Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
February 11, 2015
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 – February 11, 2015

DATE: February 2, 2015

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 February meeting.
Material is arranged in order of the agenda.

Call to Order

Public Comment Forum

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

Update on Medication Coverage Authorization Unit/Long-Acting Beta Agonist Utilization: Pediatric Members – Appendix B

Action Item – Vote to Prior Authorize Viekira Pak™ (Ombitasvir/Paritaprevir/Ritonavir/Dasabuvir) – Appendix C

Action Item – Vote to Prior Authorize Northera™ (Droxidopa) – Appendix D

Action Item – Vote to Prior Authorize Akynzeo® (Netupitant/Palonosetron) – Appendix E

30-Day Notice to Prior Authorize Myalept™ (Metreleptin) – Appendix F

Annual Review of Pulmonary Arterial Hypertension Medications and 30-Day Notice to Prior Authorize Orenitram™ (Treprostinil) and Revatio® (Sildenafil Oral Suspension) – Appendix G

Annual Review of Multiple Sclerosis Medications and 30-Day Notice to Prior Authorize Lemtrada™ (Alemtuzumab) and Plegridy™ (Peginterferon β-1a) – Appendix H

30-Day Notice to Prior Authorize Brisdelle® (Paroxetine Mesylate) – Appendix I

Annual Review of Ravicti® (Gylcerol Phenylbutyrate) – Appendix J

Annual Review of Procysbi® (Cysteamine Bitartrate Delayed-Release) – Appendix K

Annual Review of Fulyzaq® (Crofelemer) – Appendix L

FDA and DEA Updates – Appendix M

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board

(DUR Board)

Meeting – February 11, 2015 @ 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. Acknowledgment of Speakers and Agenda Items

Items to be presented by Dr. Muchmore, Chairman:

3. **Action Item – Approval of DUR Board Meeting Minutes – See Appendix A**
   A. January 14, 2015 DUR Minutes – Vote
   B. January 14, 2015 DUR Recommendations Memorandum

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

4. **Update on Medication Coverage Authorization Unit/Long-Acting Beta Agonist Utilization: Pediatric Members – See Appendix B**
   A. Medication Coverage Activity for January 2015
   B. Pharmacy Help Desk Activity for January 2015
   C. Long-Acting Beta Agonist Utilization: Pediatric Members

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

5. **Action Item – Vote to Prior Authorize Viekira Pak™ (Ombitasvir/Paritaprevir/Ritonavir/Dasabuvir) – See Appendix C**
   A. College of Pharmacy Recommendations
   B. Hepatitis C Therapy Pharmacy Agreement
   C. Hepatitis C Therapy Intent to Treat Contract

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

6. **Action Item – Vote to Prior Authorize Northera™ (Droxidopa) – See Appendix D**
   A. College of Pharmacy Recommendations

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

7. **Action Item – Vote to Prior Authorize Akynzeo® (Netupitant/Palonosetron) – See Appendix E**
   A. College of Pharmacy Recommendations

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

8. 30-Day Notice to Prior Authorize Myalept™ (Metreleptin) – See Appendix F

A. Introduction
B. Myalept™ (Metreleptin) Product Summary
C. College of Pharmacy Recommendations

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

9. Annual Review of Pulmonary Arterial Hypertension Medications and 30-Day Notice to Prior Authorize Orenitram™ (Treprostinil) and Revatio® (Sildenafil Oral Suspension) – See Appendix G

A. Introduction
B. Treatment
C. Current Prior Authorization Criteria
D. Utilization of Pulmonary Arterial Hypertension Medications
E. Prior Authorization of Pulmonary Arterial Hypertension Medications
F. Market News and Updates
G. Product Summaries
H. College of Pharmacy Recommendations
I. Utilization Details of Pulmonary Arterial Hypertension Medications

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

10. Annual Review of Multiple Sclerosis Medications and 30-Day Notice to Prior Authorize Lemtrada™ (Alemtuzumab) and Plegridy™ (Peginterferon β-1a) – See Appendix H

A. Current Prior Authorization Criteria
B. Utilization of Multiple Sclerosis Medications
C. Prior Authorization of Multiple Sclerosis Medications
D. Market News and Updates
E. Product Summaries
F. College of Pharmacy Recommendations
G. Utilization Details of Multiple Sclerosis Medications

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

11. 30-Day Notice to Prior Authorize Brisdelle® (Paroxetine Mesylate) – See Appendix I

A. Introduction
B. Brisdelle® (Paroxetine Mesylate) Product Summary
C. College of Pharmacy Recommendations

Non-presentation, Questions Only:

12. Annual Review of Ravicti® (Gylcerol Phenylbutyrate) – See Appendix J

A. Indication
B. Current Prior Authorization Criteria
C. Utilization of Ravicti® (Gylcerol Phenylbutyrate)
D. Prior Authorization of Ravicti® (Gylcerol Phenylbutyrate)
E. Market News and Updates
F. College of Pharmacy Recommendations

Non-presentation, Questions Only:

13. Annual Review of Procysbi® (Cysteamine Bitartrate Delayed-Release) – See Appendix K

A. Indication
B. Current Prior Authorization Criteria
C. Utilization of Procysbi® (Cysteamine Bitartrate Delayed-Release)

D. Prior Authorization of Procysbi® (Cysteamine Bitartrate Delayed-Release)
E. Market News and Updates
F. College of Pharmacy Recommendations
G. Utilization Details of Procysbi® (Cysteamine Bitartrate Delayed-Release)

Non-presentation, Questions Only:

14. Annual Review of Fulyzaq® (Crofelemer) – See Appendix L

A. Indication
B. Current Prior Authorization Criteria
C. Utilization of Fulyzaq® (Crofelemer)
D. Prior Authorization of Fulyzaq® (Crofelemer)
E. Market News and Updates
F. College of Pharmacy Recommendations

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

15. FDA and DEA Updates – See Appendix M

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

16. Future Business

A. Annual Reviews
B. New Product Reviews

Items to be presented by Dr. Muchmore, Chairman:

17. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF JANUARY 14, 2015

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

COLLEGE OF PHARMACY STAFF:	PRESENT	ABSENT
Terry Cothran, D.Ph.; Pharmacy Director	x	
Michyla Adams, Pharm.D.; Clinical Pharmacist	x	
Melissa Anderson, 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	
Leslie Robinson, D.Ph.; PA Coordinator		x
Ashley Teel, Pharm.D.; Clinical Pharmacist		x
Graduate Students: David George, Pharm. D.		x
Tammy Lambert, Pharm .D.	x	
Timothy Pham, Pharm. D.	x	
Visiting Pharmacy Student(s): Jodi Cagley, Allen Varghese	x	

	PRESENT	ABSENT
Marlene Asmussen, R.N.; Population Care Management Director	x	
Burl Beasley, D.Ph.; M.P.H.; M.S. Pharm	x	
Nico Gomez, Chief Executive Officer		x
Sylvia Lopez, M.D.; FAAP; Chief Medical Officer	x	
Ed Long, Chief Communications Officer		x
Kelli Brodersen, Marketing Coordinator	x	
Nancy Nesser, Pharm.D.; J.D.; Pharmacy Director	x	
Rebecca Pasternik-Ikard, Deputy State Medicaid Director	x	
Jill Ratterman, D.Ph.; Clinical Pharmacist	x	
Garth Splinter, M.D.; M.B.A.; Medicaid Director	x	
Joseph Young, Deputy Gerneral Counsel IV	x	
Kerri Wade, Pharmacy Operations Manager	x	

OTHERS PRESENT:		
Clint Degner, Novartis	Michele Puyear, Gilead	Don Kempin, Novo Nordisk
Jeremy McClure, The Med Co.	Lisa Borland, Vertex Pharm	Roger Grotzinger, BMS
Melvin Nwamadi, Abbott	Jana Shavdomtsky, Vertex Pharm	Russ Wilson, J & J
Tone Jones, Sunovion	Deepak Patel, Novo Nordisk	Larry Goolsby, J & J
Jim Dunlap, PhRMA	Shane Voegele, Actavis	Janie Huff, Takeda
Jim Chapman, AbbVie	Kyle Kawrath, Vertex Pharm	Jim Fowler, Astra Zeneca
Eric Gardner, Vertex Pharm	Ty Griffin, The Med Co.	Jon MaGuire, GSK
Sharon Jackson, GSK		

PRESENT FOR PUBLIC COMMENT:	
Gary Riley	AbbVie

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: GARY RILEY **AGENDA NO. 11**

ACTION: NONE REQUIRED

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

3A: DECEMBER 10, 2014 DUR MINUTES – VOTE

3B: DECEMBER 10, 2014 DUR RECOMMENDATIONS MEMORANDUM

Materials included in agenda packet; presented by Dr. Muchmore

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: **UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/ CHRONIC MEDICATION ADHERENCE PROGRAM UPDATE**

4A: MEDICATION COVERAGE ACTIVITY FOR DECEMBER 2014

4B: PHARMACY HELP DESK ACTIVITY FOR DECEMBER 2014

4C: CHRONIC MEDICATION ADHERENCE PROGRAM UPDATE

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NO ACTION REQUIRED

AGENDA ITEM NO. 5: **VOTE TO PRIOR AUTHORIZE DUAVEE® (CONJUGATED ESTROGENS/BAZEDOXIFENE)**

5A: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Holderread

Dr. Winegardner moved to approve; seconded by Dr. Rhymer

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE NATESTO™ (TESTOSTERONE NASAL GEL), AVEED® (TESTOSTERONE UNDECANOATE INJECTION), AND VOGELXO™ (TESTOSTERONE TOPICAL GEL)**

6A: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Anderson

Dr. Hardzog-Britt moved to approve; seconded by Dr. Garton

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: **VOTE TO PRIOR AUTHORIZE OFEV® (NINTEDANIB) AND ESBRIET® (PIRFENIDONE)**

7A: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Adams

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: **VOTE TO PRIOR AUTHORIZE ANORO™ ELLIPTA® (UMECLIDINIUM/VILANTEROL), INCRUSE™ ELLIPTA® (UMECLIDINIUM), SPIRIVA® RESPIMAT® (TIOTROPIUM), AND STRIVERDI® RESPIMAT® (OLODATEROL)**

8A: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nawaz

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: **30-DAY NOTICE TO PRIOR AUTHORIZE NORTHERA™ (DROXIDOPA)**

9A: INTRODUCTION

9B: NORTHERA™ (DROXIDOPA) PRODUCT SUMMARY

9C: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nawaz

ACTION: NONE REQUIRED

AGENDA ITEM NO. 10: **ANNUAL REVIEW OF ANTIEMETIC MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE AKYNZEO® (NETUPITANT/PALONOSETRON)**

10A: CURRENT PRIOR AUTHORIZATION CRITERIA

10B: UTILIZATION OF ANTIEMETIC MEDICATIONS

10C: PRIOR AUTHORIZATION OF ANTIEMETIC MEDICATIONS

10D: MARKET NEWS AND UPDATES

10E: AKYNZEO® (NETUPITANT/PALONOSETRON) PRODUCT SUMMARY

10F: COLLEGE OF PHARMACY RECOMMENDATIONS

10G: UTILIZATION DETAILS OF ANTIEMETIC MEDICATIONS

Materials included in agenda packet; presented by Dr. Anderson

ACTION: NONE REQUIRED

AGENDA ITEM NO. 11: **30-DAY NOTICE TO PRIOR AUTHORIZE VIEKIRA PAK™ (OMBITASVIR/PARITAPREVIR/RITONAVIR/DASABUVIR)**

11A: INTRODUCTION

11B: MARKET NEWS AND UPDATES

11C: VIEKIRA PAK™ (OMBITASVIR/PARITAPREVIR/RITONAVIR/DASABUVIR) PRODUCT SUMMARY

11D: REGIMEN COST COMPARISON

11E: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Holderread

Dr. Rhymer recommends that member contract and pharmacy agreement be added to the packet for next month.

ACTION: NONE REQUIRED

AGENDA ITEM NO. 12: **ANNUAL REVIEW OF MAKENA® (17-HYDROXYPROGESTERONE CAPROATE)**

12A: INDICATION

12B: CURRENT PRIOR AUTHORIZATION CRITERIA

12C: UTILIZATION OF MAKENA® (17-HYDROXYPROGESTERONE CAPROATE)

12D: PRIOR AUTHORIZATION OF MAKENA® (17-HYDROXYPROGESTERONE CAPROATE)

12E: MARKET NEWS AND UPDATES
12F: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Holderread
ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: ANNUAL REVIEW OF GATTEX® (TEDUGLUTIDE)
13A: INDICATION
13B: CURRENT PRIOR AUTHORIZATION CRITERIA
13C: UTILIZATION OF GATTEX® (TEDUGLUTIDE)
13D: PRIOR AUTHORIZATION OF GATTEX® (TEDUGLUTIDE)
13E: MARKET NEWS AND UPDATES
13F: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Holderread
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: FDA AND DEA UPDATES
Materials included in agenda packet; presented by Dr. Cothran
ACTION: NONE REQUIRED

AGENDA ITEM NO. 15: FUTURE BUSINESS
15A: ANNUAL REVIEWS
15B: NEW PRODUCT REVIEWS
Materials included in agenda packet; submitted by Dr. Cothran
ACTION: NONE REQUIRED

AGENDA ITEM NO. 16: ADJOURNMENT
The meeting was adjourned at 4:51PM.

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

Memorandum

Date: January 15, 2015

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

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

Subject: DUR Board Recommendations From Meeting of January 14, 2015

Recommendation 1: Vote to Prior Authorize Duavee® (Conjugated Estrogens/ Bazedoxifene)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Duavee® (conjugated estrogens/bazedoxifene) with the following criteria:

Duavee® (Conjugated Estrogens/Bazedoxifene) Approval Criteria:

1. An FDA approved diagnosis of moderate to severe vasomotor symptoms associated with menopause or for prevention of postmenopausal osteoporosis; and
2. Member must be a female with an intact uterus; and
3. For a diagnosis of moderate to severe vasomotor symptoms associated with menopause:
    a. Member must have at least 7 moderate to severe hot flushes per day or at least 50 per week prior to treatment; and
4. For a diagnosis of prevention of postmenopausal osteoporosis:
    a. A trial of Fosamax® (alendronate), Actonel® (risedronate), Boniva® (ibandronate) or Reclast® (zoledronic acid) compliantly used for at least 6 months concomitantly with calcium + vitamin D, that failed to prevent fracture or improve BMD scores; or
    b. Contraindication to, hypersensitivity to, or intolerable adverse effects with all bisphosphonates indicated for prevention of postmenopausal osteoporosis; and
5. Member must not have any of the contraindications for use of Duavee®; and

6. Members greater than 65 years of age will generally not be approved without supporting information.
7. Approvals will be for the duration of 6 months to ensure the need for continued therapy is reassessed periodically and the medication is being used for the shortest duration possible.
8. A quantity limit of 30 tablets per 30 days will apply.

Recommendation 2: Vote to Prior Authorize Natesto™ (Testosterone Nasal Gel), Aveed® (Testosterone Undecanoate Injection), and Vogelxo™ (Testosterone Topical Gel)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following changes to the Testosterone Product Based Prior Authorization category:

1. Place Natesto™, Aveed®, Testim®, and Vogelxo™ into Tier-2.
2. Tier-1 includes supplemental rebated topical product(s) and generic injectable products.

Testosterone Products		
Tier-1*	**Tier-2**	**Special PA**
methyltestosterone powder	testosterone patch (Androderm®)	fluoxymesterone oral tablet (Androxy®)
testosterone cypionate injection (Depo-Testosterone®)	testosterone topical gel (Fortesta®)	methyltestosterone oral tablet/capsule (Android®, Methitest®, Testred®)
testosterone enanthate injection	testosterone topical solution (Axiron®)	testosterone buccal tablet (Striant®)
testosterone topical gel (Androgel®)	**testosterone nasal gel (Natesto™)**	testosterone (Testopel Pellets®)
	testosterone undecanoate injection (Aveed®)	
	testosterone topical gel (Testim®, Vogelxo™)	

*Tier-1 products include generic injectable products and supplemental rebated product(s).

Initial Approval Criteria for All Testosterone Products:

1. An FDA approved diagnosis:
   a. Testicular failure due to cryptorchidism, bilateral torsions, orchitis, vanishing testis syndrome, or orchidectomy; or
   b. Idiopathic gonadotropin or luteinizing-hormone-releasing hormone (LHRH) deficiency, or pituitary hypothalamic injury from tumors, trauma, or radiation; or
   c. Delayed puberty; or
   d. Advanced inoperable metastatic mammary cancer in females one to five years postmenopausal, or premenopausal women with breast cancer benefitting from oophorectomy and have been determined to have a hormone-responsive tumor; and

2. Must include two labs showing pre-medication, morning testosterone (total testosterone) levels below 300ng/dL; and
3. Must include one lab showing abnormal gonadotropins and/or other information necessary to demonstrate diagnosis; or
4. Testosterone and gonadotropin labs are not required for authorization of testosterone therapy if documentation is provided for established hypothalamic pituitary or gonadal disease or if the pituitary gland or testes has/have been removed.

Testosterone Products Tier-2 Authorization Criteria:

1. All diagnoses and laboratory requirements listed above must be met; and
2. A trial of at least two Tier-1 products (must include at least one injectable and one topical formulation) at least 12 weeks in duration; or
3. A patient-specific, clinically significant reason why member cannot use all available Tier-1 medications; or
4. Prior stabilization on a Tier-2 medication (within the past 180 days).
5. Approvals will be for the duration of one year.

Testosterone Products Special Prior Authorization Criteria:

1. All diagnoses and laboratory requirements listed above must be met; and
2. A patient-specific, clinically significant reason why member cannot use all other available formulations of testosterone.
3. Approvals will be for the duration of one year.

Recommendation 3: Vote to Prior Authorize Ofev® (Nintedanib) and Esbriet® (Pirfenidone)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends prior authorization of Ofev® (nintedanib) and Esbriet® (pirfenidone) with the following criteria:

Ofev® (Nintedanib) Approval Criteria:

1. An FDA approved diagnosis of idiopathic pulmonary fibrosis (IPF); and
2. Member must be 18 years of age or older; and
3. Medication must be prescribed by a pulmonologist or pulmonary specialist; and
4. A quantity limit of 60 capsules per 30 days will apply.

Esbriet® (Pirfenidone) Approval Criteria:

1. An FDA approved diagnosis of idiopathic pulmonary fibrosis (IPF); and
2. Member must be 18 years of age or older; and
3. Medication must be prescribed by a pulmonologist or pulmonary specialist; and
4. A quantity limit of 270 capsules per 30 days will apply.

Recommendation 4: Vote to Prior Authorize Anoro™ Ellipta® (Umeclidinium/Vilanterol), Incruse™ Ellipta® (Umeclidinium), Spiriva® Respimat® (Tiotropium), and Striverdi® Respimat® (Olodaterol)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Anoro™ Ellipta® (umeclidinium/vilanterol inhalation powder) with the following criteria:

Anoro™ Ellipta® (Umeclidinium/Vilanterol Inhalation Powder) Approval Criteria:

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

Additionally, the College of Pharmacy recommends placement of Incruse™ Ellipta® (umeclidinium inhalation powder), Spiriva® Respimat® (tiotropium soft mist inhaler), and Striverdi® Respimat® (olodaterol inhalation spray) into Tier-2 of the Long-Acting Beta$_2$ Agonists (LABA) and Long-Acting Muscarinic Antagonist (LAMA) product based prior authorization category. Current criteria for this category will apply.

Long-Acting Beta$_2$ Agonists (LABA) and Long-Acting Muscarinic Antagonists (LAMA) Approval Criteria:

1. Tier-1 medications do not require prior authorization with a COPD diagnosis.
2. Tier-2 Approval Criteria:
   a. Member must be 18 years of age or older; and
   b. An FDA approved diagnosis of COPD, chronic bronchitis, or emphysema; and
   c. A four week trial of at least one LABA and a four week trial of one LAMA within the past 90 days; or
   d. A documented adverse effect, drug interaction, or contraindication to all available Tier-1 products.
   e. A clinical exception may apply for members who are unable to effectively use hand-actuated devices, such as Spiriva® Handihaler® or who are stable on nebulized therapy.

Long-Acting Beta$_2$ Agonists (LABA) and Long-Acting Anticholinergics (LAMA)	
Tier-1	**Tier-2**
Long Acting Beta$_2$ Agonists* (LABA)	
Serevent® (salmeterol inhalation powder)	Perforomist® (formoterol nebulizer solution)
Foradil® (formoterol aerosolized powder)	Brovana® (arformoterol nebulizer solution)
	Arcapta® (indacaterol inhalation powder)
	Striverdi® Respimat® (olodaterol inhalation spray)
Long Acting Muscarinic Antagonists (LAMA)	
Spiriva® (tiotropium inhalation powder)	Tudorza® (aclidinium inhalation powder)
	Incruse™ Ellipta® (umeclidinium Inhalation powder)
	Spiriva® Respimat® (tiotropium soft mist inhaler)

*Combination agents that contain a Tier-1 ingredient qualify as Tier-1 agents (Advair®, Symbicort®).

Recommendation 5: 30-Day Notice to Prior Authorize Northera™ (Droxidopa)

NO ACTION REQUIRED.

Recommendation 6: Annual Review of Antiemetic Medications and 30-Day Notice to Prior Authorize Akynzeo® (Netupitant/Palonosetron)

NO ACTION REQUIRED.

Recommendation 7: 30-Day Notice to Prior Authorize Viekira Pak™ (Ombitasvir/Paritaprevir/Ritonavir/Dasabuvir)

NO ACTION REQUIRED.

Recommendation 8: Annual Review of Makena® (17-Hydroxyprogesterone Caproate)

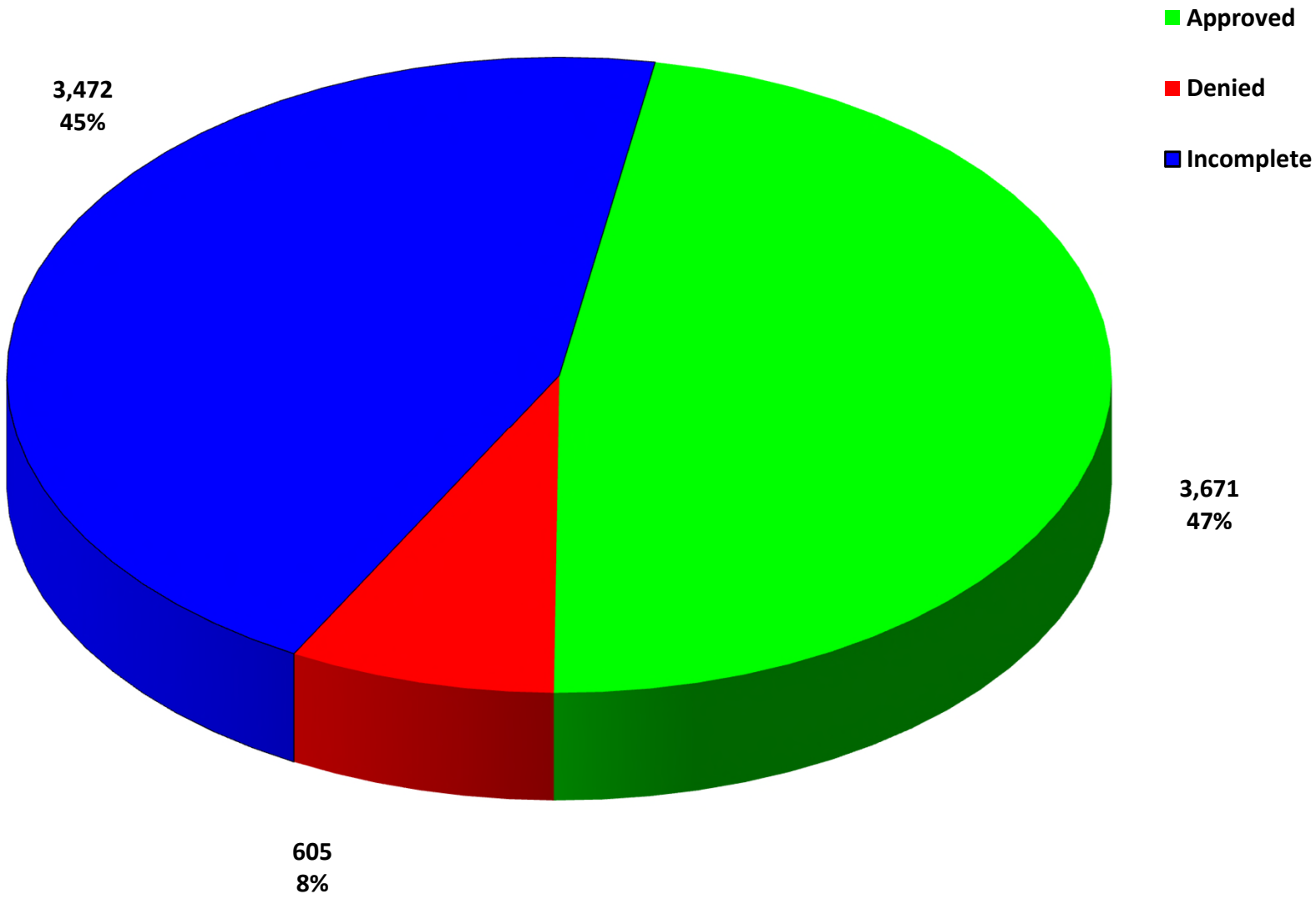
NO ACTION REQUIRED.

Recommendation 9: Annual Review of Gattex® (Teduglutide)

NO ACTION REQUIRED.

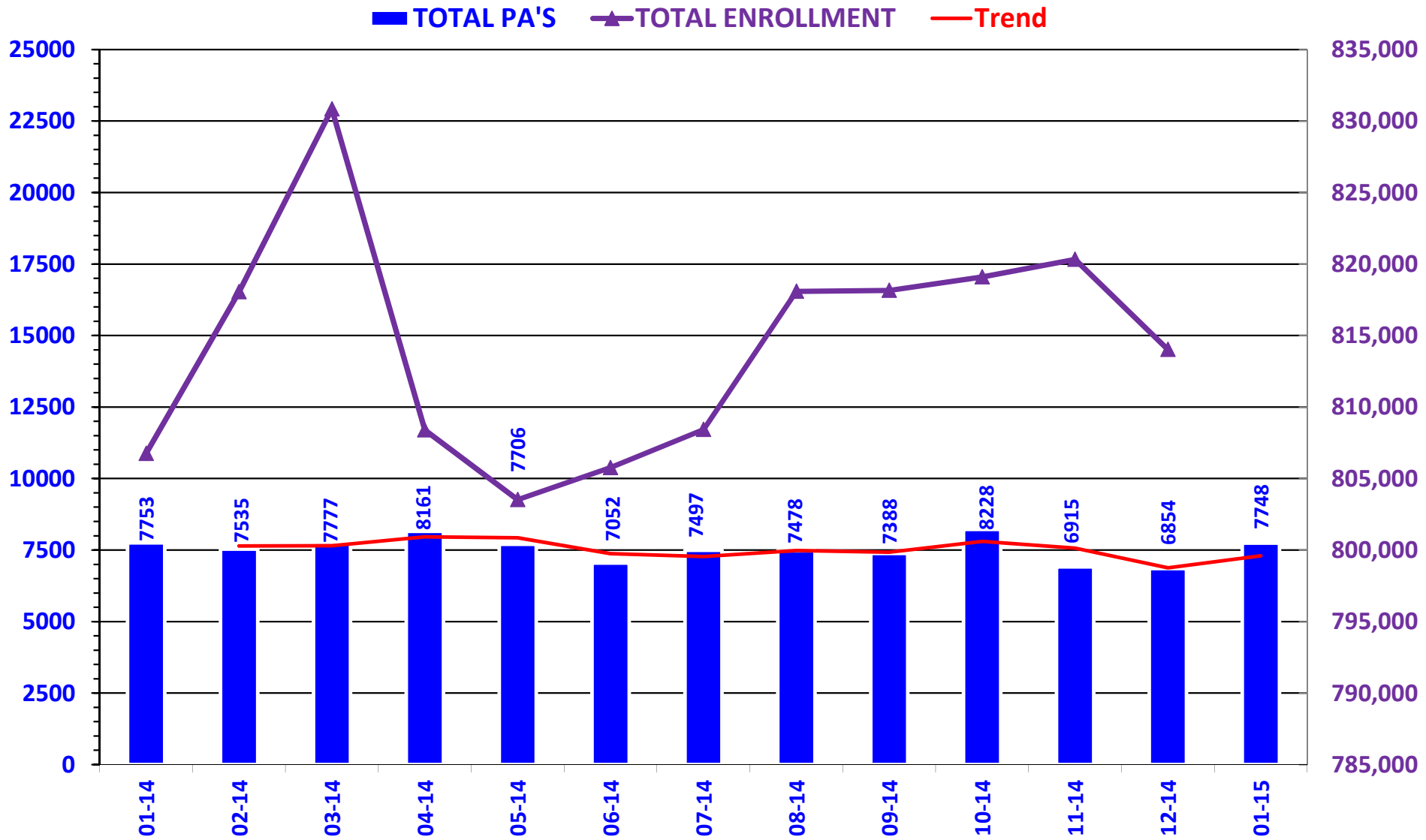
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: JANUARY



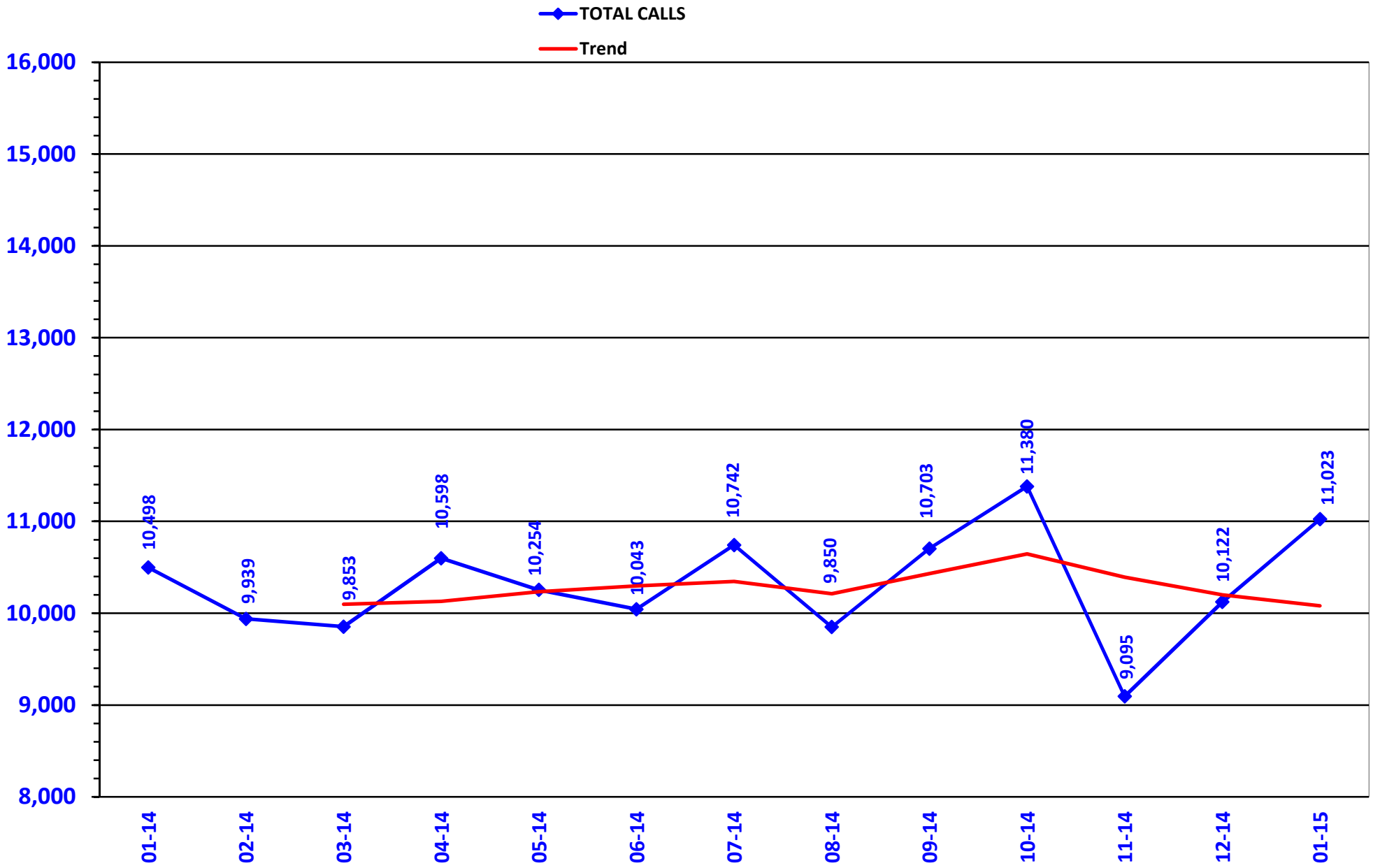
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: JANUARY 2014 – JANUARY 2015



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
JANUARY 2014 – JANUARY 2015



Prior Authorization Activity
1/1/2015 Through 1/31/2015

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	401	185	9	207	350
Analgesic - NonNarcotic	34	2	1	31	182
Analgesic, Narcotic	456	269	31	156	150
Angiotensin Receptor Antagonist	35	6	3	26	273
Antiasthma	182	85	9	88	334
Antibiotic	56	18	2	36	157
Anticonvulsant	82	34	2	46	348
Antidepressant	107	29	16	62	324
Antidiabetic	210	71	16	123	349
Antihistamine	154	125	1	28	356
Antimigraine	50	8	3	39	229
Antiulcers	219	49	47	123	211
Anxiolytic	81	49	3	29	273
Atypical Antipsychotics	422	245	3	174	340
Biologics	93	48	7	38	348
Bladder Control	89	31	13	45	359
Blood Thinners	121	86	2	33	303
Botox	26	23	1	2	354
Calcium Channel Blockers	15	4	1	10	124
Cardiovascular	30	15	3	12	267
Cephalosporins	14	3	0	11	7
Chronic Obstructive Pulmonary Disease	19	4	0	15	355
Dermatological	103	4	54	45	100
Endocrine & Metabolic Drugs	48	31	7	10	135
Erythropoietin Stimulating Agents	31	17	1	13	107
Fibromyalgia	159	31	24	104	337
Fish Oils	16	4	3	9	343
Gastrointestinal Agents	60	8	18	34	145
Genitourinary Agents	11	4	1	6	140
Glaucoma	11	1	0	10	360
Growth Hormones	67	48	3	16	155
Hematopoietic Agents	12	9	0	3	99
Hepatitis C	103	54	17	32	9
HFA Rescue Inhalers	51	24	0	27	320
Insomnia	56	15	5	36	182
Insulin	12	4	0	8	118
Linzess, Amitiza, and Relistor	77	7	9	61	242
Multiple Sclerosis	43	28	0	15	225
Muscle Relaxant	72	24	24	24	51
Nasal Allergy	66	5	18	43	302
Neurological Agents	48	35	3	10	346
Nsaids	170	28	16	126	295
Ocular Allergy	24	9	1	14	233
Ophthalmic Anti-infectives	34	2	1	31	16
Osteoporosis	22	14	2	6	344
Other*	188	30	24	134	247
Otic Antibiotic	12	4	0	8	6
Pediculicide	64	25	3	36	14
Prenatal Vitamins	13	0	2	11	0
Statins	44	16	1	27	354
Stimulant	1,153	434	48	671	350
Suboxone/Subutex	214	157	7	50	80
Synagis	161	91	13	57	77
Testosterone	80	23	5	52	340
Topical Antifungal	54	0	6	48	0
Topical Corticosteroids	82	3	16	63	241

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Vitamin	93	23	50	20	315
Pharmacotherapy	51	46	0	5	282
Emergency PAs	0	0	0	0	
Total	**6,401**	**2,647**	**555**	**3,199**	
Overrides					
Brand	35	31	1	3	325
Cumulative Early Refill	1	1	0	0	180
Dosage Change	365	326	1	38	7
High Dose	3	3	0	0	299
Ingredient Duplication	46	34	0	12	9
Lost/Broken Rx	93	81	4	8	8
NDC vs Age	38	37	0	1	230
Nursing Home Issue	60	55	0	5	3
Opioid Quantity	10	7	3	0	136
Other*	28	27	0	1	6
Prescriber Temp Unlock	1	1	0	0	85
Quantity vs. Days Supply	608	384	29	195	257
STBS/STBSM	16	15	0	1	30
Stolen	13	7	3	3	3
Temporary Unlock	9	6	3	0	27
Third Brand Request	33	18	9	6	7
Overrides Total	**1,347**	**1,024**	**50**	**273**	
Total Regular PAs + Overrides	**7,748**	**3,671**	**605**	**3,472**	

Denial Reasons	
Unable to verify required trials.	2,888
Does not meet established criteria.	614
Lack required information to process request.	552

Other PA Activity	
Duplicate Requests	459
Letters	3,981
No Process	10
Changes to existing PAs	537
Helpdesk Initiated Prior Authorizations	871
PAs Missing Information	48

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

Long-Acting Beta Agonist Utilization: Pediatric Members

Oklahoma Health Care Authority
February 2015

Introduction

The Drug Utilization Review (DUR) Board requested a review of claims for pediatric SoonerCare members utilizing single component Long-Acting Beta$_2$ Agonists (LABA). Current clinical guidelines do not recommend use of LABA medications alone in pediatric patients with asthma. Guidelines suggest using a concomitant Inhaled Corticosteroid (ICS) with a LABA medication or using an ICS alone. The purpose of this claims analysis was to evaluate potential inappropriate use of single-component LABA medications in the pediatric SoonerCare population.

Claims Analysis

The claims analysis included members 18 years of age and younger with a paid claim for a single-component LABA. The review period was for one year and members with a single-component LABA medication claim were further evaluated for a single-component ICS medication during the same month.

Results

38 Members had a paid claim for a single-component LABA medication.

11 Members (of the 38) did not have a paid claim for an ICS during the same month as the LABA medication. Most of the 11 members (8) had only one paid claim for a LABA medication.

3 Members (of the 11) had more than one paid claim for a LABA medication; the maximum number of claims was three.

2 Members (of the 11) had a paid claim for a LABA medication within the last 90 days (neither of these two members had more than one paid claim for a LABA medication).

Most of the 38 members were using nebulized Perforomist® (formoterol fumarate), a single-component LABA, with nebulized Pulmicort® (budesonide), a single-component ICS, because they required nebulized therapy due to the inability to utilize a hand-held actuation device.

Recommendations

SoonerCare claims analysis of pediatric utilization of single-component LABA medications did not reveal a pressing need for intervention. Most pediatric members utilizing single-component LABA medications required a unique dosage formulation or were being followed by a pulmonary specialist. Based on these findings the College of Pharmacy does not recommend any changes to the current LABA criteria at this time.

Appendix C

Vote to Prior Authorize Viekira Pak™ (Ombitasvir/Paritaprevir/Ritonavir/Dasabuvir)

Oklahoma Health Care Authority
February 2015

Recommendations

The College of Pharmacy recommends the prior authorization of Viekira Pak™ (ombitasvir/paritaprevir/ritonavir/dasabuvir) with the following criteria:

Viekira Pak™ (Ombitasvir/Paritaprevir/Ritonavir/Dasabuvir) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) **genotype-1** with a METAVIR fibrosis score of **F2** or greater; and
3. Viekira Pak™ must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated by a gastroenterologist, infectious disease specialist, or transplant specialist for hepatitis C therapy within the last three months; and
4. Hepatitis C Virus (HCV) genotype/subtype testing must be confirmed and indicated on prior authorization request; and
5. Pre-treatment viral load (HCV-RNA) must be confirmed and indicated on the petition. Viral load should have been taken within the last three months; and
6. The following regimens and requirements based on prior treatment experience, genotypic subtype, and cirrhosis will apply:
   a. **Genotype 1a, without cirrhosis:**
      i. Viekira Pak™ with weight-based ribavirin for 12 weeks
   b. **Genotype 1a, with cirrhosis:**
      i. Viekira Pak™ with weight-based ribavirin for 24 weeks
      ii. Viekira Pak™ with weight-based ribavirin for 12 weeks may be considered for some patients based on prior treatment history.
   c. **Genotype 1b, without cirrhosis:**
      i. Viekira Pak™ for 12 weeks
   d. **Genotype 1b, with cirrhosis:**
      i. Viekira Pak™ with weight-based ribavirin for 12 weeks
   e. New regimens will apply as approved by the FDA
7. Member must not have previously failed treatment with a hepatitis C protease inhibitor (non-responder or relapsed); and
8. Member must sign and submit the Hepatitis C Intent to Treat contract; and
9. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
10. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Viral Response (SVR-12); and

11. Member must have no illicit IV drug use or alcohol abuse in the last six months and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
12. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
13. Member must not have decompensated cirrhosis; and
14. Female members must not be pregnant and must have a pregnancy test immediately prior to therapy initiation. Female partners of male patients should also be checked for pregnancy for informational purposes. Male and female members must be willing to use two forms of non-hormonal birth control while on therapy and for six months after therapy completion; and
15. The prescriber must verify that the member's ALT levels will be monitored during the first four weeks of starting treatment and as clinically indicated thereafter; and
16. Member must not be taking the following medications: alfuzosin, carbamazepine, phenytoin, phenobarbital, gemfibrozil, rifampin, ergotamine, dihydroergotamine, ergonovine, methylergonovine, ethinyl estradiol, St. John's wort, lovastatin, simvastatin, pimozide, efavirenz, sildenafil, triazolam, oral midazolam; and
17. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight management, severe concurrent medical diseases, such as but not limited to, retinal disease or autoimmune thyroid disease; and
18. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
19. Members must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy.
20. Approvals for treatment regimen initiation for 12 weeks of therapy will not be granted prior to the 10th of a month, and for 24 weeks of therapy prior to the 15th of a month in order to prevent prescription limit issues from affecting the member's compliance.

Additionally, the College of Pharmacy recommends Viekira Pak™ (ombitasvir/paritaprevir/ritonavir/dasabuvir) and Harvoni® (sofosbuvir/ledipasvir) be the preferred regimens for treatment of chronic hepatitis C genotype-1. Use of Sovaldi® (sofosbuvir) and Olysio® (simeprevir) in combination or alone for treatment of HCV genotype-1 will require patient-specific, clinically significant reasoning why Viekira Pak™ or Harvoni® is not appropriate for the member.

SoonerCare
Oklahoma Health Care Authority

State of Oklahoma
Oklahoma Health Care Authority
Hepatitis C Therapy Pharmacy Agreement

Member Name: _____ ***Date of Birth:***_____ ***Member ID#:***_____

Pharmacy NPI: _____ ***Pharmacy Name:***_____

Pharmacy Phone: _____ ***Pharmacy Fax:*** _____ ***Drug Name:***_____

To be completed by pharmacist after discussion of therapy with member.
Agreement is required for processing of prior authorization requests.

The member will start treatment on the following date: _____

Please check each line and sign at the bottom.

- ☐ The member has been counseled on hepatitis C medications including the following:
  - ☐ Regimen
  - ☐ Potential side effects
  - ☐ Storage requirements
  - ☐ Importance of compliance
  - ☐ Drug interactions
  - ☐ SoonerCare prescription limits and the need for appropriate “punches” per month
- ☐ The member has been counseled on effective non-hormonal birth control products. Please list non-hormonal birth control options discussed with member _____
- ☐ The pharmacist agrees to contact the member and prescriber 7 days before medications run out to start the prior authorization process for refills.
- ☐ The pharmacist agrees to notify the prescriber and OHCA if the member is non-compliant within 1 day of late refills.
- ☐ The pharmacist agrees to refuse to fill SovaldiTM or OlysioTM without appropriate combination therapy as indicated on the prior authorization form.
- ☐ The pharmacist agrees to work with member to appropriately utilize SoonerCare pharmacy benefits including therapy management, transferring prescriptions, and working with OHCA and other pharmacies to stretch the benefit when required.
- ☐ I have read the above statements, and understand the agreement.

Members must be adherent for continued approval. Treatment gaps of therapy longer than 3 days will result in denial of payment for subsequent requests for continued therapy. Refills must be prior authorized.

I recommend this patient be followed by an OHCA Care Management Nurse. **Initials:**_____

Pharmacist Signature: _____ **Date:** _____
Required for processing Prior Authorization Request.

PLEASE PROVIDE THE INFORMATION REQUESTED AND RETURN TO:	CONFIDENTIALITY NOTICE
University of Oklahoma College of Pharmacy Pharmacy Management Consultants Product Based Prior Authorization Unit Fax: 1-800-224-4014 Phone: 1-800-522-0114 Option 4	*This document, including any attachments, contains information which is confidential or privileged. If you are not the intended recipient, be aware that any disclosure, copying, distribution, or use of the contents of this information is prohibited. If you have received this document in error, please notify the sender immediately by telephone to arrange for the return of the transmitted documents or to verify their destruction.*

State of Oklahoma
Oklahoma Health Care Authority

Hepatitis C Therapy Intent to Treat Contract

Member Name: _____ ***Date of Birth:***_____***Member ID#:***_____

Prescriber NPI: _____***Prescriber Name:*** _____ ***Specialty:***_____

Prescriber Phone:_____ ***Prescriber Fax:*** _____ ***Drug Name:***_____

To be completed by member after discussion of therapy with prescriber.
Contract is required for processing of prior authorization requests.

Please initial after each line and sign at the bottom.

1. I am ready to start treatment on the following date: **Initials____**
2. I have been counseled on how to take hepatitis C medications and understand how to take my medications, the potential side effects, and importance of finishing all of the therapy. **Initials____**
3. I will take my medications exactly how my doctor instructed and I will not miss doses. **Initials____**
4. I understand that if I miss taking my medications more than 3 days in a month SoonerCare will no longer provide payment for my hepatitis C medications. **Initials____**
5. For members requesting OlysioTM: I understand that after finishing 12 weeks of OlysioTM treatment I am required to continue to take pegylated interferon and ribavirin for an additional 12 or 36 weeks. **Initials____**
6. I have not used IV drugs or drunk alcohol in the past 6 months. **Initials____**
7. I will not use IV drugs or alcohol while on treatment or after completion of therapy. **Initials____**
8. I understand that random drug testing is required. **Initials____**
9. I am not pregnant or my female partner is not pregnant. **Initials____**
10. I am not planning to become pregnant or my female partner is not planning to become pregnant during treatment or within 6 months of completing treatment. **Initials____**
11. I will use the following <u>two</u> forms of effective non-hormonal birth control during treatment and for at least 6 months after completing treatment: _____ **Initials____**
12. I will undergo monthly pregnancy tests throughout treatment (female members only) or my female partner will undergo monthly pregnancy tests throughout my treatment. **Initials____**
13. For members requesting **Olysio™**: I am not currently taking any of the following medications: efavirenz, delavirdine, etravirine, nevirapine, any HIV protease inhibitor (tipranavir, indinavir, saquinavir, lopinavir, fosamprenavir, ritonavir, darunavir, atazanavir, nelfinavir), rifampin, rifabutin, rifapentine, erythromycin, clarithromycin, telithromycin, carbamazepine, oxcarbazepine, eslicarbazepine, phenobarbital, phenytoin, itraconazole, ketoconazole, posaconazole, fluconazole, voriconazole, dexamethasone, cisapride, didanosine, milk thistle, or St. John's wort. **Initials____**
14. For members requesting **Sovaldi™**: I am not currently taking any of the following medications: rifampin, rifabutin, rifapen-tine, carbamazepine, phenytoin, oxcarbazepine, eslicarbazepine, tipranavir/ritonavir, didanosine or St. John's wort. **Initials____**
15. For members requesting **Harvoni®:** I am not currently taking any of the following medications: rifampin, rifabutin, rifapen-tine, carbamazepine, eslicarbazepine, phenytoin, phenobarbital, oxcarbazepine, tipranavir/ritonavir, simeprevir, rosuvas-tatin, St. John's wort, or elvitegravir/cobicstat/emtricitabine in combination with tenofovir disoproxil fumarate. **Initials____**
16. For members requesting **Viekira Pak™:** I am not currently taking any of the following medications: alfuzosin, carbamaz-epine, phenytoin, phenobarbital, gemfibrozil, rifampin, ergotamine, dihydroergotamine, ergonovine, methylergonovine, ethinyl estradiol, St. John's wort, lovastatin, simvastatin, pimozide, efavirenz, sildenafil, triazolam, or oral midazolam. **Initials____**
17. I do not have other medical issues that will prevent me from taking my treatment as prescribed. **Initials____**
18. I understand this hepatitis C treatment will use 2 or 3 "punches"/prescriptions of my 6 total allowed per month by Sooner-Care. **Initials____**
19. I will work with <u>one</u> pharmacy to make sure my SoonerCare pharmacy benefit is used correctly during my treatment for hepatitis C. **Initials____**
    Pharmacy Name _____ **Phone**_____
20. I understand I may be contacted by an OHCA care management nurse to discuss my treatment. **Initials____**

I have read the above statements, and understand the agreement.

Member Signature:_____ **Date:** _____**Prescriber Signature:** _____**Date:**_____

PLEASE PROVIDE THE INFORMATION REQUESTED AND RETURN TO:	CONFIDENTIALITY NOTICE
University of Oklahoma College of Pharmacy Pharmacy Management Consultants Product Based Prior Authorization Unit Fax: 1-800-224-4014 Phone: 1-800-522-0114 Option 4	*This document, including any attachments, contains information which is confidential or privileged. If you are not the intended recipient, be aware that any disclosure, copying, distribution, or use of the contents of this information is prohibited. If you have received this document in error, please notify the sender immediately by telephone to arrange for the return of the transmitted documents or to verify their destruction.*

Appendix D

Vote to Prior Authorize Northera™ (Droxidopa)

Oklahoma Health Care Authority
February 2015

Recommendations

The College of Pharmacy recommends prior authorization of Northera™ (droxidopa) with the following criteria:

Northera™ (Droxidopa) Approval Criteria:

1. An FDA approved diagnosis of symptomatic neurogenic orthostatic hypotension caused by primary autonomic failure (Parkinson's disease, multiple system atrophy, and pure autonomic failure), dopamine beta-hydroxylase deficiency, or non-diabetic autonomic neuropathy; and
2. Member must be 18 years of age or older; and
3. Member must have tried and failed two of the following medications at recommended dosing within the last 90 days:
    a. Midodrine; or
    b. Fludrocortisone; or
    c. Pyridostigmine; or
    d. Have a contraindication to all preferred medications.
4. Initial approval will be for the duration of two weeks of treatment only.
5. Continued approval will require the prescriber to provide information regarding improved member response/effectiveness of this medication to determine whether Northera™ is continuing to provide a benefit.
6. Continued approval will be for the duration of three months. Each approval will require prescriber documentation of member response/effectiveness to Northera™.

Appendix E

Vote to Prior Authorize Akynzeo® (Netupitant/Palonosetron)

Oklahoma Health Care Authority
February 2015

Recommendations

The College of Pharmacy recommends the prior authorization of Akynzeo® (netupitant/palonosetron) with the following criteria:

Akynzeo® (Netupitant/Palonosetron) Approval Criteria:

1. An FDA approved diagnosis for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy; and
2. A recent trial of ondansetron (within the past six months) used for at least three days or one cycle that resulted in inadequate response.
3. Approval length based on duration of need.
4. A quantity limit of one capsule per chemotherapy cycle will apply.

Appendix F

30-Day Notice to Prior Authorize Myalept™ (Metreleptin)

Oklahoma Health Care Authority
February 2015

Introduction[1, 2]

Generalized lipodystrophy is a rare condition associated with complete or partial lack of adipose tissue. Patients with congenital generalized lipodystrophy are born with little or no adipose tissue, whereas, patients with acquired generalized lipodystrophy lose adipose tissue over time. This leads to abnormal deposition of triglycerides in other tissues such as muscle, liver, and pancreas. Additionally, due to the lack of adipose tissue, these patients may also have a leptin deficiency. Leptin is a hormone secreted by adipocytes, which is involved in regulation of food intake, energy homeostasis, and other hormones such as insulin.

Clinical manifestations include severe insulin resistance, hyperlipidemia, progressive liver disease, pancreatitis, heart disease, and increased metabolic rate. Insulin resistance is noted at an early age and diabetes mellitus usually develops in the early teen years. Diabetes in this population is typically refractory to insulin therapy. Hypertriglyceridemia associated with congenital and acquired lipodystrophy is difficult to treat and frequently leads to pancreatitis and hepatic steatosis.

The prevalence of generalized lipodystrophy has been estimated to be less than one case per one million people. In congenital generalized lipodystrophy, the absence of subcutaneous fat is often noted at or soon after birth. Acquired generalized lipodystrophy can occur in previously healthy children or adults and predominates in females.

Myalept™ (metreleptin) is the first approved therapy indicated for treating the complications of congenital and acquired generalized lipodystrophy.

Myalept™ (Metreleptin) Product Summary[3, 4, 5]

Indications: Myalept™ (metreleptin) is a leptin analog indicated as an adjunct to diet as replacement therapy to treat the complications of leptin deficiency in patients with congenital or acquired generalized lipodystrophy.

Dosing: Myalept™ is administered subcutaneously once daily.

- Body weight 40kg or less: starting dose 0.06mg/kg/day, increase or decrease by 0.02mg/kg to a maximum daily dose of 0.13mg/kg
- Males greater than 40kg: starting dose 2.5mg/day, increase or decrease by 1.25mg to 2.5mg/day to a maximum dose of 10mg/day
- Females greater than 40kg: starting dose 5mg/day, increase or decrease by 1.25mg to 2.5mg/day to a maximum of 10mg/day

Mechanism of Action: Myalept™ binds to and activates the human leptin receptor, mimicking native leptin, which is responsible for signaling the CNS with the status of energy stores in the body.

Contraindications:

- Myalept™ is contraindicated in patients with general obesity not associated with congenital leptin deficiency. Myalept™ has not been shown to be effective in treating general obesity, and the development of anti-metreleptin antibodies with neutralizing activity has been reported in obese patients treated with Myalept™.
- Myalept™ is contraindicated in patients with prior severe hypersensitivity reactions to metreleptin or to any of the product components. Known hypersensitivity reactions have included urticarial and generalized rash.

Warnings and Precautions:

- Myalept™ is available only through a restricted distribution program under the Myalept™ Risk Evaluation Mitigation Strategy (REMS) Program, because of the risks associated with the development of anti-metreleptin antibodies that neutralize endogenous leptin and/or Myalept™ and the risk of lymphoma.
- Myalept™ use can result in an increased risk for development of antibodies that neutralize endogenous leptin and/or Myalept™. Testing should be performed for anti-metreleptin antibodies with neutralizing activity in patients who develop severe infections or shows signs of loss of efficacy of Myalept™.
- The benefits and risks of Myalept™ should be carefully considered in patients with acquired generalized lipodystrophy and/or those with significant hematologic abnormalities, including leukopenia, neutropenia, bone marrow abnormalities, lymphoma, and/or lymphadenopathy.
- Dose adjustments of insulin or insulin secretagogues (e.g., sulfonylureas and meglitinides) may be necessary in some patients to minimize the risk of hypoglycemia. Blood glucose should be closely monitored in patients on concomitant insulin therapy, especially those on high doses, or insulin secretagogues.

Efficacy:

- The efficacy of Myalept™ for the treatment of patients with congenital or acquired generalized lipodystrophy, who also had diabetes mellitus, hypertriglyceridemia, and/or elevated levels of fasting insulin, was established in an open-label single-arm study with a total of 48 patients enrolled. Of the 48 patients, 32 (67%) had congenital generalized lipodystrophy and 16 (33%) had acquired generalized lipodystrophy. The ages ranged from 1 to 68 years of age, with 35 (75%) patients being less than 18 years of age. The median duration of treatment was 2.7 years.
- The mean (standard deviation [SD]) baseline HbA1c (%) was 8.5 (2) and the mean change from baseline at Month 12 was -2 (1.5).
- The mean (SD) baseline fasting glucose (mg/dL) was 174 (85) and the mean change from baseline at Month 12 was -49 (75).
- Among 12 patients who had a baseline triglyceride level 500mg/dL or greater, the median triglyceride level was 1,527mg/dL and the median reduction in triglycerides at month 12 was 1,117mg/dL.

Safety:

- The most common adverse reactions reported during clinical trials included hypoglycemia, headache, decreased weight, and abdominal pain.

Cost:

Medication Name	Cost/Vial	Cost/Month	Cost/Year
Myalept™ (metreleptin)	$1,554.43	$46,632.90	$559,594.80

Utilization:

- There has been one claim for Myalept™ since its approval in February 2014.

Recommendations

The College of Pharmacy recommends the prior authorization of Myalept™ (metreleptin) with the following criteria:

Myalept™ (Metreleptin) Approval Criteria:

1. An FDA approved diagnosis of leptin deficiency in patients with congenital or acquired generalized lipodystrophy; and
2. Approvals will not be granted for the following diagnoses:
    a. Metabolic disease without current evidence of generalized lipodystrophy
    b. HIV-related lipodystrophy
    c. General obesity not associated with congenital leptin deficiency
3. Myalept™ must be prescribed by an endocrinologist; and
4. Prescriber must agree to test for neutralizing antibodies in patients who experience severe infections or if they suspect Myalept™ is no longer effective.
    a. Baseline HbA1c, fasting glucose, and fasting triglycerides must be stated on prior authorization request
    b. Re-approvals will require recent lab values (HbA1c, fasting glucose, and fasting triglycerides) to ensure neutralizing antibodies have not developed; and
5. Prescriber and pharmacy must be enrolled in the Myalept™ REMS program; and
6. Approvals will be for the duration of six months to evaluate compliance and ensure the prescriber is assessing continued efficacy; and
7. A quantity limit of one vial per day will apply.

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[1] UpToDate. Lipodystrophic Syndromes. Available online at: http://www.uptodate.com/contents/lipodystrophic-syndromes?source=search_result&search=lipodystrophic+syndromes&selectedTitle=1%7E150. Last revised 4/18/14. Last accessed 1/26/15.

[2] Medscape. Generalized Lipodystrophy. Availabile online at: http://emedicine.medscape.com/article/128355-overview. Last revised 03/10/14. Last accessed 1/26/15.

[3] Myalept™ Package Insert. Available online at: http://myalept.com/pdfs/pi_myalept.pdf

[4] Micromedex 2.0: Myalept™ Drug Information. Available online at: http://www.micromedexsolutions.com/micromedex2/librarian/ND_T/evidencexpert/ND_PR/evidencexpert/CS/A802D4/ND_AppProduct/evidencexpert/DUPLICATIONSHIELDSYNC/15D8BE/ND_PG/evidencexpert/ND_B/evidencexpert/ND_P/evidencexpert/PFActionId/evidencexpert.IntermediateToFullDocumentLink/docId/930908/contentSetId/100/title/Metreleptin/servicesTitle/Metreleptin. Last revised 10/9/14. Last accessed 1/26/15.

[5] FDA News Release: FDA approves Myalept to treat rare metabolic disease. Available online at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm387060.htm. Last revised. 2/25/14. Last accessed 1/26/15.

Appendix G

Fiscal Year 2014 Annual Review of Pulmonary Arterial Hypertension Medications and 30-Day Notice to Prior Authorize Orenitram™ (Treprostinil) and Revatio® (Sildenafil Oral Suspension)

Oklahoma Health Care Authority
February 2015

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

Pulmonary arterial hypertension (PAH) is a complex syndrome resulting from restricted blood flow through the pulmonary arterial circulation leading to increased pulmonary vascular resistance and ultimately right heart failure. By definition, PAH is characterized by an increase in mean pulmonary arterial pressure (PAP) of ≥25 mmHg at rest and an average primary capillary wedge pressure of ≤ 15 mmHg. As PAH progresses, the blood flow to the pulmonary arteries is restricted and the right side of the heart becomes enlarged due to the increased stress of pumping blood to the lungs. As a result of the excess strain on the heart and decreased oxygenated blood flow to the left side of the heart and systemic circulation, symptoms such as breathlessness, fatigue, syncope, weakness, and angina are common.

PAH is a rare disease with an estimated prevalence of 15-50[2,4] cases per million people. Idiopathic PAH (IPAH) was estimated to have an annual incidence rate of 1-2 cases per million people in the US and Europe, and is estimated to be approximately 2-4 times more common in women than in men. The onset of PAH symptoms can occur at any age; however, the mean age of first diagnosis is approximately 45 years old. In pediatric patients diagnosed with PAH, the majority are diagnosed with IPAH or PAH associated with congenital heart disease (PAH-CHD). A recent epidemiological study revealed an annual incidence and point prevalence of 0.7 and 4.4 for IPAH and 2.2 and 15.6 for PAH-CHD cases per million children respectively.[3,5] While PAH is rare in infants and children, pediatric PAH is a challenge as current treatment decisions depend largely on results from evidence-based adult studies and clinical experience of pediatric experts.

Treatment[6]

Treatment guidelines published in *CHEST* in 2014 recommend the use of endothelin receptor antagonists (ERAs), phosphodiesterase-5 inhibitors (PDE-5), or soluble guanylate cyclase stimulators for treatment of PAH in low risk patients based on clinical assessment. Pharmacological treatment should be patient-specific and guided by high-level recommendations when sufficient evidence is available. Intravenous (IV) prostacyclin (epoprostenol or treprostinil) is recommended as first-line therapy for high risk patients and more severe cases. If the high risk patient is not a candidate for IV therapy, other therapies should be considered. Recently an oral prostacyclin vasodilator (Orenitram™ [treprostinil]) was approved by the FDA, but guidelines have not yet determined its place in therapy.

Generic	Trade	Indication	Dosage Form	Regimen	Mechanism of Action
Phosphodiesterase Type 5 (PDE-5) inhibitor					
TADALAFIL	ADCIRCA®	PAH to improve exercise ability	20 MG Tablets	2 Tablets QD (ORAL)	PDE-5 Inhibitor
SILDENAFIL	*REVATIO®	PAH to improve exercise ability and delay clinical worsening	20 MG Tablets 10 MG/Ml Oral Suspension	TID (ORAL)	PDE-5 Inhibitor
Soluble Guanylate Cyclase Stimulator					
RIOCIGUAT	ADEMPAS®	Chronic Thromboembolic Pulmonary Hypertension (CTEPH) after surgical treatment or inoperable CTEPH to improve exercise capacity and WHO functional class PAH to improve exercise capacity, improve WHO functional class and to delay clinical worsening	0.5, 1, 1.5, 2, 2.5 MG Tablets	TID (ORAL)	Soluble guanylate cyclase stimulator
Endothelin Receptor Antagonists (ERA)					
AMBRISENTAN	LETAIRIS®	PAH to improve exercise ability and delay clinical worsening	5, 10 MG Tablets	QD (ORAL)	ERA
BOSENTAN	TRACLEER®	PAH to improve exercise ability and to decrease clinical worsening	62.5, 125 MG Tablets	BID (ORAL)	ERA
MACITENTAN	OPSUMIT®	PAH to delay disease progression	10 MG Tablets	QD (ORAL)	ERA
Prostacyclin Vasodilator					
TREPROSTINIL	ORENITRAM™	PAH to improve exercise capacity	0.125, 0.25, 1 and 2.5 MG ER Tablets	BID (ORAL)	Prostacyclin vasodilator
TREPROSTINIL	REMODULIN®	PAH to improve exercise capacity	1, 2.5, 5, or 10 mg/mL	Continuous infusion	Prostacyclin vasodilator
TREPROSTINIL	TYVASO®	PAH to improve exercise capacity	1.74mg/2.9mL	9 inhalations QID (INHALED)	Prostacyclin vasodilator
ILOPROST	*VENTAVIS®	PAH to improve exercise capacity, symptoms	10 mcg/mL and 20 mcg/mL	5 mcg/dose 9 times daily (INHALED)	Prostacyclin vasodilator
EPOPROSTENOL (GLYCINE)	FLOLAN®	PAH to improve exercise capacity	0.5 mg vial and 1.5 mg vial	Continuous infusion	Prostacyclin vasodilator
EPOPROSTENOL (ARGININE)	*VELETRI	PAH to improve exercise capacity	0.5 mg vial and 1.5 mg vial	Continuous infusion	Prostacyclin vasodilator

*Available in generic formulation.

Current Prior Authorization Criteria

Adcirca® (Tadalafil) and Revatio® (Sildenafil) Approval Criteria:

1. An FDA approved diagnosis of pulmonary arterial hypertension; and
2. Medical supervision by a pulmonary specialist and/or cardiologist.
3. The following quantity limits will apply:
   a. Adcirca® (tadalafil) 20mg tablets: 60 tablets per 30 days.
   b. Revatio® (sildenafil) 20mg tablets: 90 tablets per 30 days.

Adempas® (Riociguat) Approval Criteria:

1. An FDA approved diagnosis of pulmonary arterial hypertension or chronic thromboembolic pulmonary hypertension
   a. Members with a diagnosis of pulmonary arterial hypertension must have previous failed trials of at least one of each of the following categories:
      i. Revatio® (sildenafil) or Adcirca® (tadalafil); and
      ii. Letairis® (ambrisentan) or Tracleer® (bosentan); and
   b. Members with a diagnosis of chronic thromboembolic pulmonary hypertension (CTEPH) must currently be on anticoagulation therapy; and
2. Medical supervision by a pulmonary specialist and/or cardiologist; and
3. Female members, prescribers, and dispensing pharmacies must be enrolled in the Adempas® REMS program.
4. A quantity limit of 90 tablets per 30 days will apply.

Opsumit® (Macitentan) Approval Criteria:

1. An FDA approved diagnosis of pulmonary arterial hypertension; and
2. Previous failed trials of at least one of each of the following categories:
   a. Revatio® (sildenafil) or Adcirca® (tadalafil); and
   b. Letairis® (ambrisentan) or Tracleer® (bosentan); and
3. Medical supervision by a pulmonary specialist and/or cardiologist; and
4. Female members, prescribers, and dispensing pharmacies must be enrolled in the Opsumit® REMS program.
5. A quantity limit of 30 tablets per 30 days will apply.

Tracleer® (bosentan) and Letairis® (ambrisentan) are available without prior authorization.

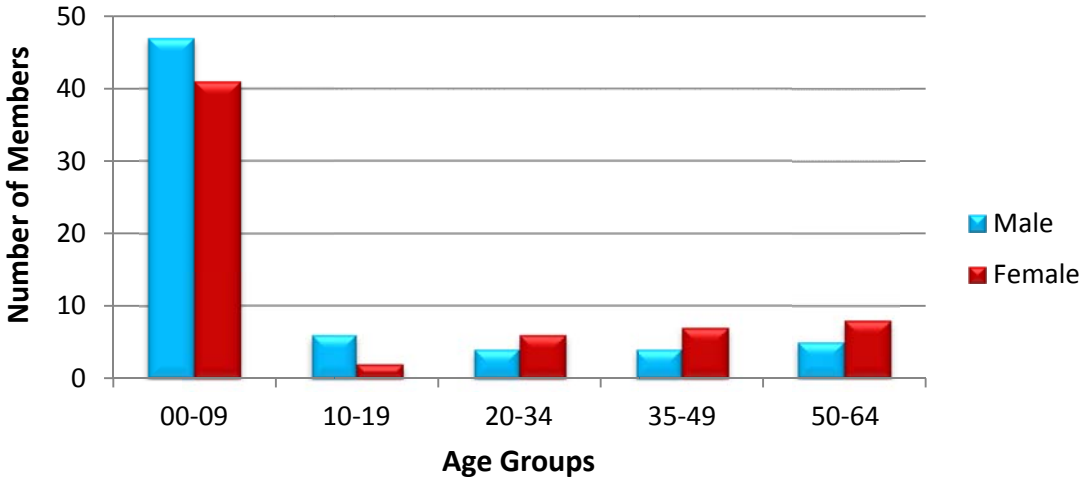
Utilization of Pulmonary Arterial Hypertension Medications

Comparison of Fiscal Years

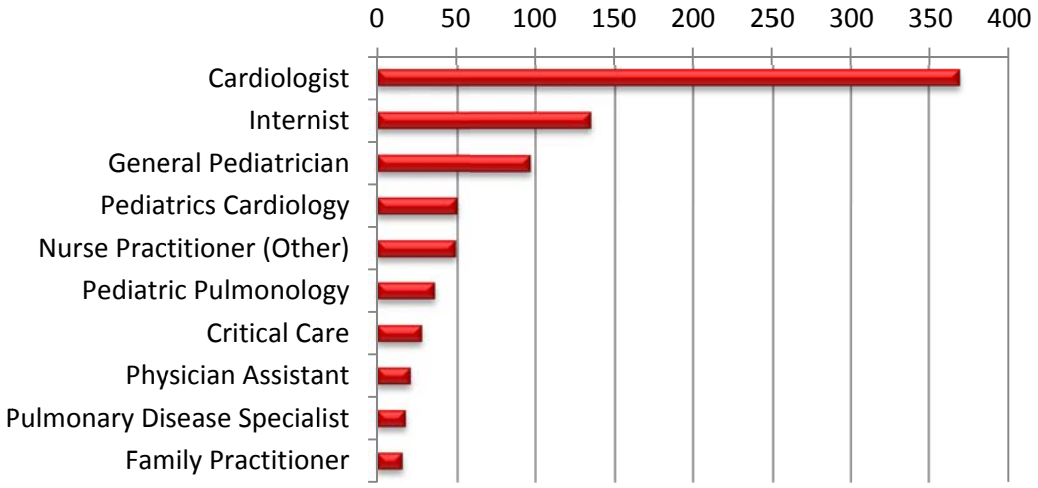
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2013	150	945	$1,829,626.21	$1,936.11	$65.52	102,253	27,925
2014	130	887	$1,697,469.53	$1,913.72	$63.63	102,073	26,677
% Change	**-13.30%**	**-6.10%**	**-7.20%**	**-1.20%**	**-2.90%**	**-0.20%**	**-4.50%**
Change	**-20**	**-58**	**-$132,156.68**	**($22.39)**	**($1.89)**	**-180**	**-1,248**

*Total number of unduplicated members.

Demographics of Members Utilizing Pulmonary Arterial Hypertension Medications



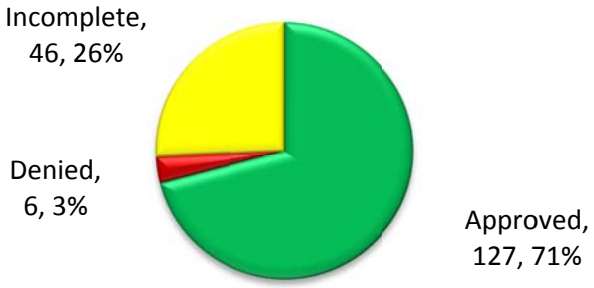
Top Prescriber Specialties of Pulmonary Arterial Hypertension Medications by Number of Claims



Prior Authorization of Pulmonary Arterial Hypertension Medications

There were 179 petitions submitted for pulmonary arterial hypertension medications during fiscal year 2014. The following chart shows the status of the submitted petitions.

Status of Petitions



Market News and Updates[7]

Anticipated Patent Expirations:

- Revatio® (sildenafil): 09/2012
  - Generic Sildenafil oral tablets became available on the market November 2012.
- Tracleer® (bosentan): 11/2015
- Letairis® (ambrisentan): 07/2018
- Adcirca® (tadalafil): 11/2020
- Adempas® (riociguat): 04/2023
- Opsumit® (macitentan): 04/2029

New FDA Approved Products:

- Orenitram™ (treprostinil) extended-release tablets: 12/2013

Orenitram™ (Treprostinil) Extended-Release Tablets Product Summary[8]

Indications: Orenitram™ (treprostinil) is a prostacyclin vasodilator indicated for treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise capacity. The study that established effectiveness included predominately patients with WHO functional class II-III symptoms and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue disease. When used as the sole vasodilator, the effect of Orenitram™ on exercise is approximately 10% of the deficit, and the effect, if any, on a background of another vasodilator is probably less than this.

Dosing:

- Orenitram™ is available as 0.125mg, 0.25mg, 1mg, and 2.5mg extended-release tablets.
- The recommended starting dose of Orenitram™ is 0.25mg twice daily or 0.125mg three times daily, not more than every 3 to 4 hours as tolerated.
- Maximum dose is determined by tolerability.
- Orenitram™ should be taken with food and swallowed whole as intact tablets.

Mechanism of Action:

- The major pharmacologic actions of Orenitram™ are direct vasodilation of pulmonary and systemic arterial vascular beds, inhibition of platelet aggregation, and inhibition of smooth muscle cell proliferation.

Contraindications:

- Severe hepatic impairment (Child Pugh Class C).

Clinical Studies:

<u>Study 1</u>

- Study 1 was a 12-week, randomized (2:1 Orenitram™ to placebo), double-blind, international efficacy and safety study of Orenitram™ in WHO Group 1 PAH patients not currently receiving PAH therapy.
- Orenitram™ was titrated to effect over the course of the 12-week trial, with a maximum dose of 12mg twice daily based on clinical response and tolerability.

- The primary efficacy endpoint was a change in 6 minute walking distance (6MWD) at 12 weeks from baseline. Orenitram™ compared to patients receiving placebo improved their 6MWD approximately 23 meters (*p*=0.013).

Study 2 and 3

- Study 2 and 3 were 16-weeks in duration and included patients on an endothelin receptor antagonist (ERA), phosphodiesterase type 5 (PDE-5) inhibitor, or both. The results did not demonstrate a benefit in exercise testing in median 6MWD at Week 16.
- FDA label includes the following statement in the indication: *As the sole vasodilator, the effect on exercise is small. Orenitram™ has not been shown to add to other vasodilator therapy.*

Revatio® (Sildenafil Oral Suspension) Product Summary[9]

Indications: Revatio® (sildenafil oral suspension) is a PDE-5 inhibitor indicated for the treatment of PAH (WHO Group I) in adults to improve exercise ability and delay clinical worsening. Studies establishing effectiveness were short-term (12 to 16 weeks), and included predominately patients with New York Heart Association (NYHA) Functional Class II–III symptoms. Etiologies studied were idiopathic or associated with connective tissue disease.

Limitation of Use: Adding Revatio® to bosentan therapy does not result in beneficial effect on exercise capacity.

Dosing:

- Revatio® suspension is available as a 10mg/mL (when reconstituted) oral suspension.
- Revatio® oral suspension is recommended to be dosed 5mg or 20mg three times a day, 4 to 6 hours apart.

Mechanism of Action:

- Revatio® is an inhibitor of cyclic guanosine monophosphate (cGMP) specific for PDE-5 in the smooth muscle of the pulmonary vasculature, where PDE-5 is responsible for degradation of cGMP. Sildenafil, therefore, increases cGMP within pulmonary vascular smooth muscle cells resulting in relaxation. In patients with PAH, this can lead to vasodilation of the pulmonary vascular bed and, to a lesser degree, vasodilation in the systemic circulation.

Contraindications:

- Use with organic nitrates
- History of hypersensitivity reaction to sildenafil or any component of the tablet, injection, or oral suspension.

Cost Comparison

MEDICATION NAME	STRENGTH	COST/ UNIT**	COST/ MONTH**
Phosphodiesterase-5 Inhibitor (PDE-5)			
Sildenafil Oral Tablet	5mg, 20mg	$0.76*	$68.40
Revatio® (sildenafil) Oral Suspension	10mg/mL	$47.11+	$8,479.80
Adcirca® (tadalafil) Oral Tablet	20mg	$40.08+	$2,404.80
Endothelin Receptor Antagonists (ERA)			
Letairis® (ambrisentan) Oral Tablet	5mg, 10mg	$259.39+	$7,781.70
Tracleer® (bostentan) Oral Tablet	62.5mg, 125mg	$144.67+	$8,680.20
Opsumit® (macitentan) Oral Tablet	10mg	$252.91+	$7,587.30
Prostacyclin Vasodilator			
Orenitram™ (treprostinil) Oral Tablet	0.125mg, 0.25mg, 1mg, 2.5mg	$5.45-$102.96+	$9,266.40
Tyvaso® (treprostinil) Inhalation Soln	1.74mg/2.9mL ampule	$198.00+	$2,296.80
SOLUABLE GUANYLATE CYCLASE STIMULATOR			
Adempas® (riociguat) Oral Tablet	0.5mg, 1mg, 1.5mg, 2mg, 2.5mg	$90.64+	$8,157.60

*State Maximum Allowable Cost
+Estimated Acquisition Cost (EAC)
**Rebates not shown.

Recommendations

The College of Pharmacy recommends the prior authorization of Orenitram™ (treprostinil) and Revatio® (sildenafil) suspension with the following criteria:

Orenitram™ (Trepostinil) Approval Criteria:

1. An FDA approved diagnosis of pulmonary arterial hypertension; and
2. Previous failed trials of at least one of each of the following categories:
    a. Revatio® (sildenafil) or Adcirca® (tadalafil), and
    b. Letairis® (ambrisentan) or Tracleer® (bosentan); and
3. Medical supervision by a pulmonary specialist and/or cardiologist; and
4. A quantity limit of 90 tablets per 30 days will apply.

Revatio® (Sildenafil) Suspension Approval Criteria:

1. An FDA approved diagnosis of pulmonary arterial hypertension; and
2. Medical supervision by a pulmonary specialist and/or cardiologist; and
3. An age restriction would apply. The oral suspension formulation would be approvable for ages six years and younger. Members 7 years and older must have a patient-specific, clinically significant reason the member is not able to use the oral tablet formulation.
4. A quantity limit of 224mL per 30 days (two bottles) will apply.

Additionally the College of Pharmacy recommends updating the current criteria for Adcirca® (tadalafil) with the following criteria:

Adcirca® (Tadalafil) Approval Criteria:

1. An FDA approved diagnosis of pulmonary arterial hypertension; and
2. Medical supervision by a pulmonary specialist and/or cardiologist.
3. A patient-specific, clinically significant reason the member cannot use generic sildenafil oral tablets; and
4. A quantity limit of 60 tablets per 30 days will apply.

Utilization Details of Pulmonary Arterial Hypertension Medications: Fiscal Year 2014

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
PHOSPHODIESTERASE-5 INHIBITOR (PDE-5)					
SILDENAFIL TAB 20MG	519	106	$29,171.02	$1.86	$56.21
ADCIRCA TAB 20MG	132	16	$152,880.65	$38.67	$1,158.19
SUBTOTAL	**651**	**122**	**$182,051.67**	**$20.27**	**$607.20**
ENDOTHELIN RECEPTOR ANTAGONISTS (ERA)					
TRACLEER TAB 62.5MG	116	22	$170,244.92	$50.49	$1,467.63
TRACLEER TAB 125MG	34	5	$251,980.70	$247.04	$7,411.20
LETAIRIS TAB 10MG	19	2	$134,582.66	$236.11	$7,083.30
LETAIRIS TAB 5MG	12	1	$84,472.98	$234.65	$7,039.42
SUBTOTAL	**181**	**30**	**$641,281.26**	**$192.07**	**$23,001.55**
PROSTACYCLIN VASODILATORS					
REMODULIN 10MG/ML INJ	30	4	$685,922.50	$762.14	$22,864.08
REMODULIN 2.5MG/ML INJ	14	3	$79,636.38	$189.61	$5,688.31
FLOLAN INJ 1.5MG	11	1	$108,577.72	$293.45	$9,870.70
SUBTOTAL	**55**	**8**	**$874,136.60**	**$415.07**	**$12,807.70**
TOTAL	**887**	**130***	**$1,697,469.53**	**$63.63**	**$1,913.72**

*Total number of unduplicated members.

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[3] Vorhies, Erika E., and David Dunbar Ivy. "Drug Treatment of Pulmonary Hypertension in Children." *Pediatric Drugs* 16.1 (2014): 43-65.

[4] Peacock, A. J., N. F. Murphy, J. J. V. Mcmurray, L. Caballero, and S. Stewart. "An Epidemiological Study of Pulmonary Arterial Hypertension." European Respiratory Journal 30.1 (2007): 104-09.

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[7] 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 1/2015. Last accessed 01/2015.

[8] Orenitram™ Product Information. United Therapeutics Corp. Available online at: http://www.orenitram.com/pdf/Orenitram_Full_Prescribing_Information.pdf. Last revised 10/2014. Last accessed 01/2015.

[9] Revatio® Product Information. Pfizer Labs. Available online at: http://labeling.pfizer.com/ShowLabeling.aspx?id=645. Last revised 03/2014. Last accessed 01/2015.

Appendix H

Fiscal Year 2014 Annual Review of Multiple Sclerosis Medications and 30-Day Notice to Prior Authorize Lemtrada™ (Alemtuzumab) and Plegridy™ (Peginterferon β-1a)

Oklahoma Health Care Authority
February 2015

Current Prior Authorization Criteria

Multiple Sclerosis Interferon Approval Criteria:

1. An FDA approved diagnosis of relapsing remitting Multiple Sclerosis; and
2. Authorization of Tier-2 medications requires previous failure of the preferred Tier-1 product defined as:
   a. Occurrence of an exacerbation after six months; or
   b. Significant increase in MRI lesions after six months; or
   c. Adverse reactions or intolerable side effects; and
3. Approvals will not be granted for concurrent use with other disease modifying therapies; and
4. Compliance will be checked for continued approval every six months.

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

*Tier structure based on supplemental rebate participation.

Ampyra® (Dalfampridine) Approval Criteria:

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

Aubagio® (Teriflunomide) Approval Criteria:

1. An FDA approved diagnosis of relapsing forms of Multiple Sclerosis; and
2. Approvals will not be granted for concurrent use with other disease modifying therapies; and
3. All of the following will be required for initiation of treatment:
   a. Verification that female members are not pregnant and currently using reliable contraception; and
   b. Verification that member has no active infection(s); and

c. Complete blood counts (CBC) and verification that levels are acceptable to the prescriber; and
d. Liver function tests and verification that levels are acceptable to the prescriber; and
e. Blood pressure measurement and verification that blood pressure is being monitored; and
f. Verification that members do not have tuberculosis, or completion of standard medical treatment for patients with tuberculosis; and

4. Initial approvals of Aubagio® will be for six months, after which time, all of the following will be required for further approval:
   a. Medication compliance; and
   b. Repeat CBC counts and verification that counts are acceptable to the prescriber; and
   c. Repeat liver function tests and verification that levels are acceptable to the prescriber; and
   d. Verification that female members are not pregnant and will continue using reliable contraception; and
   e. Verification that blood pressure and symptoms of renal failure are being monitored; and
5. Compliance will be checked for continued approval every six months; and
6. A quantity limit of 30 tablets per 30 days will apply.

Copaxone® (Glatiramer Acetate) Approval Criteria:

1. An FDA approved diagnosis of relapsing, remitting Multiple Sclerosis; and
2. Approvals will not be granted for concurrent use with other disease modifying therapies; and
3. Compliance will be checked for continued approval every six months.

Gilenya® (Fingolimod) Approval Criteria:

1. An FDA approved diagnosis of relapsing, remitting Multiple Sclerosis with at least one relapse in the previous 12 months, or transitioning from existing Multiple Sclerosis therapy; and
2. Approvals will not be granted for concurrent use with other disease modifying therapies; and
3. The first dose should be observed in the doctor's office for signs and symptoms of bradycardia for six hours after first dose; and
4. Compliance will be checked for continued approval every six months.

Tecfidera™ (Dimethyl Fumarate) Approval Criteria:

1. An FDA approved diagnosis of relapsing forms of Multiple Sclerosis; and
2. Approvals will not be granted for concurrent use with other disease modifying therapies; and
3. Verification from the prescriber that member has no active infection(s); and
4. Complete blood counts (CBC) and verification that levels are acceptable to the prescriber; and
5. Compliance will be checked for continued approval every six months; and
6. A quantity limit of 60 tablets per 30 days will apply.

Tysabri® (Natalizumab) Approval Criteria:

1. An FDA approved diagnosis of Multiple Sclerosis or Crohn's disease; and
2. Treatment with at least two different first line therapeutic categories for Multiple Sclerosis or Crohn's disease that have failed to yield an adequate clinical response, or a patient-specific, clinically significant reason why the member cannot use all available first and second line alternatives; and
3. Prescriber, infusion center, and member must enroll in the TOUCH Prescribing Program.

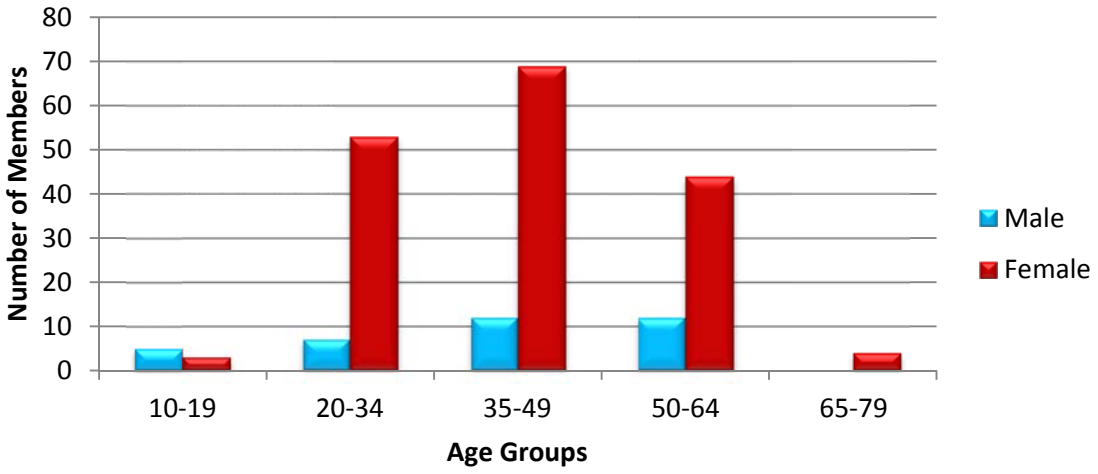
Utilization of Multiple Sclerosis Medications

Comparison of Fiscal Years: Pharmacy Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2013	189	1,441	$5,985,822.57	$4,153.94	$141.40	15,751	42,334
2014	209	1,514	$6,944,557.09	$4,586.89	$156.92	31,995	44,256
% Change	**10.60%**	**5.10%**	**16.02%**	**10.42%**	**10.98%**	**103.13%**	**4.50%**
Change	**20**	**73**	**$958,234.52**	**$432.95**	**$15.52**	**16,244**	**1,922**

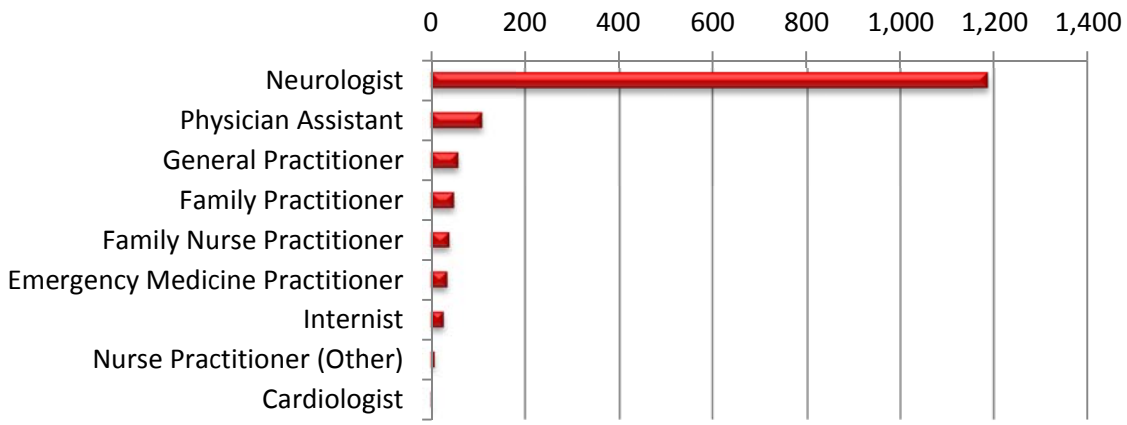
*Total number of unduplicated members

Demographics of Members Utilizing Multiple Sclerosis Medications



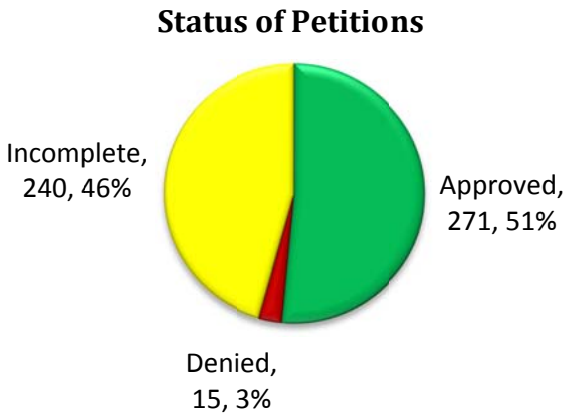
All members under the age of 21 years were verified to have a diagnosis of Multiple Sclerosis (MS) in their diagnosis history and their MS therapies were prescribed by a specialist in neurology.

Top Prescriber Specialties of Multiple Sclerosis Medications by Number of Claims



Prior Authorization of Multiple Sclerosis Medications

There were 526 petitions submitted for Multiple Sclerosis medications during fiscal year 2014. The following chart shows the status of the submitted petitions.



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

Anticipated Patent Expirations:

- Copaxone® (glatiramer acetate): There are no unexpired patents for the 20mg/mL strength however the 40mg/mL strength is patented until 08/2030.
- Gilenya® (fingolimod): 03/2026
- Ampyra® (dalfampridine): 05/2027
- Tecfidera™ (dimethyl fumarate): 02/2028
- Aubagio® (teriflunomide): 09/2030

New FDA Approvals:

- **12/2013:** The FDA approved a label change for Tysabri® (natalizumab). The label update included the option of using Tysabri® for first-line therapy at the discretion of the prescriber. The guidelines have not been updated to recommend Tysabri® as a first-line agent. Previous guidelines from the American Academy of Neurology (AAN) stated that Tysabri® is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, other MS therapies. Because of the possibility that Tysabri® therapy may be responsible for Progressive Multifocal Leukoencephalopathy (PML), it is recommended that it be reserved for use in select patients with relapsing, remitting disease who have failed other therapies either through continued disease activity, medication intolerance, or who have a particularly aggressive initial disease course.
- **08/2014:** The FDA approved Peligridy™ (peginterferon beta-1a) as a new disease-modifying therapy for people with relapsing forms of MS. Peligridy™, injected under the skin every two weeks, is a new therapy that belongs to the same interferon class as several medications that have been approved to treat MS. This new version is designed to maintain the effects of interferon in the body for a longer period of time.
- **11/2014:** Genzyme announced the FDA approval of Lemtrada™ (alemtuzumab) for the treatment of patients with relapsing forms of MS. Because of its safety profile, the use of Lemtrada™ should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.

Safety Updates:

- **08/29/2013:** The FDA released a drug safety communication alerting the public that a patient in Europe diagnosed with possible MS developed PML after taking Gilenya® (fingolimod). The FDA is continuing to investigate the PML case.
- **11/25/2014:** The FDA released a drug safety communication warning that a patient with MS who was being treated with Tecfidera™ (dimethyl fumarate), developed PML, and later died. As a result, information describing this case of PML, is being added to the Tecfidera™ drug label.

Lemtrada™ (Alemtuzumab) Product Summary[8]

FDA Approved: November 2014

Indications: Lemtrada™ (alemtuzumab) is a CD52-directed cytolytic monoclonal antibody indicated for the treatment of patients with relapsing forms of MS. Because of its safety profile, the use of Lemtrada™ should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.

Dosing: Lemtrada™ is available as a 12mg/1.2mL single use vial for injection.

- The recommended dosing is via intravenous infusion over four hours for two treatment courses:
    - First course: 12mg/day on five consecutive days
    - Second course: 12mg/day on three consecutive days 12 months after the first treatment course
- Prior to Lemtrada™ infusion the patient should be premedicated with corticosteroids for the first three days of each treatment course.

- The patient should be administered antiviral agents for herpetic prophylaxis starting on the first day of Lemtrada™ dosing and continued for a minimum of two months after completion of Lemtrada™ dosing or until CD4+ lymphocyte count is greater than 200 cells per microliter, whichever occurs later.
- Lemtrada™ injections must be diluted prior to administration.

Mechanism of Action: The precise mechanism of action by which Lemtrada™ exerts its therapeutic effects in MS is unknown but is presumed to involve binding to CD52, a cell surface antigen present on T and B lymphocytes, and on natural killer cells, monocytes, and macrophages. Following cell surface binding to T and B lymphocytes, Lemtrada™ results in antibody-dependent cellular cytolysis and complement-mediated lysis.

Boxed Warning: Autoimmunity, Infusion Reactions, and Malignancies

- Lemtrada™ can cause serious, sometimes fatal, autoimmune conditions such as immune thrombocytopenia and anti-glomerular basement membrane disease. Complete blood counts, serum creatinine levels, and urinalysis should be monitored at periodic intervals for 48 months after the last dose.
- Lemtrada™ can cause serious and life-threatening infusion reactions. Lemtrada™ must be administered in a setting with appropriate equipment and personnel to manage anaphylaxis or serious infusion reactions. Patients should be monitored for two hours after each infusion. Patients should be made aware that serious infusion reactions can also occur after the two hour monitoring period.
- Lemtrada™ may cause an increased risk of malignancies, including thyroid cancer, melanoma, and lymphoproliferative disorders. Baseline and yearly skin examinations should be performed.
- Because of the risk of autoimmunity, infusion reactions, and malignancies, Lemtrada™ is available only through restricted distribution under a Risk Evaluation Mitigation Strategy (REMS) Program.

Contraindications: Lemtrada™ is contraindicated in patients who are infected with Human Immunodeficiency Virus (HIV) because Lemtrada™ causes prolonged reductions of CD4+ lymphocyte counts.

Warnings and Precautions:

- Autoimmunity: Treatment with Lemtrada™ can result in the formation of autoantibodies and increase the risk of serious autoimmune mediated conditions.
- Infusion Reactions: Lemtrada™ can cause cytokine release syndrome resulting in infusion reactions, some of which may be serious and life-threatening.
- Malignancies: Lemtrada™ may increase the risk of thyroid cancer, melanoma, lymphoproliferative disorders, and lymphoma.
- Immune Thrombocytopenia: Immune thrombocytopenia (ITP) occurred in 2% of Lemtrada™ treated patients in clinical studies in MS. ITP has been diagnosed more than three years after the last Lemtrada™ dose.
- Glomerular Nephropathies: Glomerular nephropathies occurred in 0.3% of Lemtrada™ treated patients in clinical studies in MS. There are post-marketing cases of MS patients treated with Lemtrada™ who developed anti-glomerular basement membrane disease

(anti-GBM) and subsequently developed end-stage renal disease (ESRD) requiring renal transplantation. Cases of anti-GBM disease have been diagnosed up to 40 months after the last Lemtrada™ dose.

- Thyroid Disorders: Autoimmune thyroid disorders occurred in 34% of Lemtrada™ treated patients in clinical studies.
- Other Autoimmune Cytopenias: Autoimmune cytopenias such as neutropenia (0.1%), hemolytic anemia (0.2%), and pancytopenia (0.2%) occurred in Lemtrada™ treated patients in clinical studies in MS.
- Infections: Infections occurred in 71% of Lemtrada™ treated patients compared to 53% of patients treated with interferon beta-1a in controlled clinical trials. Infections that occurred more often in Lemtrada™ treated patients included nasopharyngitis, urinary tract infection, upper respiratory tract infection, sinusitis, herpetic infections, influenza, and bronchitis.
- Drug Products with the Same Active Ingredient: Lemtrada™ contains the same active ingredient found in Campath® an intravenous medication indicated for B-cell chronic lymphocytic leukemia.

Adverse Reactions: In clinical trials the most common adverse reactions with Lemtrada™ (in at least 10% of patients and more frequently than in interferon beta-1a) were rash, headache, pyrexia, nasopharyngitis, nausea, urinary tract infection, fatigue, insomnia, upper respiratory tract infection, herpes viral infection, urticaria, pruritus, thyroid gland disorders, fungal infection, arthralgia, pain in extremity, back pain, diarrhea, sinusitis, oropharyngeal pain, paresthesia, dizziness, abdominal pain, flushing, and vomiting.

Use in Special Populations:

- Pregnancy: Lemtrada™ is pregnancy category C. Placental transfer of anti-thyroid antibodies resulting in neonatal Graves' disease has been reported.
- Nursing Mothers: It is not known whether Lemtrada™ is excreted in human milk.
- Pediatric Patients: The safety and effectiveness of Lemtrada™ in pediatric patients younger than 17 years of age have not been established.
- Geriatric Patients: Clinical studies of Lemtrada™ did not include sufficient numbers of patients aged 65 years and older to determine whether they respond differently than younger patients.

Efficacy: The efficacy of Lemtrada™ was demonstrated in a two-year randomized open-label, rater-blinded, active comparator (interferon beta-1a 44 mcg) controlled study in patients with relapsing, remitting MS. Patients entering the study had an EDSS score of 5 or less and had to have experienced at least one relapse while on interferon beta or glatiramer acetate therapy. The clinical outcome measures were the annualized relapse rate (ARR) and the time to confirmed disability progression. The MRI outcome measure was the change in T2 lesion volume. The ARR was significantly lower in patients treated with Lemtrada™ (0.26 for Lemtrada™ and 0.52 for interferon beta-1a, $p<0.0001$, a 49% relative reduction). Time to onset of six-month confirmed disability progression was significantly delayed with Lemtrada™ (13% for Lemtrada™ and 21% for interferon beta-1a, $p=0.0084$, a 42% relative risk reduction). There was no significant difference between the treatment groups for the change in T2 lesion volume.

Plegridy™ (Peginterferon β-1a) Product Summary[9]

FDA Approved: August 2014

Indications: Plegridy™ (Peginterferon β-1a) is an interferon beta indicated for the treatment of patients with relapsing forms of MS.

Dosing:

- Plegridy™ is administered subcutaneously.
- Plegridy is available as 125mcg/0.5mL single-dose prefilled pens and syringes.
- The recommended dose of Plegridy™ is 125mcg injected subcutaneously every 14 days.
- Patients should start treatment with 63mcg on day 1. On day 15 (14 days later), the dose is increased to 94mcg, reaching the full dose of 125mcg on day 29 (after another 14 days). Patients continue with the full dose (125mcg) every 14 days thereafter.
- Healthcare professionals should train patients in the proper technique for self-administering subcutaneous injections using the prefilled pen or syringe. Patients should be advised to rotate sites for subcutaneous injections. The usual sites for subcutaneous injections are abdomen, back of the upper arm, and thigh.
- Each Plegridy™ pen and syringe is provided with the needle pre-attached. Prefilled pens and syringes are for a single dose only and should be discarded after use.
- Prophylactic and concurrent use of analgesics and/or antipyretics may prevent or ameliorate flu-like symptoms sometimes experienced during treatment with Plegridy™.

Mechanism of Action: The mechanism by which Plegridy™ exerts its effects in patients with MS is unknown.

Contraindications: History of hypersensitivity to natural or recombinant interferon beta, peginterferon, or any other component of the formulation.

Warnings and Precautions:

- Hepatic Injury: Severe hepatic injury, including hepatitis, autoimmune hepatitis, and rare cases of severe hepatic failure, have been reported with Plegridy™. Asymptomatic elevation of hepatic transaminases has also been reported, and in some patients has recurred upon rechallenge with Plegridy™.
- Depression and Suicide: Depression, suicidal ideation, and suicide occur more frequently in patients receiving Plegridy™ than in patients receiving placebo.
- Seizures: Seizures are associated with the use of Plegridy™.
- Anaphylaxis and Other Allergic Reactions: Anaphylaxis and other serious allergic reactions are rare complications of treatment with Plegridy™.
- Injection Site Reactions: Injection site reactions, including injection site necrosis, can occur with the use of Plegridy™.
- Congestive Heart Failure: Congestive heart failure, cardiomyopathy, and cardiomyopathy with congestive heart failure may occur in patients receiving Plegridy™.
- Decreased Peripheral Blood Counts: Plegridy™ can cause decreased peripheral blood counts in all cell lines, including rare instances of pancytopenia and severe thrombocytopenia.

- Autoimmune Disorders: Autoimmune disorders of multiple target organs including idiopathic thrombocytopenia, hyper- and hypothyroidism, and autoimmune hepatitis have been reported with Plegridy™.

Adverse Reactions: The most common adverse drug reactions experienced during clinical trials with Plegridy™ were injection site erythema, influenza-like illness, pyrexia, headache, myalgia, chills, injection site pain, asthenia, injection site pruritus, and arthralgia (all had incidence more than 10% and at least 2% more than placebo).

Use in Special Populations:

- Pregnancy: Plegridy™ is pregnancy category C. There are no adequate and well-controlled studies in pregnant women.
- Nursing Mothers: It is not known whether Plegridy™ is excreted in human milk.
- Pediatric Patients: The safety and effectiveness of Plegridy™ have not been established in pediatric patients.
- Geriatric Patients: The safety and effectiveness of Plegridy™ have not been established in geriatric patients.
- Renal Impairment: Patients with severe renal impairment using Plegridy™ should be monitored for adverse reactions due to increased drug exposure.

Efficacy: The efficacy of Plegridy™ was demonstrated in a randomized, double-blind, and placebo-controlled study. The trial compared clinical and MRI outcomes at 48 weeks in patients who received Plegridy™ 125mcg (n=512) or placebo (n=500) once every 14 days. The study enrolled patients who had a baseline EDSS score from 0 to 5, who had experienced at least two relapses within the previous three years, and had experienced at least 1 relapse in the previous year. The trial excluded patients with progressive forms of MS. The primary outcome was the annualized relapse rate (ARR) over one year. Secondary outcomes included the proportion of patients relapsing, number of new or newly enlarging T2 hyperintense lesions, and time to confirmed disability progression. The ARR was significantly lower in patients treated with Plegridy™ (0.26 for Plegridy™ and 0.40 for placebo, p=0.0007, a 36% relative reduction). The mean number of new or newly enlarging T2 hyperintense lesions was significantly less with Plegridy™ (3.6% for Plegridy™ and 10.9% for placebo, p<0.0001, a 67% relative risk reduction).

Recommendations

The College of Pharmacy recommends the prior authorization of Lemtrada™ (alemtuzumab) with the following criteria:

Lemtrada™ (Alemtuzumab) Approval Criteria:

1. An FDA approved diagnosis of relapsing forms of Multiple Sclerosis; and
2. Member must have had an inadequate response to two or more drugs indicated for the treatment of Multiple Sclerosis; and
3. Lemtrada™ must be administered in a setting with appropriate equipment and personnel to manage anaphylaxis or serious infusion reactions. The prescriber must agree that the member will be monitored for two hours after each infusion; and
4. The prescriber must agree to monitor complete blood counts with differential, serum creatinine levels, and urinalysis with urine counts at periodic intervals for 48 months after the last dose of Lemtrada™; and
5. The prescriber must agree that baseline and yearly skin examinations will be performed while the member is utilizing Lemtrada™ therapy; and
6. Member, prescriber, pharmacy, and healthcare facility must all enroll in the Lemtrada™ REMS Program and maintain enrollment throughout therapy.

Additionally the College of Pharmacy recommends placement of Plegridy™ (peginterferon β-1a) into Tier-2 of the Multiple Sclerosis Interferon Prior Authorization category. Current criteria for this category will apply.

Multiple Sclerosis Interferon Approval Criteria:

1. An FDA approved diagnosis of relapsing remitting Multiple Sclerosis; and
2. Authorization of Tier-2 medications requires previous failure of the preferred Tier-1 product defined as:
   d. Occurrence of an exacerbation after six months; or
   e. Significant increase in MRI lesions after six months; or
   f. Adverse reactions or intolerable side effects; and
5. Approvals will not be granted for concurrent use with other disease modifying therapies; and
6. Compliance will be checked for continued approval every six months.

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

*Tier structure based on supplemental rebate participation.

Utilization Details of Multiple Sclerosis Medications: Fiscal Year 2014

Pharmacy Claims: Fiscal Year 2014

Product Utilized	Total Claims	Total Members	Total Cost	Cost/ Day	Cost/ Claim
Tier-1 Interferon Beta-1a Products					
AVONEX PREFILLED KIT 30MCG	87	16	$407,167.98	$162.48	$4,680.09
AVONEX PEN KIT 30MCG	44	14	$207,259.19	$167.96	$4,710.44
AVONEX KIT 30MCG	6	2	$27,504.48	$163.72	$4,584.08
Subtotal	**137**	**23**	**$641,931.65**	**$164.26**	**$4,685.63**
Tier-1 Interferon Beta-1b Products					
BETASERON INJ 0.3MG	68	13	$345,269.63	$163.48	$5,077.49
Subtotal	**68**	**13**	**$345,269.63**	**$163.48**	**$5,077.49**
Tier-1 Subtotal	**205**	**36**	**$987,201.28**	**$163.99**	**$4,815.62**
Tier-2 Interferon Beta-1a Products					
REBIF INJ 44/0.5	142	23	$688,519.02	$172.22	$4,848.73
REBIF REBIDO INJ 44/0.5	45	8	$224,963.80	$178.26	$4,999.20
REBIF INJ 22/0.5	13	2	$61,231.69	$167.30	$4,710.13
REBIF REBIDO SOL TITRATN	5	5	$23,872.06	$158.09	$4,774.41
REBIF TITRTN SOL PACK	3	3	$13,909.00	$143.39	$4,636.33
Subtotal	**208**	**32**	**$1,012,495.57**	**$172.37**	**$4,867.77**
Tier-2 Interferon Beta-1b Products					
EXTAVIA INJ 0.3MG	2	1	$538.18	$9.61	$269.09
Subtotal	**2**	**1**	**$538.18**	**$9.61**	**$269.09**
Tier-2 Subtotal	**210**	**33**	**$1,013,033.75**	**$170.83**	**$4,823.97**
Dalfampridine Products					
AMPYRA TAB 10MG	142	25	$227,305.62	$53.74	$1,600.74
Subtotal	**142**	**25**	**$227,305.62**	**$53.74**	**$1,600.74**
Teriflunomide Products					
AUBAGIO TAB 14MG	19	8	$83,648.76	$157.23	$4,402.57
AUBAGIO TAB 7MG	1	1	$4,021.29	$143.62	$4,021.29
Subtotal	**20**	**9**	**$87,670.05**	**$156.55**	**$4,383.50**
Glatiramer Acetate Products					
COPAXONE KIT 20MG/ML	418	68	$2,089,481.55	$166.59	$4,998.76
COPAXONE INJ 40MG/ML	81	34	$392,365.51	$171.34	$4,844.02
Subtotal	**499**	**78**	**$2,481,847.06**	**$167.32**	**$4,973.64**
Fingolimod Products					
GILENYA CAP 0.5MG	205	26	$996,679.56	$173.64	$4,861.85
Subtotal	**205**	**26**	**$996,679.56**	**$173.64**	**$4,861.85**
Dimethyl Fumarate Products					
TECFIDERA CAP 240MG	183	35	$917,033.51	$167.04	$5,011.11
TECFIDERA MIS STARTER	36	35	$177,871.27	$164.70	$4,940.87
TECFIDERA CAP 120MG	3	2	$10,825.56	$171.83	$3,608.52
Subtotal	**222**	**45**	**$1,105,730.34**	**$166.70**	**$4,980.77**
Natalizumab Products					
TYSABRI INJ 300MG/15ML	11	2	$45,089.43	$145.45	$4,099.04
Subtotal	**11**	**2**	**$45,089.43**	**$145.45**	**$4,099.04**
Total	**1,514**	**209***	**$6,944,557.09**	**$156.92**	**$4,586.89**

*Total number of unduplicated members

Medical Claims: Fiscal Year 2014

Product Utilized	Total Claims	Total Members	Total Cost	Cost/ Claim
Natalizumab Products				
TYSABRI INJ 300MG/15ML (J2323)	64	12	$215,423.03	$3,365.98
Total	**64**	**12***	**$215,423.03**	**$3,365.98**

*Total number of unduplicated members

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[2] Multiple Sclerosis Society of America: FDA-Approved Medications: Intravenous (IV) Infusion Tysabri® (Natalizumab). Available online at: http://www.mymsaa.org/publications/msresearch-update-2014/tysabri/. Last revised 02/10/2014. Last accessed 01/27/2015.
[3] American Academy of Neurology: The use of Natalizumab (Tysabri) for the treatment of Multiple Sclerosis. Available online at: https://www.aan.com/Guidelines/home/GetGuidelineContent/306. Last revised 09/2008. Last accessed 01/27/2015.
[4] National Multiple Sclerosis Society: FDA Approves Plegridy (Pegylated Interferon Beta) For Relapsing MS. Available online at: http://www.nationalmssociety.org/About-the-Society/News/FDA-Approves-Plegridy-Pegylated-Interferon-Beta. Last revised 08/15/2014. Last accessed 01/27/2015.
[5] Genzyme: Genzyme's Lemtrada Approved by the FDA. Available online at: http://news.genzyme.com/press-release/genzymes-lemtrada-approved-fda. Last revised 11/14/2014. Last accessed 01/27/2015.
[6] FDA Drug Safety Communication: FDA Investigating Rare Brain Infection in Patient Taking Gilenya (Fingolimod). Available online at: http://www.fda.gov/Drugs/DrugSafety/ucm366529.htm. Last revised 08/29/2013. Last accessed 01/27/2015.
[7] FDA Drug Safety Communication: FDA Warns About Case of Rare Brain Infection PML with MS Drug Tecfidera (Dimethyl Fumarate). Available online at: http://www.fda.gov/drugs/drugsafety/ucm424625.htm. Last revised 11/25/2014. Last accessed 01/27/2015.
[8] Lemtrada™ Product Information. Genzyme Corporation. Available online at: http://products.sanofi.us/Lemtrada/Lemtrada.pdf. Last revised 11/2014. Last accessed 01/27/2015.
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Appendix I

30-Day Notice to Prior Authorize Brisdelle® (Paroxetine Mesylate)

Oklahoma Health Care Authority
February 2015

Introduction[1, 2, 3]

Vasomotor symptoms (VMS) are described as sudden sensations of heat centered on the face and chest that may become generalized throughout the body. They are commonly referred to as hot flushes (hot flashes) and are one of the chief complaints of women experiencing menopause. They occur most frequently during the menopausal transition period, perimenopause, and can vary in severity, duration, and frequency. Studies have shown that 87% of women who report hot flashes, have these symptoms on a daily basis, with 33% of those experiencing more than 10 episodes per day.

There are several risk factors for VMS which include obesity, smoking, reduced physical activity, socioeconomic factors, hormonal concentrations, and ethnic factors. Obese women have more adipose tissue than lean women. It is thought that adipose functions as an insulator and interferes with thermoregulatory mechanisms of heat dissipation. These women have higher serum estrone concentrations due to the increased adipose tissue; thus, they have an increased incidence of VMS. Weight loss may help reduce symptoms. A higher hormonal level of FSH is associated with increased prevalence and frequency of VMS. Ethnic factors appear to play a part in VMS with African American women experiencing more VMS than Caucasian women and Asian women experiencing the least.

The most common treatment options for moderate to severe VMS include hormonal therapy (HT) and non-hormonal therapy (NHT). HT is thought to be most effective at treating VMS frequency and severity but carries many risks that may outweigh the benefits. The most serious risks include an increase of venous thromboembolism (VTE) and breast cancer incidence. HT is a viable option for women with no contraindications, who have an intact uterus, and who only plan to use the treatment for a short duration.

NHT is an option for women who are not candidates for HT and experience moderate to severe VMS. NHT includes the use of selective serotonin reuptake inhibitors (SSRIs). Paroxetine mesylate, an SSRI, has demonstrated improvement in VMS although the mechanism of action for the treatment of VMS is unknown. When SSRIs are given for VMS doses are typically lower than when used for psychiatric disorders and the SSRI effect on VMS tends to have a quicker onset than when given for depression.

The FDA approved Brisdelle® (paroxetine mesylate) for the treatment of moderate to severe VMS associated with menopause in June 2013. It is presently the only non-hormonal therapy approved by the FDA for VMS due to menopause.

Brisdelle® (Paroxetine Mesylate) Product Summary[4]

Indications: Brisdelle® (paroxetine mesylate) is indicated for the treatment of moderate to severe vasomotor symptoms associated with menopause. It is not indicated for treating any psychiatric condition.

Dosing:

- Brisdelle® is available as 7.5mg oral capsules.
- The recommended dosage of Brisdelle® is 7.5mg once daily, at bedtime.
- Brisdelle® may be taken with or without food.

Mechanism of Action: Brisdelle® is a SSRI. It is not an estrogen. Its mechanism of action for the treatment of VMS is unknown.

Contraindications:

- Concurrent use with monoamine oxidase inhibitors (MAOI) or use within 14 days of MAOI use
- Concurrent use with thioridazine
- Concurrent use with pimozide
- Hypersensitivity to any ingredient in Brisdelle®
- Pregnancy

Efficacy:

- The efficacy of Brisdelle® for the treatment of moderate to severe VMS associated with menopause was assessed in two Phase 3 studies. The dose used in both studies was 7.5mg once nightly at bedtime. The studies included 1,174 postmenopausal women with a minimum of 7 to 8 moderate to severe vasomotor symptoms per day at baseline for 30 days prior to initiation of drug therapy.
- Study 1 lasted 12 weeks and included 606 postmenopausal women. Study 2 lasted 24 weeks and included 568 postmenopausal women. Both were randomized, double-blind, and placebo-controlled trials. The co-primary efficacy endpoints for both studies were the reduction from baseline in VMS frequency and severity at weeks 4 and 12.
- Data from Study 1 showed a statistically significant reduction from baseline in the frequency of moderate to severe vasomotor symptoms at both weeks 4 and 12 and a statistically significant reduction in the severity of moderate to severe VMS at week 4 for Brisdelle® compared to placebo.
- Data from Study 2 showed a statistically significant reduction from baseline in the frequency and severity of moderate to severe vasomotor symptoms at week 4 and week 12 for Brisdelle® compared to placebo.
- Persistence of benefit at 24 weeks in Study 2 was evaluated with a responder analysis where responders were defined as those patients who achieved greater than or equal to 50% reduction from baseline in the frequency of moderate to severe VMS at week 24. The proportion of patients achieving a greater than or equal to 50% reduction in the

frequency of moderate to severe VMS from baseline to week 24 was 48% in the Brisdelle® group and 36% in the placebo group at week 24.

Safety:

- Brisdelle® has a boxed warning for risk of suicidal thoughts and behaviors. SSRI antidepressants increase the risk of suicidal thinking and behavior in pediatric and young adult patients when used to treat major depressive disorder (MDD) and other psychiatric disorders. There is limited information regarding suicidality in women who use Brisdelle® for treatment of VMS. The trials conducted excluded women with a presence or history of previous psychiatric disorders. Prescribers should consider discontinuing Brisdelle® if depression worsens or suicidality emerges.
- Brisdelle® includes a risk of life-threatening serotonin syndrome when administered alone and concomitantly with serotonergic drugs and drugs that impair metabolism of serotonin. Patients should be monitored for the development of serotonin syndrome and Brisdelle® or any concomitant serotonergic agents should be discontinued immediately if symptoms occur.
- The concomitant use of Brisdelle® with MAOIs is contraindicated.
- Brisdelle® may decrease the efficacy of tamoxifen when co-administered.
- Brisdelle® may increase the risk of bleeding events. Concomitant use of aspirin, NSAIDs, warfarin, and other anticoagulants may increase the risk further.
- Brisdelle® may result in hyponatremia. Elderly patients may be at greater risk. Most often, it appears to be the result of the syndrome of inappropriate antidiuretic hormone secretion (SIADH). Consideration should be given to discontinuing Brisdelle® in patients with symptomatic hyponatremia.
- Brisdelle® may increase the risk of bone fracture.
- Brisdelle® is not approved for use in treating either depression or bipolar depression. However, prior to Brisdelle® therapy initiation, all patients should be screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression. It is generally believed (though not established in controlled trials) that use of an antidepressant alone may increase the likelihood of precipitation of a mixed/manic episode in patients at risk for bipolar disorder.
- Brisdelle® exhibited seizures in 0.1% of patients in premarketing testing. Brisdelle® should be used cautiously in patients with a history of seizures or with conditions that potentially lower the seizure threshold.
- Brisdelle® has been associated with the development of akathisia, characterized by an inner sense of restlessness and psychomotor agitation such as an inability to sit or stand still.
- Brisdelle® may cause mydriasis. Use caution in patients with narrow angle glaucoma.
- Brisdelle® has the potential to impair judgment, thinking, or motor skills. Patients should be cautioned about operating hazardous machinery, including motor vehicles, until they are reasonably certain that the drug treatment does not affect them adversely.
- The most common side effects of Brisdelle® are headache, feeling tired, nausea, and vomiting.

Cost Comparison:

Medication Name	Strength	Cost Per Unit*	Cost Per Month+	Cost Per Year
Brisdelle® (paroxetine mesylate)	**7.5mg**	**$5.23***	**$156.90**	**$1,882.80**
Prempro® (conjugated estrogens/medroxyprogesterone)	0.45mg	$4.70*	$140.85	$1,690.20
Micronized Estradiol	1mg	$0.13∞	$3.76	$45.07
Duavee® (conjugated estrogens/bazedoxifene)	0.45/20mg	$4.29	$128.70	$1,544.40
Paroxetine HCl	10mg	$0.11∞	$3.38	$40.50

*Cost based on Estimated Acquisition Cost (EAC)
+Cost based on recommended dosing
∞ Cost based on state maximum allowable cost (SMAC)

Utilization: There has been no utilization of Brisdelle® in the SoonerCare population since its approval in June 2013.

Recommendations

The College of Pharmacy recommends the prior authorization of Brisdelle® (paroxetine mesylate) with the following criteria:

Brisdelle® (Paroxetine Mesylate) Approval Criteria:

1. An FDA approved diagnosis of moderate to severe vasomotor symptoms associated with menopause; and
2. Approvals for Brisdelle® will not be granted for psychiatric indications; and
3. Member must not have any of the contraindications for use of Brisdelle®; and
4. Authorization requires a patient-specific clinically significant reason why paroxetine 10mg is not appropriate for the member; and
5. A quantity limit of 30 capsules per 30 days will apply.

[1] Management of Menopausal Symptoms. Practice Bulletin No. 141. American College of Obstetricians and Gynecologists. Obstet Gynecol 2014; 123:202-16.
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[4] Brisdelle® Product Information. Noven Therapeutics, LLC. Available online at: http://www.brisdelle.com/brisdelle-pdf/Full-Prescribing-Information.pdf. Last revised 07/2013. Last accessed 01/28/2014.

Appendix J

Fiscal Year 2014 Annual Review of Ravicti®
(Glycerol Phenylbutyrate)

Oklahoma Health Care Authority
February 2015

Indication[1]

Ravicti® (glycerol phenylbutyrate) is an oral liquid indicated for use as a nitrogen-binding agent for chronic management of adult and pediatric patients two years of age and older with urea cycle disorders (UCDs), who cannot be managed by dietary protein restriction and/or amino acid supplementation alone.

Current Prior Authorization Criteria

Ravicti® (Glycerol Phenylbutyrate) Approval Criteria:

1. An FDA approved diagnosis of urea cycle disorder; and
2. Active management with protein restricted diet; and
3. A patient-specific, clinically significant reason why member cannot use Buphenyl® (sodium phenylbutyrate).

Utilization of Ravicti® (Glycerol Phenylbutyrate)

There has been no utilization during fiscal years 2013 or 2014.

Prior Authorization of Ravicti® (Glycerol Phenylbutyrate)

There were no petitions submitted for Ravicti® during fiscal years 2013 or 2014.

Market News and Updates[2]

Anticipated Patent Expirations:

- Ravicti® (glycerol phenylbutyrate): 02/2032

Recommendations

The College of Pharmacy does not recommend any changes at this time.

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[1] Ravicti® Prescribing Information. Available online at: http://www.ravicti.com/hcp/PDF/RAVICTI_Prescribing_Information_Updated.pdf Last revised 06/2014. Last accessed 1/23/15.

[2] 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 1/23/15. Last accessed 1/23/15.

Appendix K

Calendar Year 2014 Annual Review of Procysbi® (Cysteamine Bitartrate Delayed-Release)

Oklahoma Health Care Authority
February 2015

Indication[1]

Procysbi® (cysteamine bitartrate delayed-release) is a cysteine depleting agent indicated for the management of nephropathic cystinosis in adults and children ages 6 years and older.

Current Prior Authorization Criteria

Procysbi® (Cysteamine Bitartrate Delayed-Release Capsules) Approval Criteria:

1. An FDA approved diagnosis of nephropathic cystinosis; and
2. A patient-specific, clinically significant reason why member cannot use the short-acting formulation Cystagon® (cysteamine bitartrate).

Utilization of Procysbi® (Cysteamine Bitartrate Delayed-Release)

There were eight claims for Procysbi® with a total cost of $99,651.53 during calendar year 2014.

Prior Authorization of Procysbi® (Cysteamine Bitartrate Delayed-Release)

There were six petitions submitted for Procysbi® during calendar year 2014, two petitions were approved.

Market News and Updates[2]

Anticipated Patent Expirations:

- Procysbi® (cysteamine bitartrate delayed-release): 09/2027

Recommendations

The College of Pharmacy does not recommend any changes at this time.

Utilization Details

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
PROCYSBI 75MG CAPSULE	8	1	$99,651.53	$415.21	$12,456.44	100%
TOTAL	**8**	**1**	**$99,651.53**	**$415.21**	**$12,456.44**	**100%**

[1] Procysbi® Prescribing Information. Available online at: http://www.procysbi.com/docs/Procysbi-Full-Prescribing-Information.pdf Last revised 04/2013. Last accessed 1/23/15.
[2] 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 1/23/15. Last accessed 1/23/15.

Appendix L

Fiscal Year 2014 Annual Review of Fulyzaq® (Crofelemer)

Oklahoma Health Care Authority
February 2015

Indication[1]

Fulyzaq® (crofelemer) is a twice daily oral tablet indicated for the symptomatic relief of non-infectious diarrhea in adult patients with HIV/AIDS on anti-retroviral therapy.

Current Prior Authorization Criteria

Fulyzaq® (Crofelemer) Approval Criteria:

1. An FDA approved diagnosis of non-infectious diarrhea in adult patients with HIV/AIDS currently on anti-retroviral therapy; and
2. The duration of diarrhea has been greater than or equal to four weeks; and
3. Trials of dietary modifications have failed; and
4. Prescribers must verify that infectious diarrhea has been ruled out via confirmation of all of the following:
    a. CD4 count has been measured and possible opportunistic infections have been ruled out; and
    b. Member does not have fever; and
    c. Stool studies for pathogens are negative including:
        i. Bacterial cultures
        ii. Ova, Parasite, Cryptosporidium and/or Giardia
        iii. *Clostridium difficile* (*Clostridium difficile* testing should include a glutamate dehydrogenase screen and if positive followed by a confirmatory test or a nucleic acid amplification test in patients with documented diarrhea. A toxin enzyme immunoassay should not be used as a stand-alone test.); and
5. If stool study results are negative and the patient has severe symptoms, particularly in the case of advanced immunodeficiency, an endoscopy with biopsy is recommended, at the doctor's discretion, to rule out inflammatory bowel disease, cancer, cytomegalovirus (CMV) infection, microsporidium, or mycobacterium avium complex (MAC); and
6. A quantity limit of 60 tablets per 30 days will apply.
7. Initial approvals will be for the duration of four weeks. An additional six month approval may be granted if the prescriber documents the member is responding well to treatment.

Utilization of Fulyzaq® (Crofelemer)

There has been no use of Fulyzaq® during fiscal year 2013 or 2014.

Prior Authorization of Fulyzaq® (Crofelemer)

There were no petitions submitted for Fulyzaq® during fiscal year 2013 or 2014.

Market News and Updates[2]

Anticipated Patent Expiration of Fulyzaq® (crofelemer): 06/2018

Recommendations

The College of Pharmacy does not recommend any changes at this time.

[1] Fulyzaq® Prescribing Information. Salix Pharmaceuticals Inc. Available online at: http://cdn.salix.com/shared/pi/fulyzaq-pi.pdf. Last revised 02/2013. Last accessed 01/28/2014.

[2] FDA: Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised 01/21/2014. Last accessed 01/21/2014.

Appendix M

FDA & DEA Updates (additional information can be found at http://www.fda.gov/Drugs/default.htm)

FDA NEWS RELEASE

For Immediate Release: January 8th, 2015

FDA approves anti-clotting drug Savaysa

The U.S. Food and Drug Administration approved the anti-clotting drug Savaysa (edoxaban tablets) to reduce the risk of stroke and dangerous blood clots in patients with atrial fibrillation that is not caused by a heart valve problem.

Atrial fibrillation is one of the most common types of abnormal heart rhythm. It occurs when the heart's two upper chambers (atria) do not contract properly, allowing blood clots to form, which can break off and travel to the brain or other parts of the body. Patients with atrial fibrillation experience an abnormal, irregular and rapid heartbeat.

Savaysa also has been approved to treat deep vein thrombosis (DVT) and pulmonary embolism (PE) in patients who have already been treated with an anti-clotting drug administered parenterally, for five to ten days.

The safety and efficacy of Savaysa in treating patients with atrial fibrillation not caused by cardiac valve disease was studied in a clinical trial of 21,105 participants. The trial compared two dose levels of Savaysa with the anti-clotting drug warfarin for their effects on rates of stroke and systemic emboli. The trial results showed the higher dose of Savaysa to be similar to warfarin for the reduction in the risk of stroke. While warfarin is highly effective in reducing the risk of stroke in patients with atrial fibrillation, it increases the risk of bleeding. Savaysa demonstrated significantly less major bleeding compared to warfarin.

Savaysa for treatment of patients with DVT and PE was studied in 8,292 participants. The study compared the safety and efficacy of Savaysa to warfarin for treating patients with a DVT and/or PE to reduce the rate of recurrence of symptomatic venous thromboembolism (VTE) events (which includes DVT, PE, and VTE-related death). In the trial, 3.2 percent of participants taking Savaysa had a symptomatic recurrent VTE compared to 3.5 percent of those taking warfarin.

The most common side effects observed in clinical trial participants were bleeding and anemia. As with other FDA-approved anti-clotting drugs, bleeding, including life-threatening bleeding, is the most serious risk with Savaysa. There is no treatment that has been proven to reverse the anti-coagulant effect of Savaysa.

Savaysa has a Boxed Warning that provides important dosing and safety information for health care professionals about specific patient groups, including a warning that Savaysa is less effective in atrial fibrillation patients with a creatinine clearance greater than 95 milliliters per minute. A patient's level of creatinine clearance shows how well a patient's kidneys are working by measuring the level of the waste product creatinine in the blood or urine. This should be assessed before initiating therapy with Savaysa. Patients with creatinine clearance greater than 95 milliliters per minute have an increased risk of stroke compared to similar patients given warfarin. Savaysa should not be used in nonvalvular atrial fibrillation patients with a higher creatinine clearance. Another anticoagulant should be used instead.

As with other anticoagulants, the Boxed Warning counsels that premature discontinuation of Savaysa increases the risk of stroke and notes that spinal or epidural hematomas (collection of blood outside of a blood vessel) may occur in patients treated with Savaysa who are receiving anesthesia injected around the spine or undergoing spinal puncture.

Savaysa will be dispensed with a patient Medication Guide that provides instructions on its use and drug safety information. Health care professionals should counsel patients about the increased risk of bleeding for those taking this product.

Savaysa is made by Tokyo-based Daiichi Sankyo Co., Ltd.

FDA NEWS RELEASE

For Immediate Release: January 21st, 2015

FDA approves new psoriasis drug Cosentyx

The U.S. Food and Drug Administration approved Cosentyx (secukinumab) to treat adults with moderate-to-severe plaque psoriasis.

Psoriasis is a skin condition that causes patches of skin redness and irritation. Psoriasis is an autoimmune disorder, and occurs more commonly in patients with a family history of the disease, and most often begins in people between the ages of 15 and 35. The most common form of psoriasis is plaque psoriasis, in which patients develop thick, red skin with flaky, silver-white patches called scales.

Cosentyx's active ingredient is secukinumab. Secukinumab is an antibody that binds to a protein (interleukin (IL)-17A) which is involved in inflammation. By binding to IL-17A, secukinumab prevents it from binding to its receptor, and inhibits its ability to trigger the inflammatory response that plays a role in the development of plaque psoriasis.

Cosentyx is administered as an injection under the skin. It is intended for patients who are candidates for systemic therapy, phototherapy, or a combination of both.

Cosentyx's safety and effectiveness were established in four clinical trials with a total of 2,403 participants with plaque psoriasis who were candidates for phototherapy or systemic therapy. Participants were randomly assigned to receive Cosentyx or a placebo. The results showed that Cosentyx achieved greater clinical response than placebo, with skin that was clear or almost clear, as assessed by scoring of the extent, nature and severity of psoriatic changes of the skin.

Cosentyx is being approved with a Medication Guide to inform patients that, because Cosentyx is a medicine that affects the immune system, patients may have a greater risk of getting an infection. Serious allergic reactions have been reported with the use of Cosentyx. Caution should be exercised when considering the use of Cosentyx in patients with a chronic infection or history of recurrent infection, and in patients with active Crohn's Disease. The most common side effects include diarrhea and upper respiratory infections.

Cosentyx is marketed by East Hanover, New Jersey-based Novartis Pharmaceuticals Corporation.

FDA NEWS RELEASE

For Immediate Release: January 26th, 2015

FDA approves first generic esomeprazole

The U.S. Food and Drug Administration approved the first generic version of Nexium (esomeprazole magnesium delayed-release capsules) to treat gastroesophageal reflux disease (GERD) in adults and children ages 1 and older. Esomeprazole is a proton pump inhibitor that reduces the amount of acid in the stomach.

Ivax Pharmaceuticals, Inc., a subsidiary of Teva Pharmaceuticals USA, has gained approval to market esomeprazole in 20 and 40 milligram capsules.

Esomeprazole capsules are also approved to reduce the risk of gastric ulcers associated with use of nonsteroidal anti-inflammatory drugs (NSAIDs), treat the stomach infection Helicobacter pylori along with certain antibiotics, and to treat conditions where the stomach makes too much acid, including Zollinger-Ellison syndrome.

Gastroesophageal reflux (GER) happens when stomach contents come back up into the esophagus. Stomach acid that touches the lining of the esophagus can cause acid indigestion (also called acid reflux or heartburn). GERD is a more serious, chronic form of GER. GER that occurs more than twice a week for a few weeks could be GERD, which over time can lead to more serious health problems, such as esophagitis and respiratory problems.

Generic esomeprazole capsules will be dispensed with a patient Medication Guide that provides important information about the medication's use and risks. The most serious risks are stomach problems, including severe diarrhea, and a warning that people who take multiple daily doses of PPIs for a long period of time may have an increased risk of bone fractures.

The most common side effects reported by those taking Nexium in clinical trials include headache, diarrhea, nausea, flatulence, abdominal pain, sleepiness, constipation, and dry mouth.

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.

FDA NEWS RELEASE

For Immediate Release: January 23rd, 2015

FDA approves Natpara to control low blood calcium levels in patients with hypoparathyroidism

The U.S. Food and Drug Administration approved Natpara (parathyroid horomone) to control hypocalcemia in patients with hypoparathyroidism, a rare disease that affects approximately 60,000 people in the United States.

Hypoparathyroidism occurs when the body secretes abnormally low levels of parathyroid hormone, which helps regulate calcium and phosphorus levels in the body.

Hypoparathyroidism is caused by loss of function of the parathyroid glands and occurs most commonly as a result of surgical removal of the parathyroid glands and more rarely as a result of autoimmune or congenital diseases. Patients with hypoparathyroidism can experience numbness, tingling, muscle twitching, spasms or cramps, abnormal heart rhythm, and seizures as a consequence of low blood calcium levels.

Hypoparathyroidism is also associated with long-term complications such as kidney damage, kidney stones, development of cataracts and calcification of soft tissues.

Natpara, a hormonal injection administered once daily, helps to regulate the body's calcium levels. The FDA granted Natpara orphan drug designation because it is intended to treat a rare disease.

The safety and effectiveness of Natpara were evaluated in a clinical trial of 124 participants who were randomly assigned to receive Natpara or a placebo. The trial was designed to determine whether Natpara can be used as a substitute for, or be used to help reduce the amount of, active forms of vitamin D or oral calcium taken by participants.

Results showed 42 percent of Natpara-treated participants achieved normal blood calcium levels on reduced doses of calcium supplements and active forms of vitamin D, compared to three percent of placebo-treated participants.

Natpara carries a boxed warning that bone cancer (osteosarcoma) has been observed in rat studies with Natpara. It is unknown whether Natpara causes osteosarcoma in humans, but because of a potential risk of osteosarcoma, Natpara is only recommended for use in patients whose hypocalcemia cannot be controlled on calcium supplementation and active forms of vitamin D, and for whom the potential benefits are considered to outweigh this potential risk. Natpara is only available through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS).

The most common side effects observed in Natpara-treated participants were sensations of tingling, tickling, pricking, or burning of the skin (paraesthesia); low blood calcium; headache; high blood calcium; and nausea.

Natpara is manufactured by NPS Pharmaceuticals, Inc., based in Bedminster, New Jersey.

FDA NEWS RELEASE

For Immediate Release: January 30th, 2015

FDA expands uses of Vyvanse to treat binge-eating disorder

The U.S. Food and Drug Administration expanded the approved uses of Vyvanse (lisdexamfetamine dimesylate) to treat binge-eating disorder in adults. The drug is the first FDA-approved medication to treat this condition.

In binge-eating disorder, patients have recurrent episodes of compulsive overeating during which they consume larger amounts of food than normal and experience the sense that they lack control. Patients with this condition eat when they are not hungry and often eat to the point of being uncomfortably full. Patients may feel ashamed and embarrassed by how much they are eating, which can result in social isolation. Binge-eating disorder may lead to weight gain and to health problems related to obesity.

Vyvanse was reviewed under the FDA's priority review program, which provides for an expedited review of drugs that are intended to treat a serious disease or condition and may provide a significant improvement over available therapy.

The efficacy of Vyvanse in treating binge-eating disorder was shown in two clinical studies that included 724 adults with moderate-to-severe binge-eating disorder. In the studies, participants taking Vyvanse experienced a decrease in the number of binge eating days per week and had fewer obsessive-compulsive binge eating behaviors compared to those on placebo.
Vyvanse is dispensed with a Medication Guide for patients, which provides important information about the medication's use and risks. The most serious risks include psychiatric problems and heart complications, including sudden death in people who have heart problems or heart defects, and stroke and heart attack in adults. Central nervous system stimulants, like Vyvanse, may cause psychotic or manic symptoms, such as hallucinations, delusional thinking, or mania, even in individuals without a prior history of psychotic illness. The most common side effects reported by people taking Vyvanse in the clinical trials included dry mouth, insomnia, increased heart rate, jittery feelings, constipation, and anxiety.
Vyvanse is not approved for, or recommended for, weight loss. Its efficacy for weight loss has not been studied.
Vyvanse was approved in 2007 as a once-daily medication to treat attention deficit hyperactivity disorder in patients ages 6 and older. Vyvanse is a Schedule II controlled substance because it has high potential for abuse, with use potentially leading to dependence.
Vyvanse is marketed by Shire U.S., Inc., based in Wayne, Pennsylvania.

Safety Announcements

FDA Drug Safety Communication: FDA has reviewed possible risks of pain medicine use during pregnancy

[January 9th, 2015] The U.S. Food and Drug Administration (FDA) is aware of and understands the concerns arising from recent reports questioning the safety of prescription and over-the-counter (OTC) pain medicines when used during pregnancy. As a result, we evaluated research studies published in the medical literature and determined they are too limited to make any recommendations based on these studies at this time. Because of this uncertainty, the use of pain medicines during pregnancy should be carefully considered. We urge pregnant women to always discuss all medicines with their health care professionals before using them.
Severe and persistent pain that is not effectively treated during pregnancy can result in depression, anxiety, and high blood pressure in the mother. Medicines including nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, and acetaminophen can help treat severe and persistent pain. However, it is important to carefully weigh the benefits and risks of using prescription and OTC pain medicines during pregnancy.
The published studies we reviewed reported on the potential risks associated with the following three types of pain medicines used during pregnancy:

- Prescription NSAIDs and the risk of miscarriage in the first half of pregnancy.
- Opioids and the risk of birth defects of the brain, spine, or spinal cord in babies born to women who took these products during the first trimester of pregnancy.
- Acetaminophen in both OTC and prescription products and the risk of attention deficit hyperactivity disorder (ADHD) in children born to women who took this medicine at any time during pregnancy.

We found all of the studies we reviewed to have potential limitations in their designs; sometimes the accumulated studies on a topic contained conflicting results that prevented us from drawing reliable conclusions. As a result, our recommendations on how pain medicines are used during pregnancy will remain the same at this time.
Pregnant women should always consult with their health care professional before taking any prescription or OTC medicine. Women taking pain medicines who are considering becoming pregnant should also consult with their health care professionals to discuss the risks and benefits of pain medicine use. Health care professionals should continue to follow the recommendations in the drug labels when prescribing pain medicines to pregnant patients.
We will continue to monitor and evaluate the use of pain medicines during pregnancy and will update the public as new safety information becomes available.

Safety Announcements

FDA's investigation into patients being injected with simulated IV fluids continues

[Updated January30th, 2015] FDA and the Centers for Disease Control and Prevention (CDC) continue to investigate multiple instances of simulated saline solution being administered to patients and to alert health care providers and regulatory officials throughout the country to raise awareness of the potential risk. FDA first became of aware of adverse events at two clinics associated with the mistaken administration of Wallcur's simulated Practi-0.9% sodium chloride IV in late December and issued a warning to all health care providers not to inject these simulated products in humans or animals on December 30, 2014. FDA's warning was disseminated through MedWatch and other communications channels, reaching more than 400,000 subscribers and followers.

Since then FDA and CDC took a number of steps to remove the simulated saline products from medical settings, raise awareness among health care providers, and provide information to state and local health officials in order to prevent exposure to additional patients.

Specifically, FDA worked with Wallcur to implement a voluntary nationwide recall of its Practi-0.9% sodium chloride solution, and issued an updated warning to the public on January 14, 2015, which included additional targeted outreach to professional associations and health care organizations. On January 16, 2015, FDA and CDC organized stakeholder and 50-State teleconference calls which included all of the State Departments of Health, several local/county Health Departments, Health Canada, health care professionals, hospitals, professional associations and others. Participants were updated on the recall and asked that they remain vigilant for the possibility that simulated saline products remain in the pharmaceutical supply chain.

FDA has also reached out to other companies that market simulated products for training purposes to make them aware of this incident. In its review of other simulated products, FDA has already worked collaboratively with one other training company that took immediate steps to remedy a potentially confusing situation between its training products and the real drugs.

To date, we are aware of more than 40 patients who have received infusions of the simulated saline products. Some of the patients experienced adverse events associated with these products including fever, chills, tremors and headache.

Current Drug Shortages Index (as of January 29th, 2015):

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

Acetohydroxamic Acid (Lithostat) Tablets	***Currently in Shortage***
Ammonium Chloride Injection	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Azathioprine Tablet	***Currently in Shortage***
Barium Sulfate for Suspension	***Currently in Shortage***
Bupivacaine Hydrochloride (Marcaine, Sensorcaine) Injection	***Currently in Shortage***
Caffeine Anhydrous (125mg/mL); Sodium Benzoate (125mg/mL) Injection	***Currently in Shortage***
Calcium Gluconate Injection	***Currently in Shortage***
Cefazolin Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***
Chloramphenicol Sodium Succinate Injection	***Currently in Shortage***
Clindamycin Phosphate (Cleocin) Injection	***Currently in Shortage***
Clonidine HCL Injection (Duraclon)	***Currently in Shortage***
Dexamethasone Sodium Phosphate Injection	***Currently in Shortage***
Dexmethylphenidate Hydrochloride (Focalin) Tablet	***Currently in Shortage***
Dextrose 5% Injection Bags	***Currently in Shortage***
Dextrose Injection USP, 70%	***Currently in Shortage***
Dimercaprol (Bal-in-Oil) Injection	***Currently in Shortage***
Disopyramide Phosphate (Norpace) Capsules	***Currently in Shortage***
Doxorubicin (Adriamycin) Lyophilized Powder	***Currently in Shortage***
Ephedrine Sulfate Injection	***Currently in Shortage***
Epinephrine 1mg/mL (Preservative Free)	***Currently in Shortage***
Epinephrine Injection	***Currently in Shortage***

Fentanyl Citrate (Sublimaze) Injection	***Currently in Shortage***
Fluorescein Sodium Injection	***Currently in Shortage***
Fluoxymesterone (Androxy) Tablets, USP	***Currently in Shortage***
Haloperidol Lactate Injection	***Currently in Shortage***
Indigo Carmine Injection	***Currently in Shortage***
Irrigation Solutions	***Currently in Shortage***
L-Cysteine Hydrochloride Injection	***Currently in Shortage***
Leucovorin Calcium Lyophilized Powder for Injection	***Currently in Shortage***
Leuprolide Acetate Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection	***Currently in Shortage***
Liotrix (Thyrolar) Tablets	***Currently in Shortage***
Magnesium Sulfate Injection	***Currently in Shortage***
Mecasermin [rDNA origin] (Increlex) Injection	***Currently in Shortage***
Memantine Hydrochloride (Namenda) XR Capsules	***Currently in Shortage***
Methyldopate Hydrochloride Injection	***Currently in Shortage***
Methylene Blue Injection	***Currently in Shortage***
Methylin Chewable Tablets	***Currently in Shortage***
Methylphenidate Hydrochloride ER Capsules/Tablets	***Currently in Shortage***
Morphine Sulfate (Astramorph PF, Duramorph, Infumorph) Injection (Preservative Free)	***Currently in Shortage***
Multi-Vitamin Infusion (Adult and Pediatric)	***Currently in Shortage***
Nalbuphine Hydrochloride (Nubain) Injection	***Currently in Shortage***
Nebivolol (BYSTOLIC) Tablets	***Currently in Shortage***
Nitroglycerin (Nitronal) Injection	***Currently in Shortage***
Nitroglycerin in 5% Dextrose Injection	***Currently in Shortage***
Pancuronium Bromide Injection	***Currently in Shortage***
Papaverine Hydrochloride Injection	***Currently in Shortage***
Peritoneal Dialysis Solutions	***Currently in Shortage***
Phentolamine Mesylate Injection	***Currently in Shortage***
Phenylephrine Hydrochloride Ophthalmic Solution	***Currently in Shortage***
Phosphate (Glycophos) Injection	***Currently in Shortage***
Piperacillin and Tazobactam (Zosyn) Injection	***Currently in Shortage***
Potassium Chloride Injection	***Currently in Shortage***
Quazepam (Doral) Tablets	***Currently in Shortage***
Radium RA-223 Dichloride (Xofigo) Injection	***Currently in Shortage***
Reserpine Tablets	***Currently in Shortage***
Secretin Synthetic Human (ChiRhoStim) Injection	***Currently in Shortage***
Selenium Injection	***Currently in Shortage***
Sincalide (Kinevac) Lyophilized Powder for Injection	***Currently in Shortage***
Sodium Chloride 0.9% Injection Bags	***Currently in Shortage***
Sodium Chloride 23.4% Injection	***Currently in Shortage***
Sodium Phosphate Injection	***Currently in Shortage***
Sterile Water for Injection Solutions	***Currently in Shortage***
Sufentanil Citrate (Sufenta) Injection	***Currently in Shortage***
Sulfamethoxazole and Trimethoprim (Bactrim) Oral Suspension	***Currently in Shortage***
Technetium tc99m Exametazime Injection (Ceretec Kit)	***Currently in Shortage***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***
Thiotepa (Thioplex) for Injection	***Currently in Shortage***
Tiopronin (Thiola)	***Currently in Shortage***
Tobramycin Injection	***Currently in Shortage***
Trace Elements	***Currently in Shortage***
Triamcinolone Hexacetonide Injectable Suspension (Aristospan)	***Currently in Shortage***
Trimipramine Maleate (SURMONTIL) Capsules	***Currently in Shortage***

Trypan Blue (Membraneblue)	***Currently in Shortage***
Vancomycin Hydrochloride for Injection, USP	***Currently in Shortage***