Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
January 14, 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 – January 14, 2015

DATE: January 6, 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 January 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/Chronic Medication Adherence Program Update – See Appendix B

Action Item – Vote to Prior Authorize Duavee® (Conjugated Estrogens/Bazedoxifene) – See Appendix C

Action Item – Vote to Prior Authorize Natesto™ (Testosterone Nasal Gel), Aveed® (Testosterone Undecanoate Injection), and Vogelxo™ (Testosterone Topical Gel) – See Appendix D

Action Item – Vote to Prior Authorize Ofev® (Nintedanib) and Esbriet® (Pirfenidone) – See Appendix E

Action Item – Vote to Prior Authorize Anoro™ Ellipta® (Umeclidinium/Vilanterol), Incruse™ Ellipta® (Umeclidinium), Spiriva® Respimat® (Tiotropium), and Striverdi® Respimat® (Olodaterol) – See Appendix F

30-Day Notice to Prior Authorize Northera™ (Droxidopa) – See Appendix G

Annual Review of Antiemetic Medications and 30-Day Notice to Prior Authorize Akynzeo® (Netupitant/Palonosetron) – See Appendix H

30-Day Notice to Prior Authorize Viekira Pak™ (Ombitasvir/Paritaprevir/Ritonavir/Dasabuvir) – See Appendix I

Annual Review of Makena® (17-Hydroxyprogesterone Caproate) – See Appendix J

Annual Review of Gattex® (Teduglutide) – See Appendix K

FDA and DEA Updates – See Appendix L

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board

(DUR Board)

Meeting – January 14, 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. December 10, 2014 DUR Minutes – Vote
   B. December 10, 2014 DUR Recommendations Memorandum

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

4. **Update on Medication Coverage Authorization Unit/ Chronic Medication Adherence Program Update – See Appendix B**
   A. Medication Coverage Activity for December 2014
   B. Pharmacy Help Desk Activity for December 2014
   C. Chronic Medication Adherence Program Update

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

5. **Action Item – Vote to Prior Authorize Duavee® (Conjugated Estrogens/Bazedoxifene) – See Appendix C**
   A. College of Pharmacy Recommendations

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

6. **Action Item – Vote to Prior Authorize Natesto™ (Testosterone Nasal Gel), Aveed® (Testosterone Undecanoate Injection), and Vogelxo™ (Testosterone Topical Gel) – See Appendix D**
   A. College of Pharmacy Recommendations

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

7. **Action Item – Vote to Prior Authorize Ofev® (Nintedanib) and Esbriet® (Pirfenidone) – See Appendix E**
   A. College of Pharmacy Recommendations

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

8. **Action Item – Vote to Prior Authorize Anoro™ Ellipta® (Umeclidinium/Vilanterol), Incruse™ Ellipta® (Umeclidinium), Spiriva® Respimat® (Tiotropium), and Striverdi® Respimat® (Olodaterol) – See Appendix F**
   A. College of Pharmacy Recommendations

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

9. **30-Day Notice to Prior Authorize Northera™ (Droxidopa) – See Appendix G**
   A. Introduction
   B. Northera™ (Droxidopa) Product Summary
   C. College of Pharmacy Recommendations

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

10. **Annual Review of Antiemetic Medications and 30-Day Notice to Prior Authorize Akynzeo® (Netupitant/Palonosetron) – See Appendix H**
    A. Current Prior Authorization Criteria
    B. Utilization of Antiemetic Medications
    C. Prior Authorization of Antiemetic Medications
    D. Market News and Updates
    E. Akynzeo® (Netupitant/Palonosetron) Product Summary
    F. College of Pharmacy Recommendations
    G. Utilization Details of Antiemetic Medications: Fiscal Year 2014

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

11. **30-Day Notice to Prior Authorize Viekira Pak™ (Ombitasvir/Paritaprevir/Ritonavir/Dasabuvir) – See Appendix I**
    A. Introduction
    B. Market News and Updates
    C. Viekira Pak™ (Ombitasvir/Paritaprevir/Ritonavir/Dasabuvir) Product Summary
    D. Regimen Cost Comparison
    E. College of Pharmacy Recommendations

Non-presentation, Questions Only:

12. **Annual Review of Makena® (17-Hydroxyprogesterone Caproate) – See Appendix J**
    A. Indication
    B. Current Prior Authorization Criteria
    C. Utilization of Makena® (17-Hydroxyprogesterone Caproate)
    D. Prior Authorization of Makena® (17-Hydroxyprogesterone Caproate)
    E. Market News and Updates
    F. College of Pharmacy Recommendations

Non-presentation, Questions Only:

13. **Annual Review of Gattex® (Teduglutide) – See Appendix K**
    A. Indication
    B. Current Prior Authorization Criteria
    C. Utilization of Gattex® (Teduglutide)
    D. Prior Authorization of Gattex® (Teduglutide)
    E. Market News and Updates
    F. College of Pharmacy Recommendations

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

14. FDA and DEA Updates – See Appendix L

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

15. Future Business

A. Annual Reviews
B. New Product Reviews

Items to be presented by Dr. Muchmore, Chairman:

16. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF DECEMBER 10, 2014

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): No Students for December		

	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 General Counsel IV	x	
Kerri Wade, Pharmacy Operations Manager	x	

OTHERS PRESENT:		
Clint Degner, Novartis	Michele Puyear, Gilead	John Brunson, Impax
Greg Kitchens, Artia Solutions	Hayley Endicott, Gilead	Roger Grotzinger, BMS
Melvin Nwamadi, Abbott	Audrey Rattan, Otsuka	Ron Caine, Pfizer
Bob Gustafson, Lundbeck	Crystal Henderson, Otsuka	Toby Thompson, Pfizer
Jim Dunlap, Phrma	Charlene Kaiser, Amgen	Brian Maves, Pfizer
Jim Chapman, Abbvie	Jason Schwier, Amgen	Jim Fowler, Astra Zeneca
Brent Hildebrand, Gilead	Caroline Howard, Jazz	Tod Hudson, Astra Zeneca

PRESENT FOR PUBLIC COMMENT:	
Michele Puyear	Gilead

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: MICHELE PUYEAR AGENDA NO. 5

ACTION: NONE REQUIRED

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

3A: NOVEMBER 12, 2014 DUR MINUTES – VOTE

3B: NOVEMBER 12, 2014 DUR RECOMMENDATIONS MEMORANDUM

Materials included in agenda packet; presented by Dr. Muchmore

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: **UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/SOONERPSYCH PROGRAM UPDATE/DRUG REBATE PROGRAM REVIEW**

4A: MEDICATION COVERAGE ACTIVITY FOR NOVEMBER 2014

4B: PHARMACY HELP DESK ACTIVITY FOR NOVEMBER 2014

4C: UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT

4D: SOONERPSYCH PROGRAM UPDATE

4E: DRUG REBATE PROGRAM REVIEW; PRESENTED BY DR. NANCY NESSER

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NO ACTION REQUIRED

AGENDA ITEM NO. 5: **VOTE TO PRIOR AUTHORIZE HARVONI® (LEDIPASVIR/SOFOSBUVIR)**

5A: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Holderread

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE ZUBSOLV® (BUPRENORPHINE/NALOXONE TABLETS) AND BUNAVAIL™ (BUPRENORPHINE/NALOXONE BUCCAL FILMS)**

6A: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nawaz

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: **ANNUAL REVIEW OF MAINTENANCE ASTHMA AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ANORO™ ELLIPTA® (UMECLIDINIUM/VILANTEROL), INCRUSE™ ELLIPTA® (UMECLIDINIUM), SPIRIVA® RESPIMAT® (TIOTROPIUM), AND STRIVERDI® RESPIMAT® (OLODATEROL)**

7A: CURRENT PRIOR AUTHORIZATION CRITERIA

7B: UTILIZATION OF MAINTENANCE ASTHMA AND COPD MEDICATIONS

7C: PRIOR AUTHORIZATION OF MAINTENANCE ASTHMA AND COPD MEDICATIONS

7D: MARKET NEWS AND UPDATES

7E: DRUG PRODUCT SUMMARIES

7F: COLLEGE OF PHARMACY RECOMMENDATIONS

7G: UTILIZATION DETAILS OF MAINTENANCE ASTHMA AND COPD MEDICATIONS

Materials included in agenda packet; presented by Dr. Nawaz

ACTION: NONE REQUIRED

AGENDA ITEM NO. 8: **30-DAY NOTICE TO PRIOR AUTHORIZE OFEV® (NINTEDANIB) AND ESBRIET® (PIRFENIDONE)**

8A: INTRODUCTION

8B: DRUG PRODUCT SUMMARIES

8C: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Adams

Dr. Winegardener recommends that authorization be limited to Pulmonologist prescribers. Dr. Muchmore recommends that diagnosis be established by a Pulmonologist.

ACTION: NONE REQUIRED

AGENDA ITEM NO. 9: **ANNUAL REVIEW OF TESTOSTERONE PRODUCTS AND 30-DAY NOTICE TO PRIOR AUTHORIZE NATESTO™ (TESTOSTERONE NASAL GEL), AVEED® (TESTOSTERONE UNDECANOATE INJECTION), AND VOGELXO™ (TESTOSTERONE TOPICAL GEL)**

9A: CURRENT PRIOR AUTHORIZATION CRITERIA

9B: UTILIZATION OF TESTOSTERONE PRODUCTS

9C: PRIOR AUTHORIZATION OF TESTOSTERONE PRODUCTS

9D: MARKET NEWS AND UPDATES

9E: DRUG PRODUCT SUMMARIES

9F: COLLEGE OF PHARMACY RECOMMENDATIONS

9G: UTILIZATION DETAILS OF TESTOSTERONE PRODUCTS

Materials included in agenda packet; presented by Dr. Anderson

Dr. Muchmore recommends adding legacy treatment of established pituitary gonadal disease.

ACTION: NONE REQUIRED

AGENDA ITEM NO. 10: **ANNUAL REVIEW OF OSTEOPOROSIS MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE DUAVEE® (CONJUGATED ESTROGENS/BAZEDOXIFENE)**

10A: CURRENT PRIOR AUTHORIZATION CRITERIA
10B: UTILIZATION OF OSTEOPOROSIS MEDICATIONS
10C: PRIOR AUTHORIZATION OF OSTEOPOROSIS MEDICATIONS
10D: MARKET NEWS AND UPDATES
10E: DUAVEE® (CONJUGATED ESTROGENS/BAZEDOXIFENE) PRODUCT SUMMARY
10F: COLLEGE OF PHARMACY RECOMMENDATIONS
10G: UTILIZATION DETAILS OF OSTEOPOROSIS MEDICATIONS

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

AGENDA ITEM NO. 11: **FDA AND DEA UPDATES**
Materials included in agenda packet; presented by Dr. Cothran
ACTION: NONE REQUIRED

AGENDA ITEM NO. 12: **FUTURE BUSINESS**
12A: ANNUAL REVIEWS
12B: NEW PRODUCT REVIEWS
Materials included in agenda packet; submitted by Dr. Cothran
ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: **ADJOURNMENT**
The meeting was adjourned at 5:18 pm

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

Memorandum

Date: December 11, 2014

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 December 10, 2014

Recommendation 1: Vote to Prior Authorize Harvoni® (Ledipasvir/Sofosbuvir)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Harvoni® (ledipasvir/sofosbuvir) with the following criteria:

Harvoni® (Ledipasvir/Sofosbuvir) 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. Harvoni® must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated for hepatitis C treatment by a gastroenterologist, infectious disease specialist, or transplant specialist within the last three months; and
4. Hepatitis C Virus (HCV) genotype 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, baseline viral load, and cirrhosis will apply:
   a. **Treatment-naïve without cirrhosis who have a pre-treatment HCV-RNA less than 6 million IU/mL:**

i. Harvoni® (ledipasvir/sofosbuvir) 90mg/400mg once daily for 8 weeks

b. Treatment-naïve with or without cirrhosis:

i. Treatment-naïve patients who are cirrhotic or have a pre-treatment HCV-RNA greater than 6 million IU/mL
ii. Harvoni® (ledipasvir/sofosbuvir) 90mg/400mg once daily for 12 weeks

c. Treatment-experienced without cirrhosis

i. Treatment-experienced patients who have failed previous treatment with either peginterferon alfa, ribavirin, or an HCV protease inhibitor
ii. Harvoni® (ledipasvir/sofosbuvir) 90mg/400mg once daily for 12 weeks

d. Treatment-experienced with cirrhosis

i. Treatment-experienced patients who have failed previous treatment with either peginterferon alfa, ribavirin, or an HCV protease inhibitor
ii. Harvoni® (ledipasvir/sofosbuvir) 90mg/400mg once daily for 24 weeks

e. New regimens will apply as approved by the FDA

7. Member must sign and submit the Hepatitis C Intent to Treat contract; and
8. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
9. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Viral Response (SVR-12); and
10. 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
11. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
12. Member must not have decompensated cirrhosis; and
13. Member must not have severe renal impairment (estimated Glomerular Filtration Rate [eGFR] <30mL/min/1.73m^2); and
14. Female members must not be pregnant and must have a pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use two forms of non-hormonal birth control while on therapy; and
15. Member must not be taking the following medications: rifampin, rifabutin, rifapentine, carbamazepine, eslicarbazepine, phenytoin, phenobarbital, oxcarbazepine, tipranavir/ritonavir, simeprevir, rosuvastatin, St. John's wort, or elvitegravir/cobicistat/emtricitabine in combination with tenofovir disoproxil fumarate; and
16. 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.
17. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
18. 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.

19. 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, due to superior SVR rates and shortened treatment durations with Harvoni®, authorization of Sovaldi™ or Olysio™ for genotype-1 will require a patient-specific, clinically significant reason why Harvoni® is not an option.

Recommendation 2: Vote to Prior Authorize Zubsolv® (Buprenorphine/ Naloxone Tablets) and Bunavail™ (Buprenorphine/Naloxone Buccal Films)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Zubsolv® and Bunavail™ with the following criteria:

Zubsolv® (Buprenorphine/Naloxone Sublingual Tablets) and
Bunavail™ (Buprenorphine/Naloxone Buccal Films) Approval Criteria:

1. Oral buprenorphine products must be prescribed by a licensed physician who qualifies for a waiver under the Drug Addiction Treatment Act (DATA) and has notified the Center for Substance Abuse Treatment of the intention to treat addiction patients and has been assigned a DEA (X) number; and
2. Member must have an FDA approved diagnosis of opiate abuse/dependence; and
3. Concomitant treatment with opioids (including tramadol) will be denied; and
4. Approvals will be for the duration of 90 days to allow for concurrent medication monitoring; and
5. The following limitations will apply:
    a. **Zubsolv®** sublingual tablets: A quantity limit of 90 tablets per 30 days.
    b. **Bunavail™** 2.1mg/0.3mg and 4.2mg/0.7mg buccal films: A quantity limit of 90 films per 30 days.
    c. **Bunavail™** 6.3mg/1mg buccal films: A quantity limit of 60 films per 30 days.

Additionally, the College of Pharmacy recommends the addition of detailed criteria for high-dose oral buprenorphine regimens:

High Dose Buprenorphine Products Criteria:

1. Each request for greater than 24mg bioequivalent buprenorphine per day should be evaluated on a case-by-case basis.
2. A taper schedule should be documented on the petition or dates of an attempted taper with reason for failure should be documented or a patient-specific, clinically significant reason a taper schedule or attempt is not appropriate for the member; and
3. Opioid urine drug screens should be submitted with high-dose requests that plan to continue high-dose treatment longer than the duration of one month.
    a. Urine drug screens must show the absence of opioid medications other than buprenorphine products for continued approval; or

b. Prescriber must document a patient-specific reason the member should continue therapy, reason for opioid use, and document a plan for member to discontinue opioid use; and

4. Symptoms associated with withdrawal at lower doses or symptoms requiring high doses should be listed on petition; and
5. Each approval will be for the duration of one month. If urine drug screen and other documentation are submitted indicating high-dose therapy is necessary an approval can be granted for the duration of three months.
6. Continued high-dose authorization after the three month approval will require a new (recent) urine drug screen.

Recommendation 3: Annual Review of Maintenance Asthma and Chronic Obstructive Pulmonary Disease Medications and 30-Day Notice to Prior Authorize Anoro™ Ellipta® (Umeclidinium/Vilanterol), Incruse™ Ellipta® (Umeclidinium), Spiriva® Respimat® (Tiotropium), and Striverdi® Respimat® (Olodaterol)

NO ACTION REQUIRED.

Recommendation 4: 30-Day Notice to Prior Authorize Ofev® (Nintedanib) and Esbriet® (Pirfenidone)

NO ACTION REQUIRED.

Recommendation 5: Annual Review of Testosterone Products and 30-Day Notice to Prior Authorize Natesto™ (Testosterone Nasal Gel), Aveed® (Testosterone Undecanoate Injection), and Vogelxo™ (Testosterone Topical Gel)

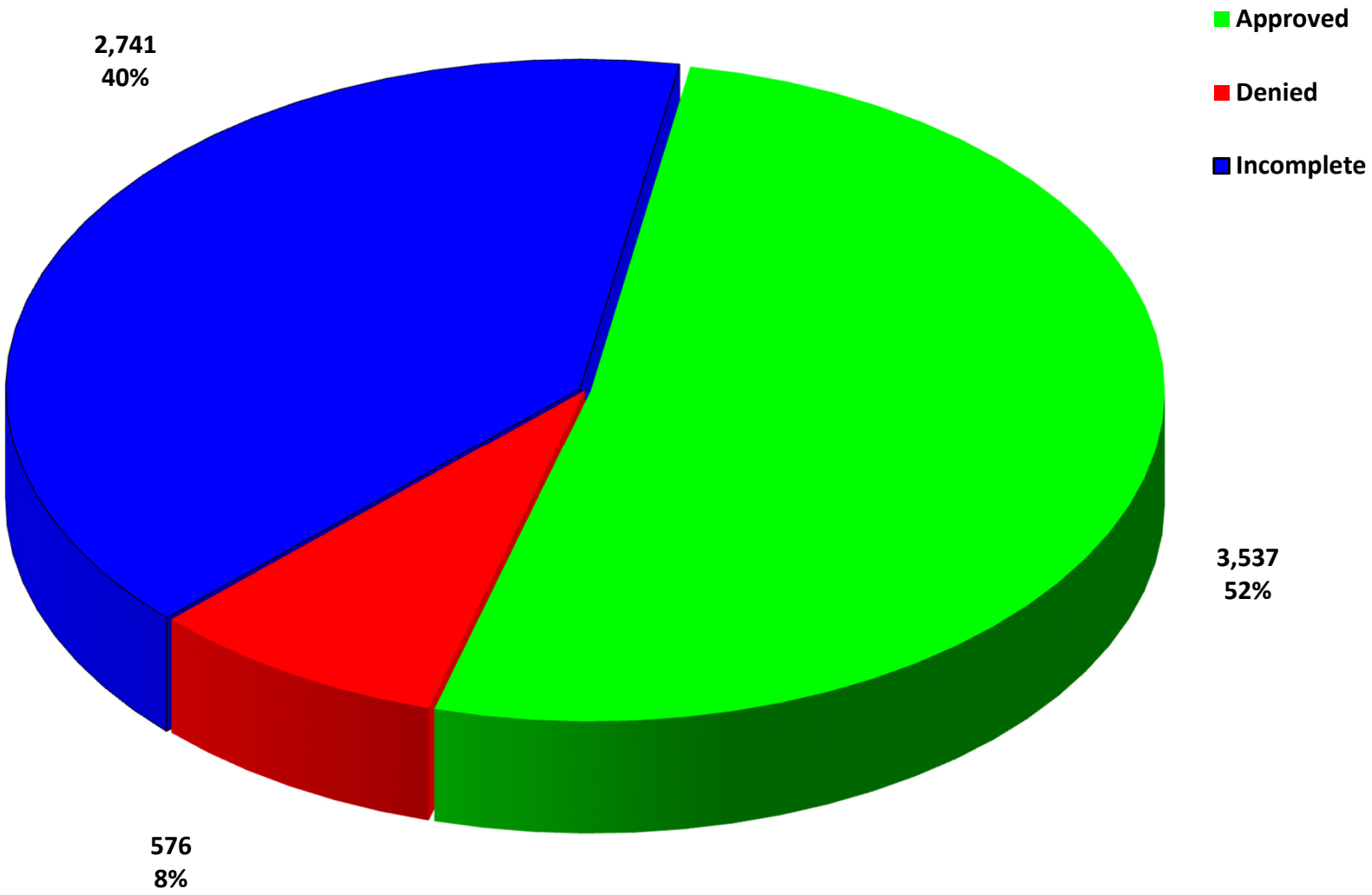
NO ACTION REQUIRED.

Recommendation 6: Annual Review of Osteoporosis Medications and 30-Day Notice to Prior Authorize Duavee® (Conjugated Estrogens/Bazedoxifene)

NO ACTION REQUIRED.

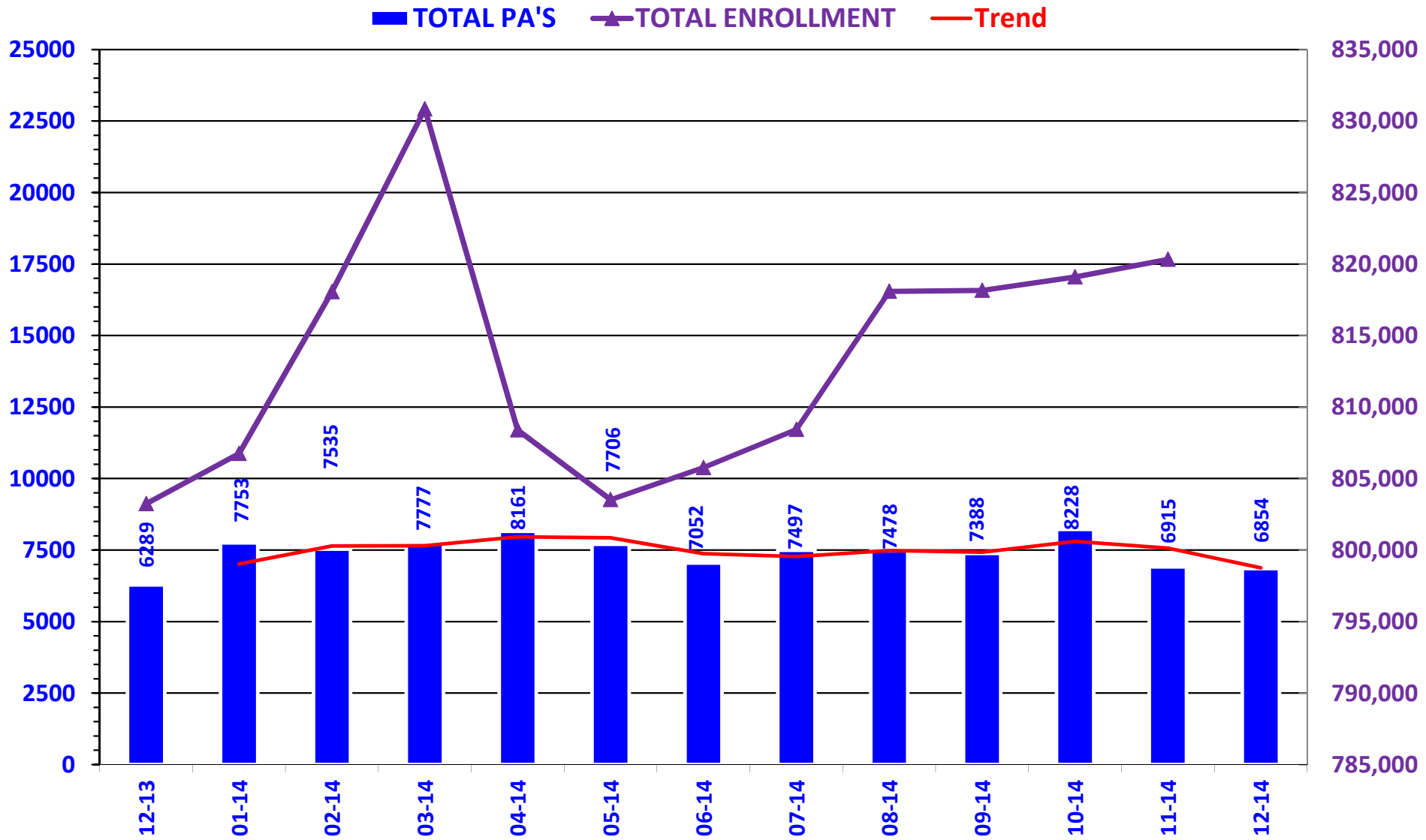
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: DECEMBER



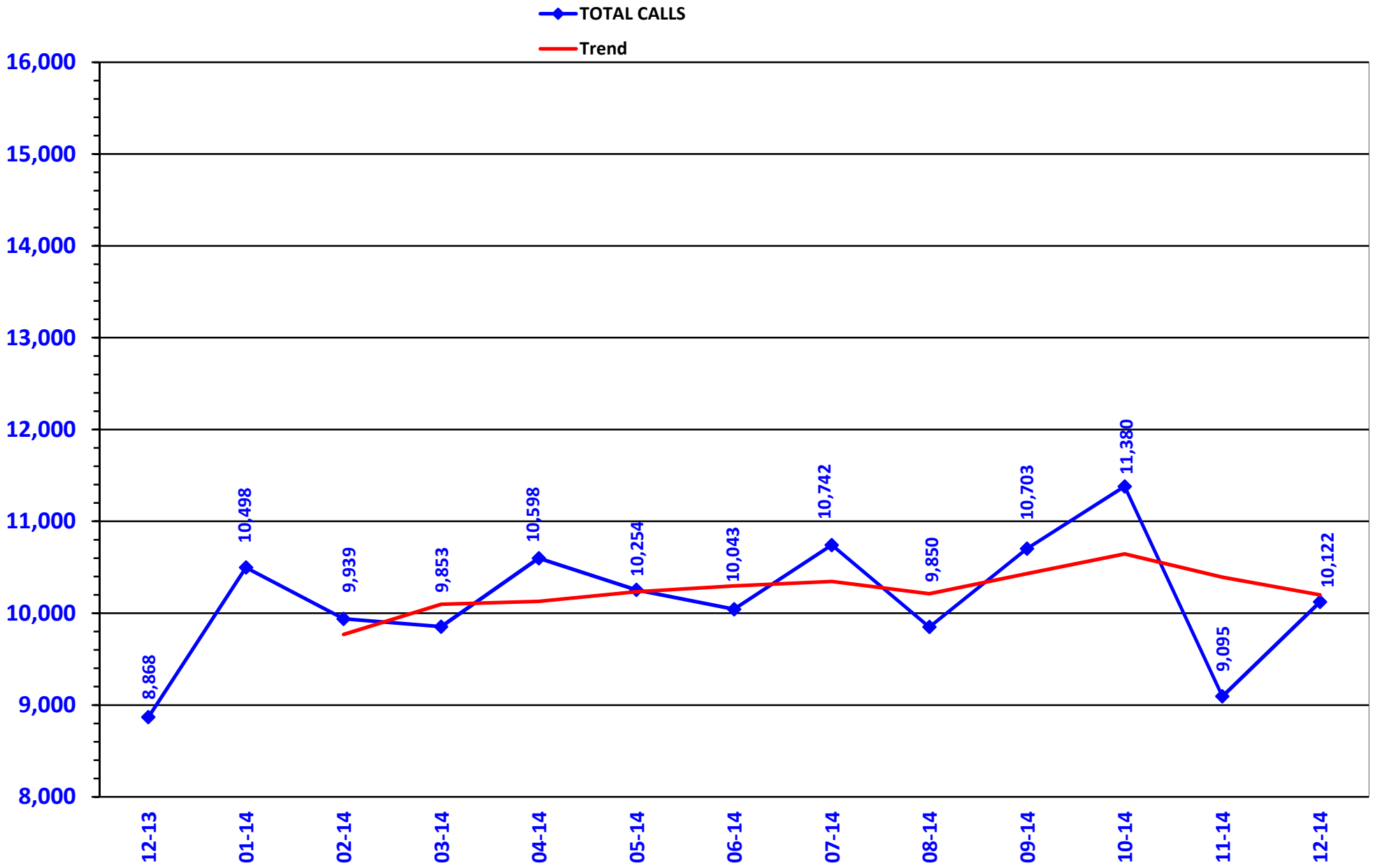
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: DECEMBER 2013 – DECEMBER 2014



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
DECEMBER 2013 – DECEMBER 2014



Prior Authorization Activity
12/1/2014 Through 12/31/2014

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	314	153	7	154	353
Analgesic - NonNarcotic	11	1	0	10	4
Analgesic, Narcotic	375	185	42	148	153
Angiotensin Receptor Antagonist	23	2	4	17	360
Antiasthma	147	69	9	69	335
Antibiotic	24	8	1	15	188
Anticonvulsant	80	32	7	41	328
Antidepressant	101	31	11	59	293
Antidiabetic	120	48	10	62	358
Antifungal	10	3	0	7	23
Antigout	11	6	0	5	358
Antihistamine	161	137	2	22	351
Antimigraine	57	15	6	36	193
Antiulcers	186	46	41	99	186
Anxiolytic	64	36	4	24	242
Atypical Antipsychotics	368	232	10	126	340
Biologics	73	45	3	25	306
Bladder Control	92	59	5	28	354
Blood Thinners	87	64	3	20	279
Botox	17	9	1	7	321
Cardiovascular	37	19	5	13	300
Chronic Obstructive Pulmonary Disease	21	7	0	14	308
Dermatological	87	8	45	34	78
Endocrine & Metabolic Drugs	63	39	3	21	130
Erythropoietin Stimulating Agents	27	18	3	6	106
Fibromyalgia	104	27	24	53	340
Fish Oils	25	7	6	12	360
Gastrointestinal Agents	57	11	18	28	127
Glaucoma	13	2	1	10	360
Growth Hormones	47	37	2	8	154
Hepatitis C	92	50	9	33	8
HFA Rescue Inhalers	51	25	5	21	337
Insomnia	52	16	3	33	155
Linzess, Amitiza, and Relistor	73	9	7	57	298
Multiple Sclerosis	69	45	3	21	191
Muscle Relaxant	81	21	28	32	38
Nasal Allergy	77	9	25	43	210
Neurological Agents	80	59	6	15	342
NSAIDS	155	24	11	120	253
Ocular Allergy	20	9	0	11	228
Ophthalmic Anti-infectives	27	8	3	16	52
Osteoporosis	13	6	1	6	359
Other*	159	34	27	98	172
Otic Antibiotic	17	4	0	13	10
Pediculicide	83	36	12	35	18
Prenatal Vitamins	11	0	1	10	0
Statins	40	13	1	26	333
Stimulant	975	442	44	489	331
Suboxone/Subutex	184	143	7	34	75
Synagis	208	119	16	73	98
Testosterone	46	19	3	24	336
Topical Antifungal	38	1	1	36	10
Topical Corticosteroids	65	0	17	48	0
Vitamin	38	18	17	3	308

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Pharmacotherapy	71	62	0	9	204
Emergency PAs	0	0	0	0	
Total	**5,527**	**2,528**	**520**	**2,479**	
Overrides					
Brand	27	21	4	2	266
Cumulative Early Refill	3	3	0	0	121
Dosage Change	394	353	5	36	5
High Dose	8	6	0	2	155
Ingredient Duplication	49	46	1	2	4
Lost/Broken Rx	79	66	2	11	4
NDC vs Age	33	31	0	2	227
Nursing Home Issue	43	41	0	2	5
Opioid Quantity	5	3	2	0	177
Other*	37	30	1	6	5
Quantity vs. Days Supply	610	387	35	188	257
STBS/STBSM	12	9	1	2	81
Stolen	7	4	2	1	8
Temporary Unlock	4	3	0	1	12
Third Brand Request	24	12	5	7	6
Overrides Total	**1,327**	**1,009**	**56**	**262**	
Total Regular PAs + Overrides	**6,854**	**3,537**	**576**	**2,741**	

Denial Reasons	
Unable to verify required trials.	2,282
Does not meet established criteria.	578
Lack required information to process request.	440

Other PA Activity	
Duplicate Requests	436
Letters	3,297
No Process	125
Changes to existing PAs	507
Helpdesk Initiated Prior Authorizations	882
PAs Missing Information	29

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

Chronic Medication Adherence Program Update

Oklahoma Health Care Authority
January 2015

Prescriber Mailing: Maintenance Diabetes Medications

The College of Pharmacy and the Oklahoma Health Care Authority have started an educational quarterly mailing to prescribers with members on chronic maintenance medications for diabetes, blood pressure, or cholesterol. The purpose of these mailings is to encourage medication adherence and improve the quality of care for SoonerCare members on these medications.

Each mailing includes a prescriber summary report with a "star rating" based on their overall percentage of patients considered adherent to chronic maintenance medications. Adherence is estimated by measuring the Proportion of Days Covered (PDC), or percent of days in the past year covered by prescription claims. A patient is considered adherent if their PDC is greater than or equal to 80%. A patient is considered non-adherent if their PDC is less than 80%. Patients must have at least two pharmacy claims for at least one medication in the drug category in the past year to be included in the calculations.

The first mailing was processed in November and addressed adherence to maintenance diabetes medications. Prescribers with three or more patients were eligible for inclusion in the mailing if their percentage of patients considered adherent was less than 60% (0 stars) or ≥82% (5 stars). The review period was for one year and patients were assigned to prescribers based on their designated medical home provider as of October 2014.

A total of 1,518 prescribers were evaluated based on the computed adherence claims. These prescribers had 2,710 flagged patients considered non-adherent based on PDC calculations. A total of 457 prescribers were included in the mailing which accounted for 2,894 patients evaluated for adherence.

Summary of Mailing

Letters/Prescribers	Count
Total Letters Mailed	457
Members	**Count**
Total Members Included	2,894

Example Star Rating[1]

Report date: <Date>
Prescriber: <Prescriber Name>
NPI: <Prescriber NPI>
SoonerCare Provider ID: <Provider ID>
Assigned medical home patients on a diabetic medication: <11>
Percentage of patients adherent to metformin-containing medications: <30%>
Percentage of patients adherent to all other diabetic medications: <33%>

Overall percentage of patients adherent to all diabetic medications: <45%>

0 out of 5 stars

Adherence is shown in the Prescriber Summary Report as a percentage for metformin-containing medications, a percentage for all other diabetic medications (excluding insulin and Symlin®), and a final percentage and star rating for all diabetic medications (metformin- and non-metformin-containing medications). Combination products, e.g. Janumet® (metformin/sitagliptin), may be shown in both of the percentages for adherence to metformin-containing products and to all other diabetic medications; however, combination products will only be included one time in the overall percentage and star rating. The star ratings for the overall percentage of patients that are adherent to all diabetic medications (excluding insulin and Symlin®) are based on the 2014 Medicare Star Ratings. However, a rating of zero stars is exclusive to SoonerCare. A key is shown below to illustrate the star ratings and adherence percentages (based on patients' PDC) for each star rating.

5 Stars: Excellent (≥ 82%)

4 Stars: Above Average (≥ 79% to < 82%)

3 Stars: Average (≥ 76% to < 79%)

2 Stars: Below Average (≥ 73% to < 76%)

1 Star: Poor (≥ 60% to < 73%)

0 Stars: Very Poor (< 60%)

Chronic Medication Adherence PDC by Drug Category

The average member PDC is listed based on drug category below. Also listed is the average prescriber percentage of adherent members (PDC ≥ 80%) for each category and the average star rating for the applicable categories. Star ratings listed as N/A are either subcategories or categories that are not included in Medicare's star ratings thus far.

Drug Category	Member PDC	Prescriber % of Adherent Members	Star Rating
Beta Blockers	67.21%	38.74%	N/A
Calcium Channel Blockers	70.93%	46.11%	N/A
Metformin	62.17%	33.34%	N/A
Other Diabetes Medications	68.07%	41.19%	N/A
Overall Diabetes Medications	67.52%	41.20%	0 stars
RAS Antagonists	70.11%	43.18%	0 stars
Statins	72.23%	47.34%	0 stars

Medication Compliance Informational Page [2, 3, 4, 5]

Medication adherence is essential for positive therapeutic outcomes. Non-adherence may lead to false medication failure, resulting in unnecessary dose increases and/or medication changes or additions, complications associated with diabetes, and increased health-care costs. Patients need to understand the importance of taking their diabetic medications as directed to reduce the risk of serious complications associated with diabetes, such as heart disease, stroke, blindness, kidney failure, lower-limb amputations, and pre-mature death. Dosing regimens, possible adverse effects, the importance of medication compliance, and long-term serious complications associated with diabetes should be discussed with the patient to address any concerns and improve medication adherence, resulting in improved glucose control and a decreased risk of complications associated with diabetes.

[1] Centers for Medicare & Medicaid Services: *Medicare 2014 Part C & D Star Rating Technical Notes*. Available online at http://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovGenIn/PerformanceData.html. Last updated 4/2/14.
[2] Centers for Disease Control and Prevention: *National Diabetes Statistics Report, 2014.* Available online at: http://www.cdc.gov/diabetes/pubs/statsreport14/national-diabetes-report-web.pdf.
[3] Centers for Disease Control and Prevention: *Diabetes Report Card, 2012.* Available online at: http://www.cdc.gov/diabetes/pubs/pdf/diabetesreportcard.pdf.
[4] Cramer, J. A Systematic Review of Adherence with Medications for Diabetes. *Diabetes Care.* 2004. 27: 1218-1224.
[5] Meece, J. Improving Medication Adherence Among Patients with Type 2 Diabetes. *Journal of Pharmacy Practice.* April 2014. 27 (2): 187-194.

Appendix C

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

Oklahoma Health Care Authority
January 2015

Recommendations

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.

Appendix D

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

Oklahoma Health Care Authority
January 2015

Recommendations

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.

Appendix E

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

Oklahoma Health Care Authority
January 2015

Recommendations

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.

Appendix F

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

Oklahoma Health Care Authority
January 2015

Recommendations

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 Anticholinergics (LAMA) product based prior authorization category. Current criteria for this category will apply.

Long-Acting $Beta_2$ Agonists (LABA) and Long-Acting Anticholinergics (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 Anticholinergics (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®).

Appendix G

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

Oklahoma Health Care Authority
January 2015

Introduction[1,2]

Orthostatic hypotension (OH) is defined as a decrease in systolic blood pressure by 20mm Hg or a decrease in diastolic blood pressure by 10mm Hg within three minutes of standing compared with blood pressure from the sitting or supine position. Standing results in blood pooling of approximately 500mL to 1000mL in the lower extremities and splanchnic circulation. This initiates the pathologic response of an increase in sympathetic outflow which increases peripheral vascular resistance, venous return, and cardiac output, thereby limiting the decrease in blood pressure. OH results from an inadequate physiologic response to postural changes in blood pressure.

OH neurologic symptoms result from decreased cerebral perfusion. Common symptoms include dizziness, lightheadedness, feeling faint, weakness, blurred vision, fatigue, and headache. More severe, less common symptoms include dyspnea, syncope, chest pain, and neck and shoulder pain. OH most commonly occurs in the elderly population and in patients with neurological disorders such as Parkinson's disease. Approximately 20% of patients older than 65 years of age are estimated to have OH while only 2% of these patients are symptomatic. Younger patients diagnosed with OH may have underlying causes such as volume depletion.

OH may be caused by a number of things including dehydration, blood loss, medications, or a disorder of the neurologic, cardiovascular, or endocrine system. Evaluation of suspected OH should start with identifying reversible causes and underlying associated medical conditions. Acute cases generally resolve with treatment of the underlying cause. Patients with chronic OH may find pharmacologic and non-pharmacologic treatment beneficial. Goals of treatment include improving orthostatic blood pressure without excessive supine hypertension, relieving orthostatic symptoms, and improving standing time.

Current medications used for the treatment of OH include fludrocortisone, midodrine, and pyridostigmine. Fludrocortisone, a synthetic mineralocorticoid, is considered first-line pharmacologic treatment for OH. Dosing should be titrated within therapeutic range until symptoms are relieved, or until the patient develops edema or greater than four pound weight gain. Midodrine, a peripheral selective alpha-1 adrenergic agonist, improves symptoms in patients with neurogenic OH by significantly increasing standing systolic blood pressure. Midodrine is FDA approved to treat OH with a recommended dose of 10mg by mouth three times daily at three to four hour intervals during daytime hours. Pyridostigmine, a cholinesterase inhibitor, improves neurotransmission at acetylcholine-mediated neurons of the autonomic nervous system. In a double-blind study, compared with placebo, pyridostigmine demonstrated a decreased drop in standing diastolic blood pressure without worsening supine hypertension.

The FDA approved Northera™ (droxidopa) for the treatment of symptomatic neurogenic OH in September of 2014. Northera™ is directly metabolized to norepinephrine which increases blood pressure by inducing peripheral vasoconstriction. Effectiveness beyond two weeks of treatment has not been demonstrated in clinical trials. The continued effectiveness of Northera™ should be assessed periodically.

Northera™ (Droxidopa) Summary[3]

Indications: Northera™ (Droxidopa) is indicated for the treatment of orthostatic dizziness, lightheadedness, or the "feeling that you are about to black out" in adult patients with symptomatic neurogenic OH caused by primary autonomic failure (Parkinson's disease, multiple system atrophy, and pure autonomic failure), dopamine beta-hydroxylase deficiency, and non-diabetic autonomic neuropathy.

Dosing:

- Northera™ is available as 100mg, 200mg, and 300mg oral capsules.
- The starting dose is 100mg three times daily, up to a maximum dose of 600mg three times daily.
- Northera™ should be taken consistently with or without food.
- To reduce the potential for supine hypertension, elevate the head of the bed and give the last dose at least three hours prior to bedtime.
- Northera™ capsules should be taken whole.

Mechanism of Action: The exact mechanism of action of Northera™ in the treatment of neurogenic OH is unknown. Northera™ is a synthetic amino acid analog that is directly metabolized to norepinephrine by dopa-decarboxylase, which is extensively distributed throughout the body. Northera™ is believed to exert its pharmacological effects through norepinephrine and not through the parent molecule or other metabolites. Norepinephrine increases blood pressure by inducing peripheral arterial and venous vasoconstriction. Northera™ in humans induces small and transient rises in plasma norepinephrine.

Contraindications: None

Efficacy:

- The efficacy of Northera™ was examined in short term (1 to 2 weeks) and longer-term (8 weeks; 3 months) studies; however, only two studies showed a treatment effect of Northera™ at Week 1, and none of the studies demonstrated continued efficacy beyond two weeks.
- Efficacy was measured using Item #1 score from the Orthostatic Hypotension Questionnaire (OHQ), a patient–reported outcome that measures symptoms of neurogenic OH. Item #1 scores dizziness, lightheadedness, feeling faint, and feeling like you might black out.
- Patients were allowed to continue taking current medications including dopa-decarboxylase inhibitors and fludrocortisone.

- Study 306B demonstrated a statistically significant mean 0.9-unit decrease in dizziness with Northera™ versus placebo at Week 1, but the effect did not persist beyond Week 1.
- In Study 301, patients showed a 0.7-unit decrease from baseline in dizziness with Northera™ versus placebo, but did not demonstrate statistical significance.
- Neither Study 302 nor 303 showed statistical significance between treatment arms on its primary endpoint.
- Considering the data from clinical trials, the effectiveness of Northera™ beyond two weeks is uncertain, and patients should be evaluated periodically to determine whether Northera™ is continuing to provide a benefit.

Safety:

- Northera™ has a boxed warning for risk of supine hypertension and may increase cardiovascular risk if supine hypertension is not well-managed. Patients should be advised to elevate the head of the bed when resting or sleeping. Blood pressure should be monitored, both in the supine position and in the recommended head-elevated sleeping position. Northera™ dosing should be reduced or discontinued if supine hypertension persists. If supine hypertension is not well-managed, Northera™ may increase the risk of cardiovascular events (strokes, heart attacks, and death).
- Northera™ can cause hyperpyrexia and confusion. Post-marketing cases of a symptom complex resembling neuroleptic malignant syndrome (NMS) have been reported with Northera™ use during post-marketing surveillance in Japan. Patients should be carefully observed when the dosage of Northera™ is changed or when concomitant levodopa is reduced abruptly or discontinued, especially if the patient is receiving neuroleptics. NMS is an uncommon but life-threatening syndrome characterized by fever or hyperthermia, muscle rigidity, involuntary movements, altered consciousness, and mental status changes. The early diagnosis of this condition is important for the appropriate management of these patients.
- Northera™ may exacerbate symptoms in patients with existing ischemic heart disease, arrhythmias, and congestive heart failure. Careful consideration should be given to this potential risk prior to initiating therapy in patients with these conditions.
- Northera™ contains FD&C Yellow No. 5 (tartrazine) which may cause allergic-type reactions (including bronchial asthma) in certain susceptible persons. Although the overall incidence of FD&C Yellow No. 5 (tartrazine) sensitivity in the general population is low, it is frequently seen in patients who also have aspirin hypersensitivity.
- The most common side effects in Northera™ patients were headache, dizziness, nausea, high blood pressure, and feeling tired.

Cost Comparison:

Medication Name	Strength	Cost/Capsule	Biweekly Cost∞	Cost/Year
Northera™ (Droxidopa)	100mg	$16.23*	$681.66	$17,771.85
Northera™ (Droxidopa)	200mg	$33.06*	$1,388.52	$36,200.70
Northera™ (Droxidopa)	300mg	$49.60*	$2,083.20-$4,166.40	$54,312.00-$108,624.00
Midodrine	10mg	$1.01+	$41.42	$1,105.95
Fludrocortisone	0.1mg	$0.45+	$18.90	$492.75
Pyridostigmine	60mg	$0.32+	$13.44	$350.40

*Cost based on Estimated Acquisition Cost (EAC)
+Cost based on State Maximum Allowable Cost.
∞Cost based on recommended dosing.

Utilization: There has been no utilization of Northera™ in the SoonerCare population since its approval in September 2014.

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, and 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™.

[1] Lanier, Jeffrey B., Matthew B. Mote, and Emily C. Clay. "Evaluation and Management of Orthostatic Hypotension." *American Family Physician* 84.5 (2011) Available online at: http://www.aafp.org/afp/2011/0901/p527.html Last accessed 12/2014.
[2] Low, Phillip A., and Wolfgang Singer. "Update on Management of Neurogenic Orthostatic Hypotension." *Lancet Neurology* (2008). Available online at: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2628163/pdf/nihms-86024.pdf>. Last assessed 12/2014.
[3] Northera™ Prescribing Information, Lundbeck NA Ltd. Available online at: http://www.lundbeck.com/upload/us/files/pdf/Products/Northera_PI_US_EN.pdf. Last revised 08/2014. Last accessed 12/14.

Appendix H

Fiscal Year 2014 Annual Review of Antiemetic Medications and 30-Day Notice to Prior Authorize Akynzeo® (Netupitant/Palonosetron)

Oklahoma Health Care Authority
January 2015

Current Prior Authorization Criteria

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

1. An FDA approved diagnosis; 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 will be based on duration of need.
4. Existing quantity limits apply.

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

1. Approval can be granted for six months for the diagnosis of HIV related loss of appetite.
2. The diagnosis of chemotherapy induced nausea and vomiting requires the following:
   a. 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 will be based on duration of need.
4. A quantity limit of 60 capsules per 30 days will apply.

Zuplenz® (Ondansetron) Approval Criteria:

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

Diclegis® (Doxylamine/Pyridoxine) Approval Criteria:

1. An FDA approved diagnosis of nausea and vomiting associated with pregnancy; and
2. Trials with at least two non-pharmacological therapies that have failed to relieve nausea and vomiting; and
3. Trials with at least three prescription medications that have failed to relieve nausea and vomiting (must include a trial of ondansetron); and
4. A patient-specific, clinically significant reason why member cannot use OTC doxylamine and OTC Vitamin B-6 (pyridoxine).

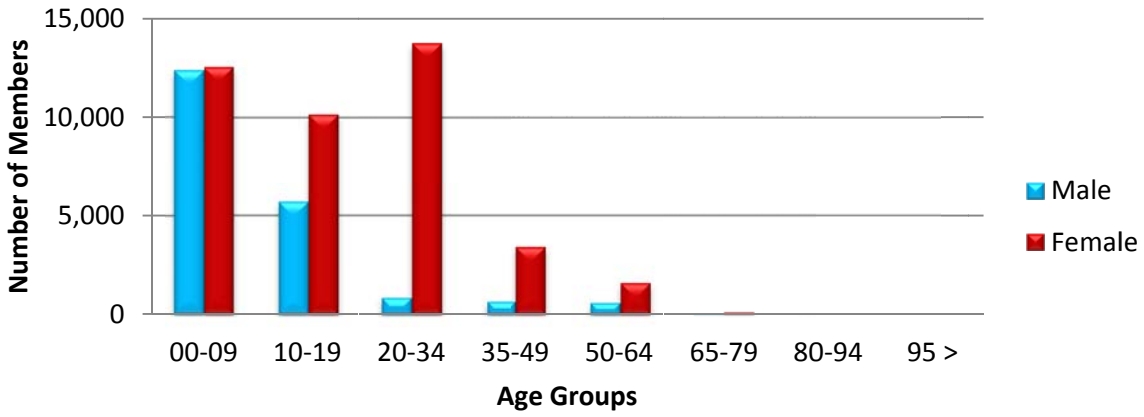
Utilization of Antiemetic Medications

Comparison of Fiscal Years

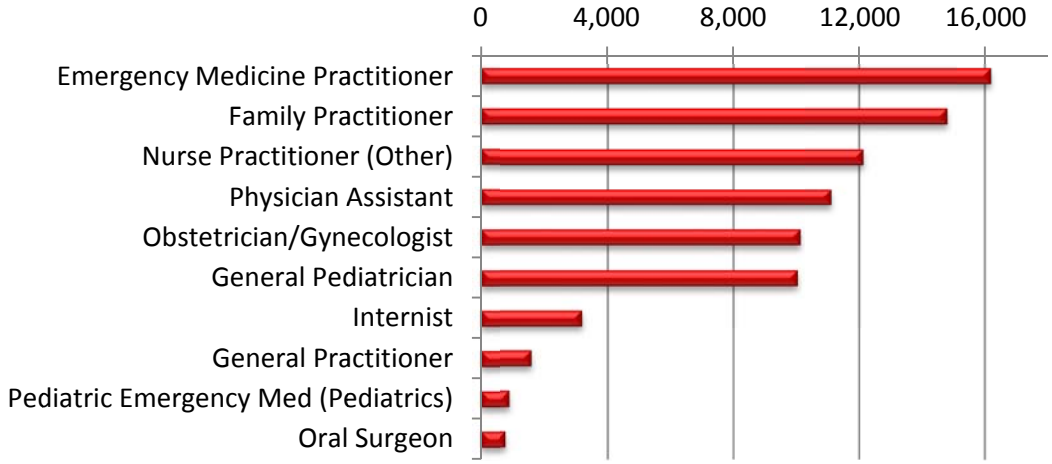
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2013	54,037	72,828	$1,007,885.85	$13.84	$0.54	832,995	1,854,831
2014	61,863	86,391	$1,207,979.00	$13.98	$1.11	1,239,832	1,084,634
% Change	**14.50%**	**18.60%**	**19.90%**	**1.00%**	**105.60%**	**48.80%**	**-41.50%**
Change	**7,826**	**13,563**	**$200,093.15**	**$0.14**	**$0.57**	**406,837**	**-770,197**

*Total number of unduplicated members.

Demographics of Members Utilizing Antiemetic Medications



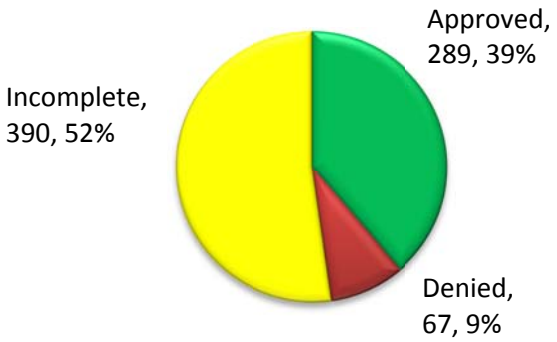
Top Prescriber Specialties of Antiemetic Medications by Number of Claims



Prior Authorization of Antiemetic Medications

There was a total of 746 petitions submitted for the antiemetic medication category during fiscal year 2014. The following chart shows the status of the submitted petitions.

Status of Petitions



Market News and Updates[1,2,3]

Anticipated Patent Expirations:

- Diclegis® (doxylamine/pyridoxine)- 01/2019
- Sancuso® (granisetron transdermal patch)- 10/2024
- Emend® (aprepitant)- 09/2027
- Zuplenz® (ondansetron film)- 11/2029

New FDA Approvals:

- Akynzeo® (netupitant/palonosetron)- 10/2014
- Aloxi® (palonosetron injection)- 05/2014 The FDA approved the indication for chemotherapy-induced nausea and vomiting in pediatrics aged one month and older.

FDA Safety Alert:

- September 2014: Labeling for the 5-HT_3 receptor antagonists have been updated to include warnings and precautions regarding serotonin syndrome. The development of serotonin syndrome has been reported with 5-HT_3 receptor antagonists. Most reports have been associated with concomitant use of serotonergic drugs.

Akynzeo® (Netupitant/Palonosetron)[4]

Indications: Akynzeo® (netupitant/palonosetron) is indicated for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy, including but not limited to, highly emetogenic chemotherapy.

Dosing:

- Akynzeo® is available as an oral capsule containing 300mg netupitant and 0.5mg palonosetron.
- The recommended dose is one capsule orally approximately one hour prior to the start of chemotherapy. With or without food.

Mechanism of Action:

- Netupitant is a selective antagonist of human substance P/neurokinin 1 (NK_1) receptors. Delayed emesis has been largely associated with the activation of tachykinin family neurokinin 1 (NK1) receptors (broadly distributed in the central and peripheral nervous systems) by substance P.
- Palonosetron is a 5-HT_3 receptor antagonist with a strong binding affinity for this receptor and little or no affinity for other receptors. Cancer chemotherapy may be associated with an incidence of nausea and vomiting, particularly when certain agents are used. Receptors for 5-HT_3 are located on the nerve terminals of the vagus in the periphery and centrally in the chemoreceptor trigger zone. Chemotherapeutic agents produce nausea and vomiting by stimulating the release of serotonin from the enterochromaffin cells of the small intestine. Serotonin then activates 5-HT_3 receptors located on vagal afferents to initiate the vomiting reflex. The development of acute emesis is known to depend on serotonin and its 5-HT_3 receptors.
- Palonosetron prevents nausea and vomiting during the acute phase and netupitant prevents nausea and vomiting during both the acute and delayed phase after cancer chemotherapy.

Warnings and Precautions:

- Hypersensitivity reactions, including anaphylaxis, have been reported in patients receiving palonosetron with or without known hypersensitivity to other 5-HT_3 receptor antagonists.
- Akynzeo® does not have any known contraindications.

Efficacy:

- The efficacy of Akynzeo® for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of chemotherapy was established in two trials.
- The first study was a multicenter, randomized, parallel, double-blind, controlled clinical trial of 694 patients undergoing highly emetogenic chemotherapy (cisplatin-based chemotherapy). Of the 694, 135 patients received the FDA approved strength of netupitant 300mg/0.5mg palonosetron combination and 136 patients received 0.5mg palonosetron alone. All patients also received oral dexamethasone.
    - The key efficacy endpoints were complete response (CR), defined as no emetic episode and no use of rescue medication for the 25-120 hour interval (delayed phase), CR for the 0-24 hour interval (acute phase), and CR within 120 hours (overall phase) after the start of the chemotherapy administration.
    - The netupitant 300mg/palonosetron 0.5mg combination resulted in 90.4% CR for the delayed phase, 98.5% CR for the acute phase, and 89.6% for the overall phase. Whereas, palonosetron 0.5mg alone resulted in 80.1%, 89.7%, and 76.5% CR, respectively.
- The second study was a multicenter, parallel, double-blind, active controlled, superiority trial of 1,455 patients receiving moderately emetogenic chemotherapy (anthracycline-cyclophosphamide). A total of 1,450 patients were randomized to receive netupitant 300mg/palonosetron 0.5mg or to receive palonosetron 0.5mg. All patients also received oral dexamethasone.

- The primary efficacy endpoint was the CR in the delayed phase. The secondary efficacy endpoint was the CR for the acute and the overall phase.
- The netupitant/palonosetron combination had a CR of 76.9% for the delayed phase, 88.4% for the acute phase, and 74.3% for the overall phase. The palonosetron alone had a CR of 69.5%, 85%, and 66.6%, respectively.

Safety:

- The most common adverse reactions reported are headache, asthenia, dyspepsia, fatigue, constipation, and erythema (incidence ≥3%).
- Use of Akynzeo® should be avoided in patients with severe hepatic impairment.
- Use of Akynzeo® should be avoided in patients with severe renal impairment or end-stage renal disease.

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.

Utilization Details of Antiemetic Medications: Fiscal Year 2014

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
ONDANSETRON PRODUCTS						
ONDANSETRON TAB 4MG	16,022	12,140	$143,818.05	$0.65	$8.98	11.91%
ONDANSETRON TAB 4MG ODT	45,641	37,626	$487,115.32	$0.93	$10.67	40.32%
ZOFRAN TAB 4MG	16	16	$85.55	$1.99	$5.35	0.01%
ONDANSETRON TAB 8MG	7,279	4,874	$74,671.58	$0.73	$10.26	6.18%
ONDANSETRON TAB 8MG ODT	12,124	8,462	$176,079.58	$1.05	$14.52	14.58%
ONDANSETRON SOL 4MG/5ML	4,850	4,387	$188,070.64	$3.10	$38.78	15.57%
ONDANSETRON INJ 4MG/2ML	133	87	$1,265.21	$1.81	$9.51	0.10%
ONDANSETRON INJ 40/20ML	26	13	$2,005.70	$5.54	$77.14	0.17%
SUBTOTAL	**86,091**	**67,065**	**$1,073,111.63**	**$1.00**	**$12.46**	**88.84%**
GRANISETRON PRODUCTS						
GRANISETRON TAB 1MG	33	10	$2,057.57	$6.66	$62.35	0.17%
GRANISOL SOL 2MG/10ML	1	1	$151.86	$50.62	$151.86	0.01%
SANCUSO DIS 3.1MG	5	3	$6,443.11	$47.03	$1,288.62	0.53%
SUBTOTAL	**39**	**14**	**$8,652.54**	**$19.27**	**$221.86**	**0.71%**
DOLASETRON PRODUCTS						
ANZEMET TAB 100MG	5	1	$10,344.29	$68.96	$2,068.86	0.86%
SUBTOTAL	**5**	**1**	**$10,344.29**	**$68.96**	**$2,068.86**	**0.86%**
APREPITANT PRODUCTS						
EMEND CAP 80MG	1	1	$241.90	$120.95	$241.90	0.02%
EMEND PAK 80 & 125	124	54	$69,494.39	$25.65	$560.44	5.75%
SUBTOTAL	**125**	**55**	**$69,736.29**	**$139.47**	**$557.89**	**5.77%**
DRONABINOL PRODUCTS						
DRONABINOL CAP 2.5MG	45	24	$8,925.69	$6.76	$198.35	0.74%
DRONABINOL CAP 5MG	68	21	$24,868.22	$12.67	$365.71	2.06%
DRONABINOL CAP 10MG	18	4	$12,340.34	$20.57	$685.57	1.02%
SUBTOTAL	**131**	**49**	**$46,134.25**	**$11.88**	**$352.17**	**3.82%**
TOTAL	**86,391**	**61,863***	**$1,207,979.00**	**$1.11**	**$13.98**	**100%**

*Total number of unduplicated members.

[1] 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 12/12/14. Last accessed 12/12/14.
[2] Aloxi® Prescribing Information. Available online at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/021372s020lbl.pdf. Last revised 09/2014. Last accessed 12/16/14.
[3] FDA: Safety Information: Serotonin-3 (5-HT3) Receptor Antagonists. Available online at: http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm418818.htm. Last revised 10/16/14. Last accessed 12/16/14.
[4] Akynzeo® Prescribing Information. Available online at: https://www.akynzeo.com/media/Prescribing_Information.pdf Last revised 10/2014. Last accessed 12/12/14.

Appendix I

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

Oklahoma Health Care Authority
January 2015

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

Hepatitis C was covered in the May and November 2014 DUR Board packets. For additional background information, please refer to those documents. Viekira Pak™ (ombitasvir/paritaprevir/ritonavir/dasabuvir) is a fixed-dose combination of a hepatitis C virus (HCV) NS5A inhibitor, a HCV NS3/4A protease inhibitor, and a CYP3A inhibitor co-packaged with a HCV non-nucleoside NS5B palm polymerase inhibitor. Viekira Pak™ efficacy has been established in individuals with genotype-1 with compensated liver disease (including cirrhosis). Viekira Pak™ is used in combination with ribavirin in certain patient populations.

Oral Products Currently Available to Treat Chronic Hepatitis C

The following table shows the various oral products currently approved to treat Chronic Hepatitis C (CHC). Regimen duration varies on host and viral factors including pretreatment viral load, fibrosis stage, cirrhosis status, and prior treatment history.

Drug Product	Indicated Genotypes	Regimen Details
Harvoni® (sofosbuvir/ledipasvir)	1	• Single Product Regimen • **Regimen Duration:** o 8 weeks o 12 weeks o 24 weeks
Olysio® (simeprevir)	1	• Never a Single Product Regimen; Multiproduct Regimen • **Regimen Duration:** o 12 weeks followed by 12 or 36 additional weeks PEG IFN + RBV o 12 weeks + sofosbuvir o 24 weeks + sofosbuvir
Sovaldi® (sofosbuvir)	1, 2, 3, & 4	• Never a Single Product Regimen; Multiproduct Regimen • **Regimen Duration:** o 12 weeks + PEG IFN +RBV o 12 weeks + RBV o 24 weeks + RBV o 12 weeks + simeprevir o 24 weeks + simeprevir
Victrelis® (boceprevir)	1	• Never a Single Product Regimen; Multiproduct Regimen • **Regimen Duration:** o PEG IFN + RBV for 4 weeks then add boceprevir, treatment duration varies from 28 to 48 weeks

Drug Product	Indicated Genotypes	Regimen Details
Viekira Pak™ (ombitasvir/paritaprevir/ ritonavir/dasabuvir)	1	• Can be a Single Product Regimen; Multiproduct Regimen • **Regimen Duration:** o 12 weeks + RBV o 24 weeks + RBV o 12 weeks

Market News and Updates [1, 7]

Guideline Updates:

- **11/2014:** The American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA) in collaboration with the International Antiviral Society-USA (IAS-USA) met and reviewed data to update the guidance based on the US FDA approval of Harvoni® (ledipasvir/sofosbuvir).
- **12/2014:** The AASLD/IDSA/IAS-USA updated the guidance. Sections regarding the initial, retreatment, monitoring and unique populations (HIV/HCV Coinfection, Cirrhosis, Post-Liver Transplantation, and Renal Impairment) were extensively revised based on newly available therapies and data. The guidelines have been updated to include the newly FDA approved therapies Viekira Pak™ and Harvoni®. Viekira Pak™, Harvoni® and Sovaldi® in combination with Olysio® are all recommended as first line regimens for genotype-1 HCV.

Market and Pipeline Updates:

- **12/2014:** The FDA approved AbbVie's Viekira Pak™, an all-oral, interferon free regimen, with or without ribavirin for the treatment of patients with chronic hepatitis C genotype-1, including those with compensated cirrhosis. Viekira Pak™ is the only FDA-approved regimen that contains three distinct mechanisms of action that work together to attack the virus at three separate stages of the disease lifecycle to inhibit reproduction.

Viekira Pak™ (Ombitasvir/Paritaprevir/Ritonavir/Dasabuvir) Product Summary[2]

FDA Approved: December 2014

Indications: Viekira Pak™ (ombitasvir/paritaprevir/ritonavir/dasabuvir) is indicated for the treatment of patients with genotype-1 chronic HCV infection including those with compensated cirrhosis. Viekira Pak™ includes ombitasvir, a HCV NS5A inhibitor, paritaprevir, a HCV NS3/4A protease inhibitor, ritonavir, a CYP3A inhibitor and dasabuvir, a HCV non-nucleoside NS5B palm polymerase inhibitor.

Limitations of Use: Viekira Pak™ is not recommended for use in patients with decompensated liver disease.

Dosing:

- Viekira Pak™ contains two separate tablet formulations. Ombitasvir 12.5mg, paritaprevir 75mg, and ritonavir 50mg fixed dose combination tablets are co-packaged with dasabuvir 250mg tablets.

- The recommended dosage of Viekira Pak™ is two ombitasvir, paritaprevir, and ritonavir tablets orally once daily (in the morning) and one dasabuvir tablet orally twice daily (morning and evening).
- Viekira Pak™ should be taken with a meal without regard to fat or calorie content.
- Viekira Pak™ is used in combination with ribavirin in certain patient populations. When administered with Viekira Pak™, the recommended dosage of ribavirin is based on weight.
    - 1000mg/day for subjects less than or equal to 75kg
    - 1200mg/day for subjects greater than 75kg
    - Ribavirin should be administered twice daily with food
- The recommended treatment duration for Viekira Pak™ is dependent on cirrhosis stage, genotypic subtype, and prior treatment history. The following table delineates the regimens.

Patient Population	Treatment Regimen	Treatment Duration
Genotype 1a, without cirrhosis	Viekira Pak™ + RBV	12 weeks
Genotype 1a, with cirrhosis	Viekira Pak™ + RBV	24 weeks**
Genotype 1b, without cirrhosis	Viekira Pak™	12 weeks
Genotype 1b, with cirrhosis	Viekira Pak™ + RBV	12 weeks

RBV= Ribavirin
HCV/HIV co-infection: For patients with HCV/HIV co-infection, follow the dosage recommendations in the table above.
Liver Transplant Recipients: In liver transplant recipients with normal hepatic function and mild fibrosis (METAVIR fibrosis ≤2), the recommended duration of Viekira Pak™ with ribavirin is 24 weeks.
Follow the genotype 1a dosing recommendations in patients with an unknown genotype 1 subtype or with mixed genotype 1 infection.
**Viekira Pak™ administered with ribavirin for 12 weeks may be considered for some patients based on prior treatment history.

Contraindications:

- If Viekira Pak™ is administered with ribavirin, the contraindications to ribavirin also apply to this combination regimen. Ribavirin contraindications include the following:
    - Pregnant women and men whose female partners are pregnant
    - Hemoglobinopathies
    - Coadministration with didanosine
- Viekira Pak™ is contraindicated in patients with severe hepatic impairment due to the risk of potential toxicity.
- Viekira Pak™ is contraindicated with drugs that are highly dependent on CYP3A for clearance.
    - Drugs that are strong inducers of CYP3A and CYP2C8 may lead to reduced efficacy of Viekira Pak™.
    - Drugs that are strong inhibitors of CYP2C8 may increase dasabuvir plasma concentrations and the risk of QT prolongation.

Warnings and Precautions:

- Increased risk of ALT elevations when Viekira Pak™ is used concomitantly with ethinyl estradiol containing medications. Ethinyl estradiol medications must be discontinued prior to therapy with Viekira Pak™. Hepatic laboratory testing should be performed during the first four weeks of starting treatment and as clinically indicated thereafter. Consideration should be given to discontinuing Viekira Pak™ if ALT levels remain persistently greater than ten times the upper limit of normal.

- If Viekira Pak™ is administered with ribavirin, the warnings and precautions to ribavirin also apply to this combination regimen.
- The ritonavir component of Viekira Pak™ is also an HIV-1 protease inhibitor and can select for HIV-1 protease inhibitor resistance associated substitutions. Any HCV/HIV co-infected patients treated with Viekira Pak™ should also be on a suppressive antiretroviral drug regimen to reduce the risk of HIV-1 protease inhibitor drug resistance.

Adverse Reactions: The most common adverse reactions (≥5%) experienced with Viekira Pak™ in combination with ribavirin during clinical trials were fatigue, nausea, pruritus, skin reactions, insomnia, and asthenia.

Drug Interactions: The following table provides a listing of drugs that are contraindicated with use of Viekira Pak™.

Concomitant Drug Class: Drug Name	Clinical Comment
Alpha 1-Adrenoreceptor Antagonist: alfuzosin HCL	Potential for hypotension.
Anticonvulsants: carbamazepine, phenytoin, phenobarbital	Ombitasvir, paritaprevir, ritonavir, and dasabuvir exposures may decrease leading to a potential loss of therapeutic activity of Viekira Pak™.
Antihyperlipidemic Agents: gemfibrozil	Increase in dasabuvir exposures by 10-fold which may increase the risk of QT prolongation.
Antimycobacterials: rifampin	Ombitasvir, paritaprevir, ritonavir, and dasabuvir exposures may decrease leading to a potential loss of therapeutic activity of Viekira Pak™.
Ergot Derivatives: ergotamine, dihydroergotamine, ergonovine, methylergonovine	Acute ergot toxicity characterized by vasospasm and tissue ischemia has been associated with co-administration of ritonavir and ergotamine, dihydroergotamine, ergonovine, or methylergonovine.
Ethinyl Estradiol Containing Products: Ethinyl estradiol containing medications such as combined oral contraceptives	Potential for ALT elevations.
Herbal Supplements: St. John's wort	Ombitasvir, paritaprevir, ritonavir, and dasabuvir exposures may decrease leading to a potential loss of therapeutic activity of Viekira Pak™.
HMG-CoA Reductase Inhibitors: lovastatin, simvastatin	Potential for myopathy including rhabdomyolysis
Neuroleptics: pimozide	Potential for cardiac arrhythmias.
HIV Antiretrovirals: efavirenz	Co-administration was poorly tolerated and resulted in liver enzyme elevations.
Pulmonary Arterial Hypertension Medications: sildenafil when dosed for PAH	Increased potential for sildenafil associated adverse effects such as visual disturbances, hypotension, priapism and syncope.
Sedatives/Hypnotics: triazolam, orally administered midazolam	Large increases in concentration of these benzodiazepines. The potential exists for prolonged or increased sedation or respiratory depression.

PAH = Pulmonary Arterial Hypertension

Use in Specific Populations:

- Pregnancy: Viekira Pak™ is pregnancy category B. There are no adequate and well controlled studies with Viekira Pak™ in pregnant women. If Viekira Pak™ is administered with ribavirin, the combination regimen is contraindicated in pregnant women and in men whose female partners are pregnant.
- Nursing Mothers: It is not known whether Viekira Pak™ and its metabolites are present in human breast milk.
- Pediatric Patients: The safety and effectiveness of Viekira Pak™ have not been established in pediatric patients.
- Geriatric Patients: No overall differences in safety or effectiveness with Viekira Pak™ were observed in subjects 65 years and older when compared to younger subjects.
- Renal Impairment: No dosage adjustment of Viekira Pak™ is required for mild, moderate, or severe renal impairment. Viekira Pak™ has not been studied in patients on dialysis.
- Hepatic Impairment: No dosage adjustment of Viekira Pak™ is required for patients with mild hepatic impairment (Child-Pugh A). Viekira Pak™ is not recommended in patients with moderate hepatic impairment (Child-Pugh B). Viekira Pak™ is contraindicated in patients with severe hepatic impairment (Child-Pugh C).

Mechanism of Action: Viekira Pak™ combines three direct-acting HCV antiviral agents with distinct mechanisms of action and non-overlapping resistance profiles to target HCV at multiple steps in the viral life-cycle.

- Ombitasvir is an inhibitor of HCV NS5A, which is essential for viral RNA replication and virion assembly.
- Paritaprevir is an inhibitor of the HCV NS3/4A protease which is necessary for the proteolytic cleavage of the HCV encoded polyprotein and essential for viral replication.
- Dasabuvir is a non-nucleoside inhibitor of the HCV RNA-dependent RNA polymerase encoded by the NS5B gene, which is essential for replication of the viral genome.
- Ritonavir is not active against HCV. Ritonavir is a potent CYP3A inhibitor that increases peak and trough plasma drug concentrations of paritaprevir and overall drug exposure.

Efficacy:

The efficacy of Viekira Pak™ was evaluated in six randomized clinical trials in 2,308 subjects with genotype-1 (GT1) chronic HCV:

- SAPPHIRE-I: GT1 (a and b) treatment naïve without cirrhosis
- SAPPHIRE-II: GT1 (a and b) treatment-experienced without cirrhosis
- PEARL-II: GT1 (b) treatment-experienced without cirrhosis
- PEARL-III: GT1 (b) treatment naïve without cirrhosis
- PEARL-IV: GT1 (a) treatment naïve without cirrhosis
- TURQUOISE-II: GT1 (a and b) treatment naïve and experienced with cirrhosis

Viekira Pak™ was also evaluated in the following two studies:

- CORAL-1: GT1 infected liver transplant recipients
- TURQUOISE-I: GT1 co-infected with HIV

Treatment experienced in all studies was defined as either: prior relapsers, prior partial responders, or prior null responders to PEG-IFN/RBV treatment. SVR was the primary efficacy endpoint in all studies.

GT1a and GT1b Treatment-Naïve and Treatment Experienced Without Cirrhosis

GT1a Treatment-Naïve	Viekira Pak™ with RBV x 12 Weeks
SAPPHIRE-I SVR12	96% (308/322)
PEARL-IV SVR12	97% (97/100)
GT1a Treatment-Experienced	**Viekira Pak™ with RBV x 12 Weeks**
SAPPHIRE-II SVR12	96% (166/173)
GT1b Treatment-Naïve	**Viekira Pak™ x 12 Weeks**
PEARL-III SVR12	100% (209/209)
GT1b Treatment-Experienced	**Viekira Pak™ x 12 Weeks**
PEARL-II SVR12	100% (91)

GT1a and GT1b Treatment-Naïve and Treatment Experienced With Compensated Cirrhosis

	GT1a		GT1b
	Viekira Pak™ w/RBV x 24 Weeks	Viekira Pak™ w/RBV x 12 Weeks	Viekira Pak™ w/RBV x 12 Weeks
SVR12	95% (115/121)	89% (124/140)	99%(67/68)
SVR12 for Naïve	95% (53/56)	92% (59/64)	100% (22/22)
SVR12 by Prior PEG-IFN Experience			
Null Responder	93% (39/42)	80% (40/50)	100% (25/25)
Partial Responder	100% (10/10)	100% (11/11)	86% (6/7)
Relapser	100% (13/13)	93% (14/15)	100% (14/14)

Clinical Trial of Selected Liver Transplant Recipients– CORAL-I

A total of 34 subjects with GT1 HCV and who were at least 12 months post transplantation at enrollment with normal hepatic function and mild fibrosis were treated. Subjects received 24 weeks of treatment with Viekira Pak™ with RBV. The overall SVR was found to be 97% (33/34).

Clinical Trial in Subjects with HCV/HIV-1 Co-infection– TURQUOISE-I

In an open-label trial 63 subjects with GT1 co-infected with HIV-1 were treated for 12 or 24 weeks with Viekira Pak™ in combination with RBV. Subjects were on a stable HIV-1 antiretroviral therapy (ART) regimen that included tenofovir disoproxil fumarate plus emtricitabine or lamivudine, administered with ritonavir boosted atazanavir or raltegravir. Subjects on atazanavir stopped the ritonavir component of their HIV-1 ART regimen upon initiating treatment with Viekira Pak™. Of the treated subjects 19% of subjects had compensated cirrhosis; 67% of subjects were HCV treatment-naïve; 33% of subjects had failed prior treatment with PEG-IFN/RBV; 89% of subjects had HCV genotype 1a infection. The SVR12 rates were 91% (51/56) for subjects with HCV GT1a infection and 100% (7/7) for those with HCV GT1b infection. One subject had confirmed HIV-1 RNA >400 copies/mL during the post-treatment period. This subject had no evidence of resistance to the ART regimen. No subjects switched their ART regimen due to loss of plasma HIV-1 RNA suppression.

Cost[1, 2, 3, 4, 5, 8, 9]

The following table shows the cost for each regimen. SVR rates found in clinical studies should not be compared across clinical studies, but can be used as a measure of clinical efficacy for each regimen. Specific regimens are used in specific patient populations depending on pre-treatment viral load, prior hepatitis C treatment experience, and fibrosis score. The table contains only regimens for genotype-1 as Viekira Pak™ is only indicated in genotype-1.

Treatment Regimen	Length of Therapy	Total Cost	SVR in Clinical Studies
Treatment-Naïve Without Cirrhosis			
Sovaldi™ + PEG IFN + RBV	12 weeks	$99,544.44	92% (252/273)
Harvoni®	8 weeks	$66,528.00	97% (119/123)
Viekira Pak™ + RBV	12 weeks	$88,317.60	96% (308/322)
Viekira Pak™	12 weeks	$87,984.96	GT1b: 100% (209/209)
Treatment-Naïve With Cirrhosis			
Sovaldi™ + PEG IFN + RBV	12 weeks	$99,544.44	80% (43/54)
Harvoni®	12 weeks	$99,792.00	94% (32/34)
Viekira Pak™ + RBV	12 weeks	$88,317.60	GT1a: 92% (59/64) GT1b: 100% (22/22)
Viekira Pak™ + RBV	24 weeks	$176,635.20	GT1a: 95% (53/56)
Treatment-Experienced Without Cirrhosis			
Sovaldi™ + Olysio™	12 weeks	$158,780.16	93% (13/14)
Harvoni®	12 weeks	$99,792.00	95% (83/87)
Viekira Pak™ + RBV	12 weeks	$88,317.60	96% (166/173)
Viekira Pak™	12 weeks	$87,984.96	GT1b: 100% (91/91)
Treatment-Experienced With Cirrhosis			
Sovaldi™ + Olysio™	24 weeks	$317,560.32	93% (13/14)
Harvoni®	24 weeks	$199,584.00	100% (22/22)
Viekira Pak™ + RBV	12 weeks	$88,317.60	GT1a: 86% (65/76) GT1b: 98% (45/46)
Viekira Pak™ + RBV	24 weeks	$176,635.20	GT1a: 95% (62/65)

If genotypic subtype not indicated then both GT1a and GT1b were included in the SVR results.
RBV= Ribavirin
PEG IFN= peginterferon alfa
GT= Genotype
RBV Dosing based >75kg patient (1200mg)

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 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.

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.

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[4] Olysio™ Product Information. Janssen Therapeutics, LP. Available online at: www.olysio.com/shared/product/olysio/prescribing-information.pdf. Last revised: 11/2014. Last accessed 12/30/2014.

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[9] Poordad F, Hezode C, Trinh R, et al. ABT-450/r-Ombitasvir and Dasabuvir with Ribavirin for Hepatitis C with Cirrhosis. *N Engl J Med*. May 2014: 370:1973-82.

Appendix J

Fiscal Year 2014 Annual Review of Makena® (17-Hydroxyprogesterone Caproate)

Oklahoma Health Care Authority
January 2015

Indication

Makena® (17-hydroxyprogesterone caproate) is a once weekly progestin intramuscular injection indicated to reduce the risk of preterm birth in women with a singleton pregnancy who have a history of singleton spontaneous preterm birth.

Current Prior Authorization Criteria

Makena® (17-hydroxyprogesterone caproate) was approved by the FDA in February 2011, and was covered as a medical benefit. Medical prior authorization was implemented in January 2012, and coverage switched from a medical benefit to a pharmacy benefit in September 2012. Makena® is currently covered as a pharmacy-only benefit, and the current approval criteria are as follows:

Makena® (17-Hydroxyprogesterone Caproate) Approval Criteria:

1. Documented history of previous singleton spontaneous preterm delivery (SPTD) prior to 37 weeks gestation; and
2. Current singleton pregnancy; and
3. Gestational age between 16 weeks, 0 days and 20 weeks, 6 days of gestation.
4. Authorizations will be for once a week administration by a healthcare professional through 36 weeks, 6 days of gestation.

When it is determined by the treating physician to be medically necessary and appropriate to use the compounded hydroxyprogesterone caproate product, it is covered as a SoonerCare medical benefit without prior authorization.

Utilization of Makena® (17-Hydroxyprogesterone Caproate)

Comparison of Fiscal Years: Makena® (Pharmacy)

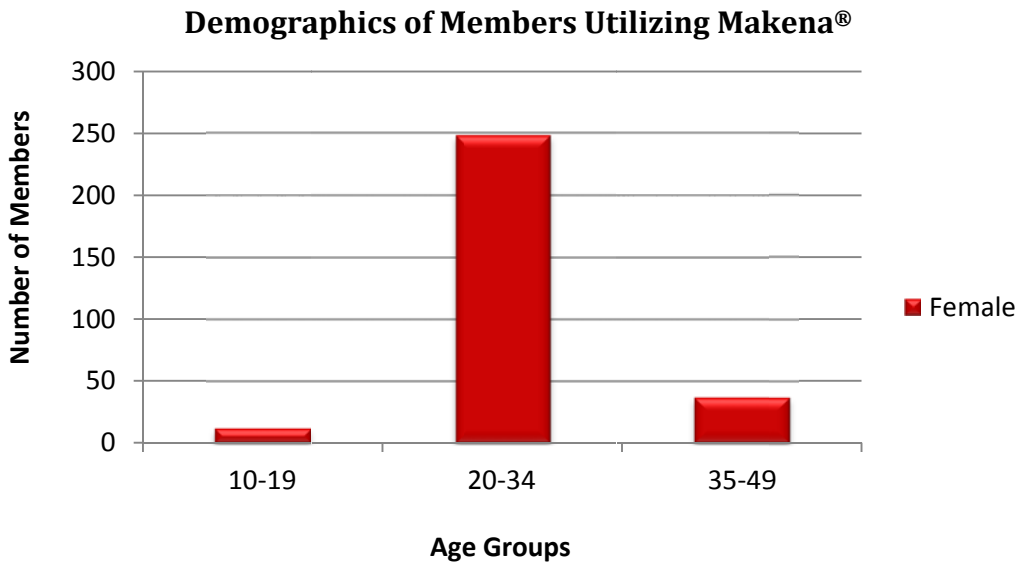
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2013	153	364	$1,316,576.42	$3,616.97	$120.88	1,820	10,892
2014	297	788	$2,864,118.32	$3,634.67	$120.91	3,940	23,688
% Change	**94.10%**	**116.50%**	**117.50%**	**0.50%**	**0.00%**	**116.50%**	**117.50%**
Change	**144**	**424**	**$1,547,541.90**	**$17.70**	**$0.03**	**2,120**	**12,796**

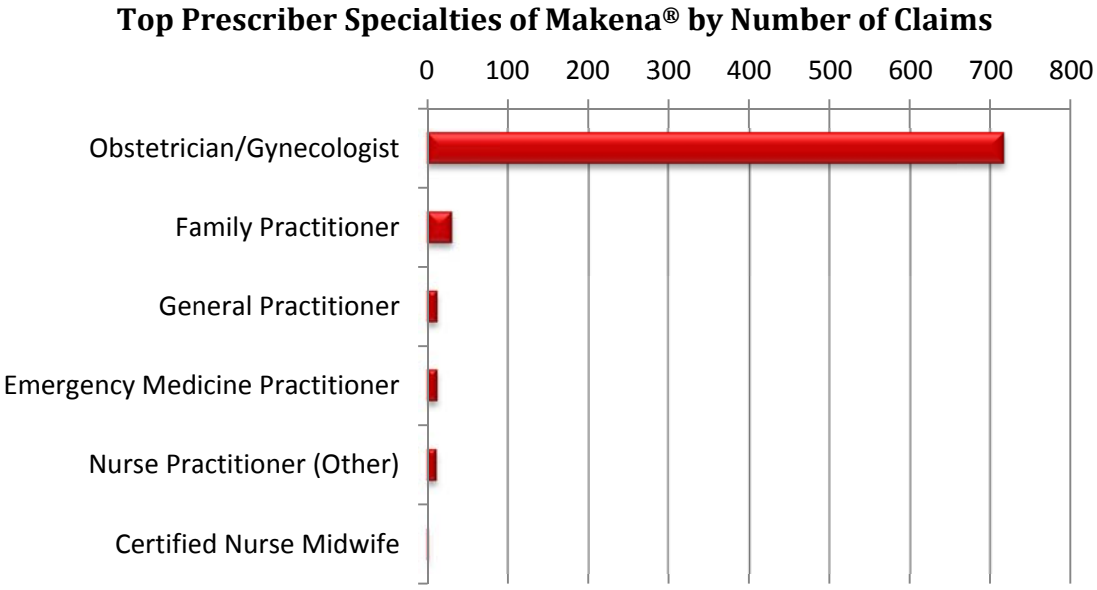
*Total number of unduplicated members.

Comparison of Fiscal Years: Compounded Hydroxyprogesterone Caproate (Medical)

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Total Units
2013	250	1,575	$17,286.72	$10.98	1,575
2014	153	1,173	$13,472.50	$11.49	1,173
% Change	**-38.80%**	**-25.52%**	**-22.06%**	**4.60%**	**-25.52%**
Change	**-97**	**-402**	**-$3,814.22**	**$0.51**	**-402**

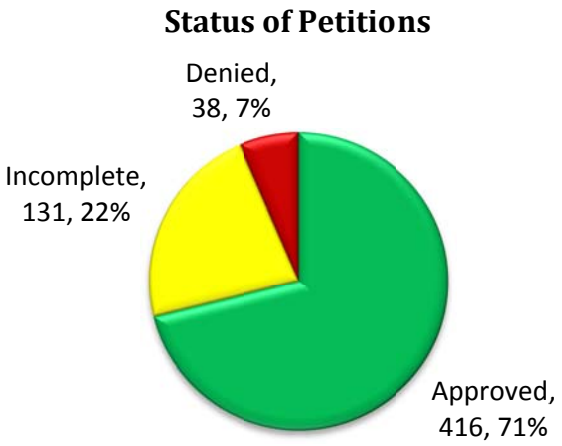
*Total number of unduplicated members.





Prior Authorization of Makena® (17-Hydroxyprogesterone Caproate)

There were 585 petitions submitted for this medication during fiscal year 2014. The following chart shows the status of the petitions.



Market News and Updates[1,2]

- Anticipated exclusivity expiration of Makena® (17-hydroxyprogesterone caproate): 2/2018
- The FDA released a statement in June 2012 regarding the compounding of hydroxyprogesterone caproate when a commercially available product (Makena®) is accessible. The FDA emphasized that the compounding of any drug should not exceed the scope of traditional pharmacy compounding, and the FDA generally prioritizes enforcement actions related to compounded drugs using a risk-based approach, giving the highest priority to pharmacies that compound products that are causing harm or that amount to health fraud.
    - There have not been any updates from the FDA regarding compounding of generic hydroxyprogesterone caproate; however, pharmacy compounding of the generic product has decreased.

Recommendations

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

[1] 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 12/16/14. Last accessed 12/17/14.
[2] FDA News & Events: Updated FDA Statement on Compounded Versions of hydroxyprogesterone caproate (the active ingredient in Makena®), 6/15/12. Available online at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm308546.htm. Last accessed 12/17/14.

Appendix K

Fiscal Year 2014 Annual Review of Gattex® (Teduglutide)

Oklahoma Health Care Authority
January 2015

Indication

Gattex® (Teduglutide [rDNA origin]) for injection is a glucagon-like peptide-2 (GLP-2) analog indicated for the treatment of adult patients with short bowel syndrome (SBS) who are dependent on parental support.

Current Prior Authorization Criteria

Gattex® (Teduglutide [rDNA origin]) Approval Criteria:

1. Member must have a diagnosis of severe short bowel syndrome; and
2. Require parenteral nutrition at least 3 times per week, every week, for the past 12 months, with
3. Documentation of all of the following:
    a. Prior use of supportive therapies such as anti-motility agents, proton pump inhibitors, bile acid sequestrants, and octreotide; and
    b. Colonoscopy within the previous 6 months, with removal of polyps if present; and
    c. Gastro-intestinal malignancy has been ruled out.
4. Initial approval will be for the duration of 3 months, after which time, prescriber must verify benefit of medication by documented reduction of at least 20% in parenteral support.
5. Subsequent approvals will be for the duration of a year.

Utilization of Gattex® (Teduglutide)

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

Prior Authorization of Gattex® (Teduglutide)

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

Market News and Updates[1]

Anticipated Patent Expiration of Gattex® (teduglutide [rDNA origin]): 11/2025

Recommendations

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

[1] 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 12/16/14. Last accessed 12/17/14.

Appendix L

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

FDA NEWS RELEASE

For Immediate Release: December 17th, 2014
FDA approves Xtoro to treat swimmer's ear

The U.S. Food and Drug Administration approved Xtoro (finafloxacin otic suspension), a new drug used to treat acute otitis externa, commonly known as swimmer's ear.
Acute otitis externa is an infection in the outer ear and ear canal, usually caused by bacteria in the ear canal. Activities in which the ear is underwater can create a moist environment where bacteria may sometimes grow. The infection causes inflammation of the ear canal leading to pain, swelling, redness of the ear and discharge from the ear.
Xtoro is an eardrop approved to treat acute otitis externa caused by Pseudomonas aeruginosa and Staphylococcus aureus. Xtoro is the newest drug belonging to the fluoroquinolone antimicrobial drug class to be approved by the FDA. It joins several other antibacterial drug products previously approved to treat ear infections.
Xtoro's safety and efficacy were primarily established in two clinical trials where 1,234 participants between the ages of 6 months and 85 years were randomly assigned to receive Xtoro or its vehicle (a solution without a fluoroquinolone). Clinical cure was achieved if the ear tenderness, redness and swelling were completely resolved.
Among 560 participants whose acute otitis externa was confirmed to be caused by Pseudomonas aeruginosa or Staphylococcus aureus, 70 percent who received Xtoro achieved clinical cure versus 37 percent who received the vehicle. In addition, Xtoro was superior to the vehicle for clearing the bacteria based on ear culture, and eased ear pain sooner than the vehicle.
The most common side effects reported in Xtoro-treated participants were itching of the ear (pruritis) and nausea.
Xtoro is manufactured Alcon Laboratories, Inc., based in Fort Worth, Texas.

FDA NEWS RELEASE

For Immediate Release: December 19th, 2014
FDA approves Viekira Pak to treat hepatitis C

The U.S. Food and Drug Administration approved Viekira Pak (ombitasvir, paritaprevir and ritonavir tablets co-packaged with dasabuvir tablets) to treat patients with chronic hepatitis C virus (HCV) genotype 1 infection, including those with a type of advanced liver disease called cirrhosis.
Hepatitis C is a viral disease that causes inflammation of the liver that can lead to reduced liver function, liver failure or liver cancer. Most people infected with HCV have no symptoms of the disease until liver damage becomes apparent, which may take decades. According to the Centers for Disease Control and Prevention, about 3.2 million Americans are infected with HCV, and without proper treatment, 15-30 percent of these people will go on to develop cirrhosis.
Viekira Pak contains three new drugs—ombitasvir, paritaprevir and dasabuvir—that work together to inhibit the growth of HCV. It also contains ritonavir, a previously approved drug, which is used to increase blood levels of paritaprevir. Viekira Pak can be used with or without ribavirin, but it is not recommended for patients whose liver is unable to function properly (decompensated cirrhosis).
Viekira Pak is the fourth drug product approved by the FDA in the past year to treat chronic HCV infection. The FDA approved Olysio (simeprevir) in November 2013, Sovaldi (sofosbuvir) in December 2013 and Harvoni (ledipasvir and sofosbuvir) in October 2014.
Viekira Pak's efficacy was evaluated in six clinical trials enrolling 2,308 participants with chronic HCV infection with and without cirrhosis. In different trials, participants were randomly assigned to receive Viekira Pak or placebo; Viekira Pak with or without ribavirin; or Viekira Pak with ribavirin for 12 or 24 weeks.
The trials were designed to measure whether the hepatitis C virus was no longer detected in the blood at least 12 weeks after finishing treatment (sustained virologic response, or SVR), indicating that a participant's HCV infection has been cured. Results from multiple populations, including those considered

difficult to treat, showed 91 to 100 percent of participants who received Viekira Pak at the recommended dosing achieved SVR. The recommended dosing for Viekira Pak is two ombitasvir, paritaprevir, ritonavir 12.5 milligrams (mg)/75 mg/50 mg tablets once daily and one dasabuvir 250 mg tablet twice daily.
The most common side effects reported in clinical trial participants were feeling tired, itching, feeling weak or lack of energy, nausea and trouble sleeping.
Viekira Pak is the eleventh new drug product with breakthrough therapy designation to receive FDA approval. The FDA can designate a drug as a breakthrough therapy at the request of the sponsor if preliminary clinical evidence indicates the drug may demonstrate a substantial improvement over available therapies for patients with serious or life-threatening diseases. Viekira Pak was reviewed under the FDA's priority review program, which provides for an expedited review of drugs that treat serious conditions and, if approved, would provide significant improvement in safety or effectiveness.
Viekira Pak is marketed by AbbVie Inc., based in North Chicago, Illinois.

FDA NEWS RELEASE

For Immediate Release: December 19th, 2014
FDA approves Lynparza to treat advanced ovarian cancer

The U.S. Food and Drug Administration granted accelerated approval to Lynparza (olaparib), a new drug treatment for women with advanced ovarian cancer associated with defective BRCA genes, as detected by an FDA-approved test.
The National Cancer Institute estimates that 21,980 American women will be diagnosed with and 14,270 will die from ovarian cancer in 2014.
Lynparza is a poly ADP-ribose polymerase (PARP) inhibitor that blocks enzymes involved in repairing damaged DNA. It is intended for women with heavily pretreated ovarian cancer that is associated with defective BRCA genes.
Lynparza is approved for patients with specific abnormalities in the BRCA gene and is an example of how a greater understanding of the underlying mechanisms of disease can lead to targeted, more personalized treatment.
The FDA approved Lynparza with a genetic test called BRACAnalysis CDx, a companion diagnostic that will detect the presence of mutations in the BRCA genes (gBRCAm) in blood samples from patients with ovarian cancer. The BRCA genes are involved with repairing damaged DNA and normally work to suppress tumor growth. Women with mutations resulting in defective BRCA genes are more likely to get ovarian cancer, and it is estimated that 10 to 15 percent of all ovarian cancer is associated with these hereditary BRCA mutations.
The FDA evaluated the BRACAnalysis CDx's safety and efficacy under the agency's premarket approval pathway used for high-risk medical devices. Until now, the manufacturer, a clinical laboratory, had been marketing this test, although not specifically for use as a companion diagnostic, without FDA approval as a laboratory developed test (LDT). The new test is approved as a companion diagnostic, specifically to identify patients with advanced ovarian cancer who may be candidates for treatment with Lynparza.
The FDA's approval of the BRACAnalysis CDx is based on data from the clinical study used to support approval of Lynparza. Blood samples from clinical trial participants were tested to validate the test's use for detecting BRCAmutations in this population.
Lynparza's efficacy was examined in a study where 137 participants with gBRCAm-associated ovarian cancer received the drug. The study was designed to measure objective response rate (ORR), or the percentage of participants who experienced partial shrinkage or complete disappearance of the tumor. Results showed 34 percent of participants experienced ORR for an average of 7.9 months.
Common side effects of Lynparza included nausea, fatigue, vomiting, diarrhea, distorted taste (dysgeusia), indigestion (dyspepsia), headache, decreased appetite, common cold-like symptoms (nasopharyngitis), cough, joint paint (arthralgia), musculoskeletal pain, muscle pain (myalgia), back pain, rash (dermatitis) and abdominal pain. Serious side effects included the development of myelodysplastic syndrome, a condition where the bone marrow is unable to produce enough functioning blood cells; acute myeloid leukemia, a bone marrow cancer; and lung inflammation.
The most common laboratory abnormalities were increased creatinine, increased average volume of red blood cells (mean corpuscular volume elevation), decreased red blood cell count (hemoglobin), decreased white blood cell count (lymphocytes and neutrophils) and decreased platelet levels.

In June, Lynparza was reviewed by the FDA's Oncologic Drugs Advisory Committee for potential use as maintenance therapy (treatment given to keep cancer from returning). The committee advised the agency in a vote of 11 to 2 that the data did not support Lynparza's accelerated approval for this use. After the meeting, the company submitted additional information supporting Lynparza's use for a different use: in patients with gBRCAm-associated ovarian cancer who have received three or more chemotherapy treatments.

The FDA is approving Lynparza under the agency's accelerated approval program, which allows approval of a drug to treat a serious or life-threatening disease based on clinical data showing the drug has an effect on a surrogate endpoint reasonably likely to predict clinical benefit to patients. This program provides earlier patient access to promising new drugs while the company conducts confirmatory clinical trials. Lynparza's application 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, if approved, would offer significant improvement compared to marketed products.

BRACAnalysis CDx's application was reviewed under the FDA's priority review program for devices, which provides for priority review of devices that meet certain criteria, including that the devices are intended to treat or diagnose a life-threatening or irreversibly debilitating disease or condition and, if approved, would offer significant, clinically meaningful advantages compared to marketed products.

Lynparza is marketed by AstraZeneca Pharmaceuticals, based in Wilmington, Delaware. BRACAnalysis CDx is manufactured by and performed at Salt Lake City, Utah-based Myriad Genetic Laboratories, Inc.

FDA NEWS RELEASE

For Immediate Release: December 19th, 2014

FDA approves new antibacterial drug Zerbaxa

The U.S. Food and Drug Administration approved Zerbaxa (ceftolozane/tazobactam), a new antibacterial drug product, to treat adults with complicated intra-abdominal infections (cIAI) and complicated urinary tract infections (cUTI).

Zerbaxa is a combination product containing ceftolozane, a cephalosporin antibacterial drug, and tazobactam, a beta-lactamase inhibitor. Zerbaxa is used to treat cUTI, including kidney infection (pyelonephritis). It is used in combination with metronidazole to treat cIAI.

Zerbaxa is the fourth new antibacterial drug approved by the FDA this year. The agency approved Dalvance (dalbavancin) in May, Sivextro (tedizolid) in June and Orbactiv (oritavancin) in August.

Zerbaxa is the fourth new antibacterial drug product designated as a Qualified Infectious Disease Product (QIDP) to receive FDA approval. Under the Generating Antibiotic Incentives Now (GAIN) title of the FDA Safety and Innovation Act, Zerbaxa was granted QIDP designation because it is an antibacterial or antifungal human drug intended to treat a serious or life-threatening infection.

As part of its QIDP designation, Zerbaxa was given priority review, which provides an expedited review of the drug's application. The QIDP designation also qualifies Zerbaxa for an additional five years of marketing exclusivity to be added to certain exclusivity periods already provided by the Food, Drug and Cosmetic Act.

Zerbaxa's efficacy to treat cIAI in combination with metronidazole was established in a clinical trial with a total of 979 adults. Participants were randomly assigned to receive Zerbaxa plus metronidazole or meropenem, an FDA-approved antibacterial drug. Results showed Zerbaxa plus metronidazole was effective for the treatment of cIAI.

The efficacy of Zerbaxa to treat cUTI was established in a clinical trial where 1,068 adults were randomly assigned to receive Zerbaxa or levofloxacin, an antibacterial drug approved by the FDA to treat cUTI. Zerbaxa demonstrated it was effective in treating cUTI.

The Zerbaxa label includes a warning about decreased efficacy seen in patients with renal impairment. The most common side effects identified in the clinical trials were nausea, diarrhea, headache and fever (pyrexia).

Zerbaxa and Sivextro are marketed by Cubist Pharmaceuticals, based in Lexington, Massachusetts. Dalvance is marketed by Chicago-based Durata Therapeutics, and Orbactiv is marketed by Parsippany, New Jersey-based The Medicines Company.

FDA NEWS RELEASE

For Immediate Release: December 22nd, 2014

FDA approves Rapivab to treat flu infection

On December 19, the U.S. Food and Drug Administration approved Rapivab (peramivir) to treat influenza infection in adults.

Flu infections can range from mild to severe and can sometimes lead to hospitalization and death. According to the Centers for Disease Control and Prevention (CDC), 5-20 percent of the American population gets the flu and more than 200,000 people are hospitalized from seasonal flu-related complications each year.

Rapivab is an inhibitor of influenza virus neuraminidase, an enzyme that releases viral particles from infected cells. Neuraminidase inhibitors are commonly used to treat flu infection. Rapivab is the first neuraminidase inhibitor approved for intravenous (IV) administration and is administered as a single IV dose. It is intended for patients 18 years and older who have acute uncomplicated influenza and have shown symptoms of flu for no more than two days.

Other neuraminidase inhibitors approved by the FDA to treat flu include oseltamivir, administered orally, and zanamivir, which is inhaled. Older antiviral drugs for flu, amantadine and rimantadine, are no longer recommended by CDC because circulating influenza strains are resistant to these drugs.

Rapivab's efficacy was established in 297 participants with confirmed influenza who were randomly assigned to receive Rapivab 300 milligrams (mg), Rapivab 600 mg or placebo. Overall, participants receiving Rapivab 600 mg had their combined influenza symptoms alleviated 21 hours sooner, on average, than those receiving placebo, which is consistent with other drugs in the same class. Those receiving Rapivab 600 mg also recovered to normal temperature approximately 12 hours sooner compared to placebo. Supportive trials confirmed these findings. However, efficacy could not be established in patients with serious influenza requiring hospitalization.

Common side effects seen in Rapivab-treated participants include diarrhea. Rare but serious side effects include serious skin or hypersensitivity reactions such as Stevens-Johnson syndrome and erythema multiforme. Patients with influenza may be at an increased risk of hallucinations, delirium and abnormal behavior early in their illness and should be monitored for abnormal behavior. These events have been reported with neuraminidase inhibitor drugs, but it is not clear that the drug caused the abnormal behavior.

Rapivab and other antiviral drugs used to treat flu are not substitutes for early, annual flu vaccination, as recommended by CDC's Advisory Committee on Immunization Practices. CDC recommends all persons ages 6 months and older receive an annual flu vaccine.

Rapivab is manufactured by BioCryst Pharmaceuticals, based in Durham, North Carolina.

FDA NEWS RELEASE

For Immediate Release: December 23rd, 2014

FDA approves weight-management drug Saxenda

The U.S. Food and Drug Administration approved Saxenda (liraglutide [rDNA origin] injection) as a treatment option for chronic weight management in addition to a reduced-calorie diet and physical activity. The drug is approved for use in adults with a body mass index (BMI) of 30 or greater (obesity) or adults with a BMI of 27 or greater (overweight) who have at least one weight-related condition such as hypertension, type 2 diabetes, or high cholesterol (dyslipidemia).

BMI, which measures body fat based on an individual's weight and height, is used to define the obesity and overweight categories. According to the Centers for Disease Control and Prevention, more than one-third of adults in the United States are obese.

Saxenda, used responsibly in combination with a healthy lifestyle that includes a reduced-calorie diet and exercise, provides an additional treatment option for chronic weight management for people who are obese or are overweight and have at least one weight-related comorbid condition.

Saxenda is a glucagon-like peptide-1 (GLP-1) receptor agonist and should not be used in combination with any other drug belonging to this class, including Victoza, a treatment for type 2 diabetes. Saxenda and Victoza contain the same active ingredient (liraglutide) at different doses (3 mg and 1.8 mg, respectively). However, Saxenda is not indicated for the treatment of type 2 diabetes, as the safety and efficacy of Saxenda for the treatment of diabetes has not been established.

The safety and effectiveness of Saxenda were evaluated in three clinical trials that included approximately 4,800 obese and overweight patients with and without significant weight-related conditions. All patients received counseling regarding lifestyle modifications that consisted of a reduced-calorie diet and regular physical activity.

Results from a clinical trial that enrolled patients without diabetes showed that patients had an average weight loss of 4.5 percent from baseline compared to treatment with a placebo at one year. In this trial, 62 percent of patients treated with Saxenda lost at least 5 percent of their body weight compared with 34 percent of patients treated with placebo. Results from another clinical trial that enrolled patients with type 2 diabetes showed that patients had an average weight loss of 3.7 percent from baseline compared to treatment with placebo at one year. In this trial, 49 percent of patients treated with Saxenda lost at least 5 percent of their body weight compared with 16 percent of patients treated with placebo.

Patients using Saxenda should be evaluated after 16 weeks to determine if the treatment is working. If a patient has not lost at least 4 percent of baseline body weight, Saxenda should be discontinued, as it is unlikely that the patient will achieve and sustain clinically meaningful weight loss with continued treatment.

Saxenda has a boxed warning stating that tumors of the thyroid gland (thyroid C-cell tumors) have been observed in rodent studies with Saxenda but that it is unknown whether Saxenda causes thyroid C-cell tumors, including a type of thyroid cancer called medullary thyroid carcinoma (MTC), in humans. Saxenda should not be used in patients with a personal or family history of MTC or in patients with multiple endocrine neoplasia syndrome type 2 (a disease in which patients have tumors in more than one gland in their body, which predisposes them to MTC).

Serious side effects reported in patients treated with Saxenda include pancreatitis, gallbladder disease, renal impairment, and suicidal thoughts. Saxenda can also raise heart rate and should be discontinued in patients who experience a sustained increase in resting heart rate.

In clinical trials, the most common side effects observed in patients treated with Saxenda were nausea, diarrhea, constipation, vomiting, hypoglycemia, and decreased appetite.

The FDA is requiring the following post-marketing studies for Saxenda:

- clinical trials to evaluate dosing, safety, and efficacy in pediatric patients;
- a study to assess potential effects on growth, sexual maturation, and central nervous system development and function in immature rats;
- an MTC case registry of at least 15 years duration to identify any increase in MTC incidence related to Saxenda; and
- an evaluation of the potential risk of breast cancer with Saxenda in ongoing clinical trials.

In addition, the cardiovascular safety of liraglutide is being investigated in an ongoing cardiovascular outcomes trial.

The FDA approved Saxenda with a Risk Evaluation and Mitigation Strategy (REMS), which consists of a communication plan to inform health care professionals about the serious risks associated with Saxenda.

Saxenda is manufactured by Novo Nordisk A/S, Bagsvaerd, Denmark and is distributed by Novo Nordisk, Inc. Plainsboro, New Jersey.

FDA NEWS RELEASE

For Immediate Release: December 22nd, 2014

FDA approves Opdivo for advanced melanoma

The U.S. Food and Drug Administration granted accelerated approval to Opdivo (nivolumab), a new treatment for patients with unresectable or metastatic melanoma who no longer respond to other drugs.

Melanoma is the fifth most common type of cancer in the United States. It forms in the body's melanocyte cells, which develop the skin's pigment. The National Cancer Institute estimates that 76,100 Americans will be diagnosed with melanoma and 9,710 will die from the disease this year.

Opdivo works by inhibiting the PD-1 protein on cells, which blocks the body's immune system from attacking melanoma tumors. Opdivo is intended for patients who have been previously treated with ipilimumab and, for melanoma patients whose tumors express a gene mutation called BRAF V600, for use after treatment with ipilimumab and a BRAF inhibitor.

Other FDA-approved treatments for melanoma include ipilimumab (2011), peginterferon alfa-2b (2011), vemurafenib (2011), dabrafenib (2013), trametinib (2013) and pembrolizumab (2014). Opdivo is being

approved more than three months ahead of the prescription drug user fee goal date of March 30, 2015, the date when the agency was scheduled to complete its review of the application.
The FDA granted Opvido breakthrough therapy designation, priority review and orphan product designation because the sponsor demonstrated through preliminary clinical evidence that the drug may offer a substantial improvement over available therapies; the drug had the potential, at the time of the application was submitted, to be a significant improvement in safety or effectiveness in the treatment of a serious condition; and the drug is intended to treat a rare disease, respectively.
Opvido is being approved under the FDA's accelerated approval program, which allows approval of a drug to treat a serious or life-threatening disease based on clinical data showing the drug has an effect on a surrogate endpoint reasonably likely to predict clinical benefit to patients. This program provides earlier patient access to promising new drugs while the company conducts additional clinical trials to confirm the drug's benefit.
Opdivo's efficacy was demonstrated in 120 clinical trial participants with unresectable or metastatic melanoma. Results showed that 32 percent of participants receiving Opdivo had their tumors shrink (objective response rate). This effect lasted for more than six months in approximately one-third of the participants who experienced tumor shrinkage.
Opdivo's safety was evaluated in the overall trial population of 268 participants treated with Opdivo and 102 participants treated with chemotherapy. The most common side effects of the drug were rash, itching, cough, upper respiratory tract infections, and fluid retention (edema). The most serious side effects are severe immune-mediated side effects involving healthy organs, including the lung, colon, liver, kidneys and hormone-producing glands.
Opdivo is marketed by Princeton, New Jersey-based Bristol-Myers Squibb.

FDA NEWS RELEASE

For Immediate Release: December 4th, 2014
FDA approves Jakafi to treat patients with a chronic type of bone marrow disease

The U.S. Food and Drug Administration approved a new use for Jakafi (ruxolitinib) to treat patients with polycythemia vera, a chronic type of bone marrow disease. Jakafi is the first drug approved by the FDA for this condition.
Polycythemia vera occurs when too many red blood cells are made in the bone marrow. Patients may also experience an increase in white blood cells and platelets. An overabundance of blood cells can cause the spleen to swell, bleeding problems and blood clots in the veins near the skin surface (phlebitis). In addition, it puts patients at increased risk of stroke or heart attack.
Jakafi's new use is intended to treat polycythemia vera patients who have an inadequate response to or cannot tolerate hydroxyurea, another medicine often prescribed to reduce the number of red blood cells and platelets in the blood. Jakafi works by inhibiting enzymes called Janus Associated Kinase (JAK) 1 and 2 that are involved in regulating blood and immunological functioning. The drug's approval to treat polycythemia vera will help decrease the occurrence of an enlarged spleen (splenomegaly) and the need for phlebotomy, a procedure to remove excess blood from the body.
Jakafi's safety and effectiveness to treat polycythemia vera were evaluated in a clinical study involving 222 participants who had the disease for at least 24 weeks, had an inadequate response to or could not tolerate hydroxyurea, had undergone a phlebotomy procedure and exhibited an enlarged spleen. Participants were randomly assigned to receive Jakafi or the best available therapy, as determined by the investigator on a participant-by-participant basis.
The study was designed to measure the reduced need for phlebotomy beginning at Week 8 and continuing through Week 32, in addition to at least 35 percent reduction in spleen volume at Week 32. Results showed 21 percent of Jakafi-treated participants experienced a reduction in the need for a phlebotomy and a reduction in spleen volume, compared to 1 percent of participants who received best available therapy.
The most common side effects associated with use of Jakafi in participants with polycythemia vera were low red blood cell counts (anemia) and low blood platelet counts (thrombocytopenia). The most common non-blood related side effects were dizziness, constipation and shingles.
The FDA reviewedJakafi's use for polycythemia vera under the agency's priority review program because, at the time the application was submitted, the drug demonstrated the potential to be a significant improvement in safety or effectiveness over available therapy in the treatment of a serious condition. Priority

review provides an expedited review of a drug's application. Jakafi also received orphan product designation because it is intended to treat a rare disease.
In 2011, the FDA approved Jakafi for treatment of patients with another bone marrow disorder, intermediate or high-risk myelofibrosis, including primary myelofibrosis, post-polycythemia vera myelofibrosis and post-essential thrombocythemia myelofibrosis.
Jakafi is marketed by Wilmington, Delaware-based Incyte Corp.

FDA NEWS RELEASE

For Immediate Release: December 12th, 2014

FDA expands approved use of Cyramza to treat aggressive non-small cell lung cancer

The U.S. Food and Drug Administration expanded the approved use of Cyramza (ramucirumab) to treat patients with metastatic non-small cell lung cancer (NSCLC).
The most common type of lung cancer, NSCLC occurs when cancer cells form in the tissues of the lung. The National Cancer Institute estimates that 224,210 Americans will be diagnosed and 159,260 will die from lung cancer in 2014.
Cyramza works by blocking the blood supply that fuels tumor growth. The drug is intended for patients whose tumor has grown (progressed) during or following treatment with platinum-based chemotherapy, and it is to be used in combination with docetaxel, another type of chemotherapy.
On April 21, the FDA approved Cyramza as a single agent to treat patients with advanced stomach cancer or gastroesophageal junction (GEJ) adenocarcinoma, a form of cancer located in the region where the esophagus joins the stomach. On November 5, the FDA expanded Cyramza's use to treat patients with advanced gastric or GEJ adenocarcinoma to include paclitaxel, another chemotherapy drug.
The approval of Cyramza plus docetaxel for metastatic NSCLC is based on a clinical study of 1,253 participants with previously treated and progressive lung cancer. Study participants were randomly assigned to receive Cyramza plus docetaxel or a placebo plus docetaxel. Treatment was given until disease progression or development of intolerable side effects.The trial was designed to measure overall survival, the length of time a participant lived before death. Results showed that half of the participants treated with Cyramza plus docetaxel survived an average of 10.5 months from the start of treatment, compared to an average of 9.1 months from the start of treatment for half of the participants who received placebo plus docetaxel.
The most common side effects associated with Cyramza plus docetaxel observed in the clinical study included a decrease in infection-fighting white blood cells called neutrophils (neutropenia) fatigue and inflammation of the lining of the mouth (stomatitis). Cyramza can cause severe bleeding, blood clots, elevation in blood pressure and may impair wound healing.
The FDA reviewed Cyramza's application for this new use under the agency's priority review program, which provides for an expedited review of drugs that are intended to treat a serious disease or condition and, if approved, would offer significant improvement compared to marketed products.
Cyramza is marketed by Indianapolis-based Eli Lilly.

Safety Announcements

FDA Drug Safety Communication: FDA reporting mental health drug ziprasidone (Geodon) associated with rare but potentially fatal skin reactions

[December 11th, 2014] The U.S. Food and Drug Administration (FDA) is warning that the antipsychotic drug ziprasidone (marketed under the brand name, Geodon, and its generics) is associated with a rare but serious skin reaction that can progress to affect other parts of the body. A new warning has been added to the Geodon drug label to describe the serious condition known as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS). Patients who have a fever with a rash and/or swollen lymph glands should seek urgent medical care. Health care professionals should immediately stop treatment with ziprasidone if DRESS is suspected.
Ziprasidone is an antipsychotic drug used to treat the serious mental health disorders schizophrenia and bipolar I disorder. Ziprasidone helps restore certain natural substances in the brain and can decrease hallucinations, delusions, other psychotic symptoms, and mania. To work properly, ziprasidone should be taken every day as prescribed. Patients should not stop taking their medicine or change their dose without first talking to their health care professional.

DRESS may start as a rash that can spread to all parts of the body. It can include fever, swollen lymph nodes, and inflammation of organs such as the liver, kidney, lungs, heart, or pancreas. DRESS also causes a higher-than-normal number of a particular type of white blood cell called eosinophils in the blood. DRESS can lead to death.
FDA reviewed information from six patients in whom the signs and symptoms of DRESS appeared between 11 and 30 days after ziprasidone treatment was started. None of these patients died. Based on this information, FDA required the manufacturer of Geodon to add a new warning for DRESS to the Warnings and Precautions section of the drug labels for the capsule, oral suspension, and injection formulations.

Current Drug Shortages Index (as of January 6th, 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[12]	***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***
Cyanocobalamin (Vitamin B12) Injection	***Currently in Shortage***
Daunorubicin Hydrochloride Solution for Injection	***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***
Dihydroergotamine Mesylate 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)[13]	***Currently in Shortage***
Epinephrine Injection	***Currently in Shortage***
Erythrocin Lactobionate Lyophilized Powder for Injection	***Currently in Shortage***
Famotidine Injection	***Currently in Shortage***
Fentanyl Citrate (Sublimaze) Injection	***Currently in Shortage***
Fluorescein Sodium Injection	***Currently in Shortage***
Haloperidol Lactate Injection	***Currently in Shortage***
Indigo Carmine Injection	***Currently in Shortage***
Irrigation Solutions	***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***
Methylin Chewable Tablets	***Currently in Shortage***
Methylphenidate Hydrochloride ER Capsules/Tablets[14]	***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***
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***
Succinylcholine (Anectine, Quelicin) Injection	***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 Solution for 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***
Verapamil Hydrochloride Injection, USP	***Currently in Shortage***
Zinc Injection	***Currently in Shortage***