tazarotene.
- Photosensitivity and Risk for Sunburn: Due to higher burning susceptibility, exposure to sunlight (including sunlamps) should be avoided if possible or minimized during use of tazarotene. Patients must be advised to use sunscreens (minimum SPF 15) and protective clothing while using tazarotene. Patients with sunburns should be advised not to use tazarotene until fully recovered.

Adverse Reactions:

- *Acne Vulgaris*: The most common adverse reactions occurring in 10 to 30% of patients include:

- Desquamation
- Dry skin
- Erythema
- Burning/stinging sensation

Adverse reactions occurring in 1 to 10% of patients include:

- Irritation
- Skin pain
- Fissuring
- Localized edema
- Skin discoloration

- *Plaque Psoriasis*: The most common adverse reactions occurring in 10 to 23% of patients include:
  - Pruritus
  - Erythema
  - Burning

  Adverse reactions occurring in 1 to 10% of patients include:
  - Rash
  - Desquamation
  - Irritant contact dermatitis
  - Skin inflammation
  - Fissuring
  - Bleeding
  - Dry skin

Use in Special Populations:

- Pregnancy: Tazarotene is pregnancy category X. Females of child-bearing potential should be warned of the potential risk and should use adequate birth control measures when tazarotene is used.
- Nursing Mothers: The safe use of tazarotene during lactation has not been established.
- Pediatric Use: The safety and efficacy of tazarotene have not been established in patients with psoriasis under the age of 18 years, or in patients with acne under the age of 12 years.
- Geriatric Use: Currently there is no clinical experience on the differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Efficacy:

- *Acne Vulgaris*: Tazarotene 0.1% cream and gel each had two large vehicle-controlled, 12-week studies comparing efficacy and safety to vehicle. Subjects were age 12 years and older with facial acne of a severity suitable for monotherapy. Clinically significant improvement was defined as a between-group difference (in favor of tazarotene) of greater than or equal to a 15% reduction from baseline in total lesions at twelve weeks. Tazarotene 0.1% cream and gel applied once daily was significantly more effective than vehicle in the treatment of facial acne vulgaris of mild-to-moderate severity. The charts below summarize the trial results.

	Tazarotene Cream 0.1%		Vehicle Cream	
Median Percent Reduction in:	Trial 1 (N=218)	Trial 2 (N=206)	Trial 1 (N=218)	Trial 2 (N=205)
Non-inflammatory lesions	46%	41%	27%	21%
Inflammatory lesions	41%	44%	27%	25%
Total lesions	44%	42%	24%	21%

Table modified from tazarotene prescribing information. Allergan Inc.

Median Percent Reduction in:	Tazarotene Gel 0.1%		Vehicle Gel	
	Trial 1 (N=218)	Trial 2 (N=206)	Trial 1 (N=218)	Trial 2 (N=205)
Non-inflammatory lesions	55%	43%	35%	27%
Inflammatory lesions	42%	47%	30%	28%
Total lesions	52%	45%	33%	27%

Table modified from tazarotene prescribing information. Allergan Inc.

- *Psoriasis*: Tazarotene 0.05% and 0.1% cream and gel each had two large, vehicle-controlled, 12-week studies comparing efficacy and safety to vehicle. The primary efficacy variable was clinical success, which was based on an overall lesional assessment (OLA); a measure of clinical judgement of a patient's psoriasis with respect to plaque elevation, scaling, and erythema. The criterion for clinical effectiveness was defined as a between-group difference (in favor of tazarotene) of greater than or equal to 15% in clinical success rate, defined as the percentage of patients with an OLA score of none, minimal, or mild after twelve weeks of treatment. The percentages of patients who achieved clinical success, were significantly higher with both tazarotene 0.1% and 0.05% than with vehicle at most visits during the treatment period. Efficacy of tazarotene was confirmed by the results of the treatment success rates of 50% to 60%. Tazarotene was effective in inducing significant reductions in the severity of plaque elevation and scaling, but erythema was less responsive; however, tazarotene 0.1% was shown to be significantly better than vehicle in reducing erythema after eight and twelve weeks of treatment.

Cost:

Medication	Cost Per Gram or mL	Cost Per 30 Days of Therapy*
tazarotene 0.1% cream	**$7.23**	**$216.82**
Tazorac® 0.1% cream	$11.63	$348.92◊
Tazorac® 0.1% gel	$11.56	$346.74◊
benzoyl peroxide 10% gel	$0.20+	$5.49+
clindamycin 1% solution	$0.68	$20.29
fluocinonide 0.05% cream	$1.08	$32.53

Cost does not reflect rebated price or net cost. Costs based on National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC is unavailable.

*Cost based on use of one 30-gram tube per month, except for benzoyl peroxide 10% gel, which is based on a 28-gram tube.

◊FDA Approved in 1997 and has significant federal rebate.

+Cost based off of Walgreens generic 28-gram tube from walgreens.com, last checked 05/18/2017.

Recommendations

The College of Pharmacy recommends the prior authorization of Aczone® Gel (dapsone) and generic tazarotene cream with the following criteria based, in part, on cost after rebates:

Aczone® (Dapsone Gel) Approval Criteria:

1. An FDA approved indication of acne vulgaris; and
2. Member must be 20 years of age or younger; and

3. A previous trial of benzoyl peroxide or a patient-specific, clinically significant reason why benzoyl peroxide is not appropriate for the member; and
4. A previous trial of a topical antibiotic, such as clindamycin or erythromycin, or a patient-specific, clinically significant reason why a topical antibiotic is not appropriate for the member.

Tazorac® (Tazarotene Cream and Gel) Approval Criteria:

1. An FDA approved indication of acne vulgaris or plaque psoriasis; and
2. Female members must not be pregnant and must be willing to use an effective method of contraception during treatment; and
3. Authorization of generic tazarotene (in place of brand Tazorac®) will require a patient-specific, clinically significant reason the member cannot use the brand formulation (brand formulation is preferred); and
4. For a diagnosis of acne vulgaris, the following must be met:
    a. Member must be 20 years of age or younger; and
5. A quantity limit of 60 grams per 30 days will apply.

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[1] Zaenglein AL, Pathy AL, Scholsser BJ, et al. Guidelines of care for the management of acne vulgaris. *J Am Acad Dermatol*. 2016; 74: 945-73.

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[3] U.S. Food and Drug Administration (FDA). First Generic Drug Approvals. Available online at: https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/DrugandBiologicApprovalReports/ANDAGenericDrugApprovals/. Last revised 5/4/2017. Last accessed 05/15/2017.

[4] U.S. Food and Drug Administration (FDA). FDA approves Differin Gel 0.1% for over-the-counter use to treat acne. Available online at: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm510362.htm. Last revised 7/8/2016. Last accessed 04/22/2017.

[5] Allergan, Inc. Allergan Announces FDA Approval of Aczone® (dapsone) Gel, 7.5% for Treatment of Acne Vulgaris. Available online at: https://www.allergan.com/news/news/thomson-reuters/allergan-announces-fda-approval-of-aczone-dapsone. Last revised 2/25/2016. Last accessed 5/17/2017.

[6] Aczone® 7.5% Gel Prescribing Information. Allergan, Inc. Available online at: https://www.allergan.com/assets/pdf/aczone7-5_pi. Last revised 02/2016. Last accessed 05/2017.

[7] Tazorac® Cream Prescribing Information. Allergan, Inc. Available online at: https://www.allergan.com/assets/pdf/tazorac_cream_pi. Last revised 12/2013. Last accessed 04/2017.

[8] Tazorac® Gel Prescribing Information. Allergan, Inc. Available online at: https://www.allergan.com/assets/pdf/tazorac_gel_pi. Last revised 02/2011. Last accessed 04/2017.

Appendix R

Calendar Year 2016 Annual Review of H.P. Acthar® Gel (Corticotropin Injection)

Oklahoma Health Care Authority
June 2017

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

H.P. Acthar® Gel (corticotropin injection) is an adrenocorticotropic hormone (ACTH) analogue, which stimulates the adrenal cortex to secrete cortisol, corticosterone, aldosterone, and other weak androgenic substances. The elevated cortisol levels suppress ACTH release. H.P. Acthar® Gel was originally approved by the U.S. Food and Drug Administration (FDA) in 1952 and is FDA-approved to treat a variety of diseases and disorders. Examples of diseases for which ACTH may be used include infantile spasms (IS) and acute multiple sclerosis (MS) exacerbations. The wholesale acquisition cost (WAC) per 5mL multi-dose vial of H.P. Acthar® Gel 80 units/mL is $36,382.00.

IS is a rare seizure disorder that typically presents in the first year of life. In the United States, it is estimated that 2,500 children are diagnosed with IS each year. In 2010, the FDA approved H.P. Acthar® Gel for the treatment of IS. Corticotropin is recommended as first-line treatment of IS in most patients. The optimal dose and duration of corticotropin injection gel for the treatment of IS is not known and may differ among patients. The recommended dose for the treatment of IS per the H.P. Acthar® Gel package insert is 150 units/m^2 divided into twice daily intramuscular injections of 75 units/m^2. Following two weeks of treatment, dosing should be gradually tapered and discontinued over a two week period.

H.P. Acthar® Gel was approved in 1978 by the FDA as a short-term treatment for acute exacerbations of MS. For acute exacerbations, glucocorticoids (e.g., methylprednisolone) are typically used. H.P. Acthar® Gel may be an alternative treatment option for patients who cannot tolerate the adverse effects of high dose glucocorticoids or have poor venous access and have difficulty receiving intravenous medications. The recommended dose of H.P. Acthar® Gel is daily intramuscular or subcutaneous doses of 80 to 120 units for 2 to 3 weeks for acute exacerbations. The dosage should be individualized according to the medical condition.

Current Prior Authorization Criteria

H.P. Acthar® Gel (Corticotropin Injection) Approval Criteria:

1. An FDA approved diagnosis of infantile spasms; and
    a. Member must be two years of age or younger; and
    b. Must be prescribed by, or in consultation with, a neurologist or an advanced care practitioner with a supervising prescriber that is a neurologist; or
2. An FDA approved diagnosis of multiple sclerosis (MS); and
    a. Member is experiencing an acute exacerbation; and

b. Must be prescribed by, or in consultation with, a neurologist or an advanced care practitioner with a supervising prescriber that is a neurologist or a physician that specializes in MS; and
c. A patient-specific, clinically significant reason why the member cannot use alternative corticosteroid therapy (e.g., IV methylprednisolone); and
d. Therapy will be limited to five weeks per approval (three weeks of treatment, followed by taper). Additional approval, beyond the initial five weeks, will require prescriber documentation of response to initial treatment and need for continued treatment; or

3. An FDA approved diagnosis of nephrotic syndrome without uremia of the idiopathic type or that is due to lupus erythematosus to induce a diuresis or a remission of proteinuria; and
    a. Must be prescribed by, or in consultation with, a nephrologist or an advanced care practitioner with a supervising prescriber that is a nephrologist; and
    b. A patient-specific, clinically significant reason why the member cannot use alternative corticosteroid therapy (e.g., prednisone); or
4. An FDA approved diagnosis of the following disorders and diseases: rheumatic; collagen; dermatologic; allergic states; ophthalmic; respiratory; and edematous states; and
    a. A patient-specific, clinically significant reason why the member cannot use alternative corticosteroid therapy.

Utilization of H.P. Acthar® Gel (Corticotropin Injection): Calendar Year 2016

Comparison of Calendar Years

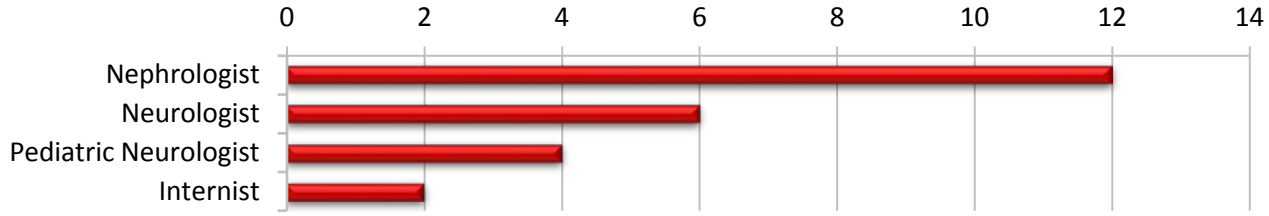
Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2015	19	56	$3,119,010.24	$55,696.61	$2,707.47	460	1,152
2016	11	24	$1,356,258.56	$56,510.77	$3,082.41	190	440
% Change	**-42.10%**	**-57.10%**	**-56.50%**	**1.50%**	**13.80%**	**-58.70%**	**-61.80%**
Change	**-8**	**-32**	**-$1,762,751.68**	**$814.16**	**$374.94**	**-270**	**-712**

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

Demographics of Members Utilizing H.P. Acthar® Gel (Corticotropin Injection)

- Due to the small number of members utilizing H.P. Acthar® Gel (corticotropin injection) during calendar year 2016, detailed demographic information could not be provided.

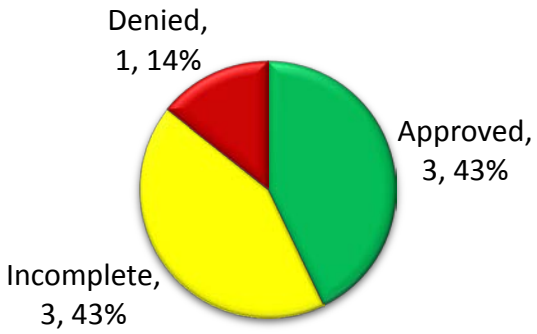
Top Prescriber Specialties of H.P. Acthar® Gel (Corticotropin Injection) by Number of Claims



Prior Authorization of H.P. Acthar® Gel (Corticotropin Injection)

There were seven prior authorization requests submitted for H.P. Acthar® Gel (corticotropin injection) during calendar year 2016. The following chart shows the status of the submitted petitions for calendar year 2016. The prior authorization criteria went into effect on November 3, 2016.

Status of Petitions



Market News and Updates[7]

News:

- **June 2017:** Questcor Pharmaceuticals settled an antitrust suit with Baylor University. The lawsuit alleged Questcor acquired the U.S. rights to Synacthen, a potential competitor to Acthar®, to block competition from the market. The company increased the price of Acthar® from $40 per vial to $34,000 per vial following the acquisition. Questcor must also transfer the rights to Synacthen to another company.

Recommendations

The College of Pharmacy does not recommend any changes to the H.P. Acthar® Gel (corticotropin injection) prior authorization criteria at this time.

[1] H.P. Acthar® Gel Prescribing Information. Mallinckrodt™ Pharmaceuticals. Available online at: http://www.acthar.com/pdf/Acthar-PI.pdf. Last revised 01/2015. Last accessed 04/28/2017.
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Appendix S

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: May 5th, 2017

FDA approves drug to treat ALS

The FDA approved Radicava™ (edaravone) to treat patients with amyotrophic lateral sclerosis (ALS), commonly referred to as Lou Gehrig's disease.

ALS is a rare disease that attacks and kills the nerve cells that control voluntary muscles. Voluntary muscles produce movements such as chewing, walking, breathing and talking. The nerves lose the ability to activate specific muscles, which causes the muscles to become weak and leads to paralysis. ALS is progressive, meaning it gets worse over time. The Centers for Disease Control and Prevention estimates that approximately 12,000 to 15,000 Americans have ALS. Most people with ALS die from respiratory failure, usually within three to five years from when the symptoms first appear.

Radicava™ is an intravenous infusion given by a health care professional. It is administered with an initial treatment cycle of daily dosing for 14 days, followed by a 14-day drug-free period. Subsequent treatment cycles consist of dosing on 10 of 14 days, followed by 14 days drug-free.

The efficacy of edaravone for the treatment of ALS was demonstrated in a six-month clinical trial conducted in Japan. In the trial, 137 participants were randomized to receive edaravone or placebo. At Week 24, individuals receiving edaravone declined less on a clinical assessment of daily functioning compared to those receiving a placebo.

The most common adverse reactions reported by clinical trial participants receiving edaravone were bruising and gait disturbance.

Radicava™ is also associated with serious risks that require immediate medical care, such as hives, swelling, or shortness of breath, and allergic reactions to sodium bisulfite, an ingredient in the drug. Sodium bisulfite may cause anaphylactic symptoms that can be life-threatening in people with sulfite sensitivity.

The FDA granted this drug orphan drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases.

The FDA granted approval of Radicava™ to Mitsubishi Tanabe Pharma America, Inc.

FDA NEWS RELEASE

For Immediate Release: May 23rd, 2017

FDA approves first cancer treatment for any solid tumor with a specific genetic feature

The FDA granted accelerated approval to a treatment for patients whose cancers have a specific genetic feature (biomarker). This is the first time the agency has approved a cancer treatment based on a common biomarker rather than the location in the body where the tumor originated.

Keytruda® (pembrolizumab) is indicated for the treatment of adult and pediatric patients with unresectable or metastatic solid tumors that have been identified as having a biomarker referred to as microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR). This indication covers patients with solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options and patients with colorectal cancer that has progressed following treatment with certain chemotherapy drugs.

MSI-H and dMMR tumors contain abnormalities that affect the proper repair of DNA inside the cell. Tumors with these biomarkers are most commonly found in colorectal, endometrial and gastrointestinal cancers, but also less commonly appear in cancers arising in the breast, prostate, bladder, thyroid gland and other places. Approximately 5 percent of patients with metastatic colorectal cancer have MSI-H or dMMR tumors.

Keytruda® works by targeting the cellular pathway known as PD-1/PD-L1 (proteins found on the body's immune cells and some cancer cells). By blocking this pathway, Keytruda® may help the body's immune system fight the cancer cells. The FDA previously approved Keytruda® for the treatment of certain patients with metastatic melanoma, metastatic non-small cell lung cancer, recurrent or metastatic head and neck cancer, refractory classical Hodgkin lymphoma, and urothelial carcinoma.

Keytruda® was approved for this new indication using the Accelerated Approval pathway, under which the FDA may approve drugs for serious conditions where there is unmet medical need and a drug is shown to have certain effects that are reasonably likely to predict a clinical benefit to patients. Further study is required

to verify and describe anticipated clinical benefits of Keytruda®, and the sponsor is currently conducting these studies in additional patients with MSI-H or dMMR tumors.
The safety and efficacy of Keytruda® for this indication were studied in patients with MSI-H or dMMR solid tumors enrolled in one of five uncontrolled, single-arm clinical trials. In some trials, patients were required to have MSI-H or dMMR cancers, while in other trials, a subgroup of patients were identified as having MSI-H or dMMR cancers by testing tumor samples after treatment began. A total of 15 cancer types were identified among 149 patients enrolled across these five clinical trials. The most common cancers were colorectal, endometrial and other gastrointestinal cancers. The review of Keytruda® for this indication was based on the percentage of patients who experienced complete or partial shrinkage of their tumors (overall response rate) and for how long (durability of response). Of the 149 patients who received Keytruda® in the trials, 39.6% had a complete or partial response. For 78 percent of those patients, the response lasted for six months or more.
Common side effects of Keytruda® include fatigue, itchy skin (pruritus), diarrhea, decreased appetite, rash, fever (pyrexia), cough, difficulty breathing (dyspnea), musculoskeletal pain, constipation and nausea.
Keytruda® can cause serious conditions known as immune-mediated side effects, including inflammation of healthy organs such as the lungs (pneumonitis), colon (colitis), liver (hepatitis), endocrine glands (endocrinopathies), and kidneys (nephritis). Complications or death related to allogeneic hematopoietic stem cell transplantation after using Keytruda® has occurred.
Patients who experience severe or life-threatening infusion-related reactions should stop taking Keytruda®.
Women who are pregnant or breastfeeding should not take Keytruda® because it may cause harm to a developing fetus or newborn baby. The safety and effectiveness of Keytruda® in pediatric patients with MSI-H central nervous system cancers have not been established.
The FDA granted this application Priority Review designation, under which the FDA's goal is to take action on an application within six months where the agency determines that the drug, if approved, would significantly improve the safety or effectiveness of treating, diagnosing or preventing a serious condition.
The FDA granted accelerated approval of Keytruda® to Merck & Co.

FDA NEWS RELEASE

For Immediate Release: May 26th, 2017

FDA broadens ceritinib indication to previously untreated ALK-positive metastatic NSCLC

The FDA granted regular approval to ceritinib (Zykadia®, Novartis Pharmaceuticals Corp.) for patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test.
In April 2014, ceritinib received accelerated approval for patients with ALK-positive metastatic NSCLC whose disease has progressed or who are intolerant to crizotinib based on a blinded independent review committee (BIRC)-assessed overall response rate (ORR) of 44% among 163 patients in a single-arm trial.
The current approval is based on data from ASCEND-4 (NCT01828099), a randomized, multicenter, open-label, active-controlled trial conducted in patients with untreated ALK-positive NSCLC. All patients were required to have evidence of ALK-rearrangement identified by the VENTANA ALK (D5F3) test performed through central laboratory testing.
ASCEND-4 randomized 376 patients (1:1) to receive either ceritinib (n=189) 750mg orally once daily until disease progression or platinum-pemetrexed doublet chemotherapy (n=187). Patients in the chemotherapy arm received pemetrexed (500mg/m^2) with either cisplatin (75mg/m^2) or carboplatin (AUC 5-6) on day 1 of every 21-day cycle for up to 4 cycles, followed by pemetrexed maintenance therapy.
ASCEND-4 demonstrated an improvement in progression-free survival (PFS) as assessed by BIRC, with a hazard ratio (HR) of 0.55 (95% CI: 0.42, 0.73, p-value <0.0001). The estimated median PFS was 16.6 months (95% CI: 12.6, 27.2) in the ceritinib arm and 8.1 months (95% CI: 5.8, 11.1) in the chemotherapy arm. Confirmed ORR, was 73% (95% CI: 66%, 79%) and 27% (95% CI: 21%, 34%) in the ceritinib and chemotherapy arms, respectively. Estimated median response durations were 23.9 months (95% CI: 16.6, not estimable [NE]) and 11.1 months (95% CI: 7.8, 16.4) in the ceritinib and chemotherapy arms, respectively. Overall survival data are immature.
In patients with measurable central nervous system (CNS) lesions on baseline brain scans, the confirmed overall intracranial response rate (OIRR), assessed by BIRC neuro-radiologist, was 57% (95% CI: 37%, 76%) in the ceritinib arm and 22% (95% CI 9%, 42% in the chemotherapy arm. The median CNS response duration was 16.6 months (95% CI: 8.1, NE) and not estimable (95% CI: 1.5, NE) in the ceritinib and chemotherapy arms, respectively.

The most common adverse reactions (occurring in at least 25% of ceritinib-treated patients in ASCEND-4) were diarrhea, nausea, vomiting, fatigue, abdominal pain, decreased appetite, and cough. Serious adverse reactions occurred in 38% of patients treated with ceritinib. Adverse reactions leading to ceritinib discontinuation occurred in 12%. Adverse reactions that led to ceritinib discontinuation in 1% or more of patients were increased creatinine, increased amylase, and increased lipase. Dose interruption due to adverse reactions occurred in 77% of ceritinib-treated patients, while dose reductions were required in 66%. The recommended ceritinib dose is 750mg orally once daily, to be taken at least 1 hour before or at least 2 hours after a meal.
Full prescribing information is available at: Highlights of Prescribing Information Zykadia®.

FDA NEWS RELEASE

For Immediate Release: May 30th, 2017

FDA approves first generic Strattera® for the treatment of ADHD

The FDA approved the first generic versions of Strattera® (atomoxetine) to treat attention-deficit/hyperactivity disorder (ADHD) in pediatric and adult patients.
Apotex Inc., Teva Pharmaceuticals USA Inc., Aurobindo Pharma Limited and Glenmark Pharmaceuticals Limited gained approval to market atomoxetine in multiple strengths.
Generic prescription drugs approved by the FDA have the same high quality and strength as brand-name drugs. Generic prescription drug manufacturing and packaging sites must pass the same quality standards as those of brand-name drugs.
ADHD is marked by an ongoing pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development.
In the clinical trials for atomoxetine in children and adolescents, the most common side effects reported were upset stomach, decreased appetite, nausea or vomiting, dizziness, tiredness, and mood swings. In the clinical trials in adults, the most common side effects reported were constipation, dry mouth, nausea, decreased appetite, dizziness, sexual side effects, and problems passing urine.
Atomoxetine must be dispensed with a patient Medication Guide that describes the drug's uses and warnings. This medication has a boxed warning for the increased risk of suicidal ideation in children and adolescents. Patients taking this medication should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dose changes. Other important warnings include the risk of severe liver damage and potential for serious cardiovascular events.

Safety Announcements

FDA approves label changes for use of general anesthetic and sedation drugs in young children

[5/1/17] On April 27, 2017 the FDA notified the public that they have approved previously announced label changes regarding the use of general anesthetic and sedation medicines in children younger than 3 years. These changes include:

- A new Warning stating that exposure to these medicines for lengthy periods of time or over multiple surgeries or procedures may negatively affect brain development in children younger than 3 years.
- And, additional information to the sections of the labels about pregnancy and pediatric use to describe studies in young animals and pregnant animals that showed exposure to general anesthetic and sedation drugs for more than 3 hours can cause widespread loss of nerve cells in the developing brain; and studies in young animals suggested these changes resulted in long-term negative effects on the animals' behavior or learning.

General anesthetic and sedation drugs are necessary for patients, including young children and pregnant women, who require surgery or other painful and stressful procedures. In the U.S., surgeries during the third trimester of pregnancy requiring general anesthesia are performed only when medically necessary and rarely last longer than 3 hours. The FDA is advising that in these situations, pregnant women should not delay or avoid surgeries or procedures during pregnancy as doing so can negatively affect them and their infants. Also, surgeries or procedures in children younger than 3 years should not be delayed or avoided when medically necessary. Consideration should be given to delaying potentially elective surgery in young children where medically appropriate.

Parents, caregivers, and pregnant women should talk to their health care professionals if they have any questions or concerns about general anesthesia and sedation drugs.
Health care professionals should continue to follow their usual practices of patient counseling including discussing the benefits and risks of surgeries or procedures that require general anesthesia and sedation drugs.
The FDA will continue to monitor the use of these drugs in children and will update the public if additional information becomes available. Side effects involving general anesthetics and sedation drugs or other medicines should be reported to the FDA MedWatch program at www.fda.gov/Medwatch.

Safety Announcements

FDA Drug Safety Communication: FDA confirms increased risk of leg and foot amputations with the diabetes medicine canagliflozin (Invokana®, Invokamet®, Invokamet XR®)

[5/27/17] Based on new data from two large clinical trials, the FDA has concluded that the type 2 diabetes medicine canagliflozin (Invokana®, Invokamet®, Invokamet XR®) causes an increased risk of leg and foot amputations. The FDA is requiring new warnings, including their most prominent Boxed Warning, to be added to the canagliflozin drug labels to describe this risk.
Patients taking canagliflozin should notify their health care professionals right away if they develop new pain or tenderness, sores or ulcers, or infections in thier legs or feet. Patients should talk to their health care professional if they have questions or concerns and should not stop taking their diabetes medicine without first talking to their health care professional.
Health care professionals should, before starting canagliflozin, consider factors that may predispose patients to the need for amputations. These factors include a history of prior amputation, peripheral vascular disease, neuropathy, and diabetic foot ulcers. Patients receiving canagliflozin should be monitored for the signs and symptoms described above and canagliflozin should be discontinued if these complications occur.
Untreated, type 2 diabetes can lead to serious problems, including blindness, nerve and kidney damage, and heart disease. Canagliflozin is a prescription medicine used with diet and exercise to lower blood sugar in adults with type 2 diabetes. It belongs to a class of drugs called sodium-glucose cotransporter-2 (SGLT2) inhibitors. Canagliflozin lowers blood sugar by causing the kidneys to remove sugar from the body through the urine.
Final results from two clinical trials – the CANVAS (Canagliflozin Cardiovascular Assessment Study) and CANVAS-R (A Study of the Effects of Canagliflozin on Renal Endpoints in Adult Participants With Type 2 Diabetes Mellitus) – showed that leg and foot amputations occurred about twice as often in patients treated with canagliflozin compared to patients treated with placebo. The CANVAS trial showed that over a year's time, the risk of amputation for patients in the trial were equivalent to:

- 5.9 out of every 1,000 patients treated with canagliflozin
- 2.8 out of every 1,000 patients treated with placebo

The CANVAS-R trial showed that over a year's time, the risk of amputation for patients in the trial were equivalent to:

- 7.5 out of every 1,000 patients treated with canagliflozin
- 4.2 out of every 1,000 patients treated with placebo

Amputations of the toe and middle of the foot were the most common; however, amputations involving the leg, below and above the knee, also occurred. Some patients had more than one amputation, some involving both limbs.
The FDA urges health care professionals and patients to report side effects involving canagliflozin and other medicines to the FDA MedWatch program.

Safety Announcements

FDA identifies no harmful effects to date with brain retention of gadolinium-based contrast agents for MRIs; review to continue

[5-22-2017] A FDA review to date has not identified adverse health effects from gadolinium retained in the brain after the use of gadolinium-based contrast agents (GBCAs) for magnetic resonance imaging (MRI). All GBCAs may be associated with some gadolinium retention in the brain and other body tissues. However, because the FDA identified no evidence to date that gadolinium retention in the brain from any of the GBCAs, including GBCAs associated with higher retention of gadolinium, is harmful, restricting GBCA use is not

warranted at this time. The FDA will continue to assess the safety of GBCAs and plan to have a public meeting to discuss this issue in the future.
The FDA's recommendations for health care professionals and patients remain unchanged from July 2015 when they informed the public that they were investigating this potential risk with GBCAs. As is appropriate when considering the use of any medical imaging agent, **health care professionals** should limit GBCA use to circumstances in which additional information provided by the contrast agent is necessary, and assess the necessity of repetitive MRIs with GBCAs. **Patients, parents, and caregivers** should talk to their health care professionals if they have any questions or concerns about the use of GBCAs with MRIs. Retention of gadolinium affects only GBCAs, and does not apply to other types of scanning agents used for other imaging procedures, such as those that are iodine-based or radioisotopes.
GBCAs contain gadolinium, a type of heavy metal, that is linked to a carrier molecule. MRIs are a way to scan the body for problems such as cancer, infections, or bleeding. GBCAs are injected into a vein to enhance the quality of the MRI images of internal organs, blood vessels, and tissues, which helps health care professionals diagnose medical conditions. There are two types of GBCAs based on their chemical structures, *linear* GBCAs and *macrocyclic* GBCAs.
The FDA evaluated scientific publications and adverse event reports submitted to FDA. Some human and animal studies looked at GBCA use over periods longer than a year. These publications and reports show that gadolinium is retained in organs such as the brain, bones, and skin. The publications show that *linear* GBCAs retain more gadolinium in the brain than *macrocyclic* GBCAs. However, the FDA's review did not identify adverse health effects related to this brain retention.
To date, the only known adverse health effect related to gadolinium retention is a rare condition called nephrogenic systemic fibrosis (NSF) that occurs in a small subgroup of patients with pre-existing kidney failure. NSF is a painful skin disease characterized by thickening of the skin, which can involve the joints and cause significant limitation of motion within weeks to months. Recent publications report cases of reactions involving thickening and hardening of the skin and other tissues in patients with normal kidney function who received GBCAs and did not have NSF; some of these patients also had evidence of gadolinium retention. The FDA is continuing to evaluate such reports to determine if these fibrotic reactions are an adverse health effect of retained gadolinium.
The manufacturer of OptiMARK® (gadoversetamide), a linear GBCA, updated its label with information about gadolinium retention in various body organs such as the brain, skin, and other organs. The FDA is reviewing the labels of other GBCAs to determine if changes are needed.
A recent review by the Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicines Agency (EMA) also identified no adverse health effects with gadolinium retention in the brain, but that Committee recommended suspending the marketing authorization of certain *linear* GBCAs because they cause a greater retention of gadolinium in the brain compared to *macrocyclic* GBCAs. The Committee's recommendation is currently undergoing an appeal, which will be further reviewed by the PRAC and subsequently by the EMA's Committee for Medicinal Products for Human Use.
The FDA is continuing to assess the safety of GBCAs. The FDA's National Center for Toxicological Research (NCTR) is conducting a study on brain retention of GBCAs in rats. Other research is also being conducted about how gadolinium is retained in the body. The FDA will update the public when new information becomes available and they plan to have a public meeting to discuss this issue in the future.
The FDA urges patients and health care professionals to report side effects involving GBCAs or other medicines to the FDA MedWatch program.

Current Drug Shortages Index (as of June 1st, 2017):

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

Asparaginase Erwinia Chrysanthemi (Erwinaze)	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Belatacept (Nulojix) Lyophilized Powder for Injection	***Currently in Shortage***
Bleomycin Sulfate for Injection	***Currently in Shortage***
Calcium Chloride Injection, USP	***Currently in Shortage***
Calcium Gluconate Injection	***Currently in Shortage***
Cefepime Injection	***Currently in Shortage***
Cefotaxime Sodium (Claforan) Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***

Dextrose 50% Injection	***Currently in Shortage***
Dihydroergotamine Mesylate Injection	***Currently in Shortage***
Disopyramide Phosphate (Norpace) Capsules	***Currently in Shortage***
Epinephrine Injection	***Currently in Shortage***
Epinephrine Injection, 0.1 mg/mL	***Currently in Shortage***
Estradiol Valerate Injection, USP	***Currently in Shortage***
Ethiodized Oil (Lipiodol) Injection	***Currently in Shortage***
Etoposide Phosphate (Etopophos) Injection	***Currently in Shortage***
Fentanyl Citrate (Sublimaze) Injection	***Currently in Shortage***
Gemifloxacin Mesylate (Factive) Tablets	***Currently in Shortage***
Imipenem and Cilastatin for Injection, USP	***Currently in Shortage***
Indigotindisulfonate Sodium (Indigo Carmine) Injection	***Currently in Shortage***
L-Cysteine Hydrochloride Injection	***Currently in Shortage***
Labetalol Hydrochloride Injection	***Currently in Shortage***
Leucovorin Calcium Lyophilized Powder for Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection	***Currently in Shortage***
Liotrix (Thyrolar) Tablets	***Currently in Shortage***
Mecasermin [rDNA origin] (Increlex) Injection	***Currently in Shortage***
Methotrexate Sodium Injection	***Currently in Shortage***
Methylprednisolone Sodium Succinate for Injection, USP	***Currently in Shortage***
Multi-Vitamin Infusion (Adult and Pediatric)	***Currently in Shortage***
Mupirocin Calcium Nasal Ointment	***Currently in Shortage***
Nitrous Oxide, Gas	***Currently in Shortage***
Penicillin G Benzathine (Bicillin L-A) Injection	***Currently in Shortage***
Penicillin G Benzathine and Penicillin G Procaine (Bicillin C-R) Injection	***Currently in Shortage***
Penicillin G Procaine Injection	***Currently in Shortage***
Peritoneal Dialysis Solutions	***Currently in Shortage***
Piperacillin and Tazobactam (Zosyn) Injection	***Currently in Shortage***
Potassium Chloride Injection	***Currently in Shortage***
Potassium Phosphate Injection	***Currently in Shortage***
Procainamide Hydrochloride Injection, USP	***Currently in Shortage***
Promethazine (Phenergan) Injection	***Currently in Shortage***
Ranitidine Injection, USP	***Currently in Shortage***
Rocuronium Bromide Injection	***Currently in Shortage***
Sacrosidase (Sucraid) Oral Solution	***Currently in Shortage***
Sclerosol Intrapleural Aerosol	***Currently in Shortage***
Scopolamine (Transderm Scop) Transdermal System Patch	***Currently in Shortage***
Sincalide (Kinevac) Lyophilized Powder for Injection	***Currently in Shortage***
Sodium Acetate Injection, USP	***Currently in Shortage***
Sodium Bicarbonate Injection, USP	***Currently in Shortage***
Sodium Chloride 0.9% Injection Bags	***Currently in Shortage***
Sodium Chloride 23.4% Injection	***Currently in Shortage***
Sterile Talc Powder	***Currently in Shortage***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***
Theophylline Extended Release Tablets and Capsules	***Currently in Shortage***
Tolmetin Sodium Tablets, USP	***Currently in Shortage***