BRIAN SANDOVAL
Governor

STATE OF NEVADA
DEPARTMENT OF HEALTH AND HUMAN SERVICES
DIVISION OF HEALTH CARE FINANCING AND POLICY
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Director

MARTA JENSEN
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NOTICE OF PUBLIC MEETING – PHARMACY AND THERAPEUTICS COMMITTEE

AGENDA

Date of Posting:	**xxxxx**
Date of Meeting:	**Thursday, March 24, 2016 at 1:00 PM**
Name of Organization:	**The State of Nevada, Department of Health and Human Services, Division of Health Care Financing and Policy (DHCFP), Pharmacy and Therapeutics Committee.**
Place of Meeting:	**Spring Preserve** **Desert Living Center** **333 S. Valley View Blvd** **Las Vegas, NV 89107** **Phone: (702) 822-7700** **Please check with staff to verify room location** **A visual and audio feed will also be broadcast via the internet for those who are unable to attend in person. See below for details.**
Webinar Event:	**https://catamaranrx.webex.com/catamaranrx/onstage/g.php?MTID=e8b6885a729934e824206461dc7b6bbd5** **Or** **www.webex.com, select "Join", enter Meeting Number 748 759 611, your name and email and then select, "Join"**
Event Number:	**748 759 611** **Follow the instructions that appear on your screen to join the teleconference. Audio will be broadcast over the internet (VoIP).**

Reasonable efforts will be made to assist and accommodate physically challenged persons desiring to attend the meeting. Please call Tanya Benitez at: 775-684-3722 or email Tanya.Benitez@dhcfp.nv.gov in advance, but no later than two working days prior to the meeting, so that arrangements may be conveniently made.

Items may be taken out of order.
Items may be combined for consideration by the public body.
Items may be pulled or removed from the agenda at any time.

Public comment is limited to 5 minutes per individual, organization, or agency, but may be extended at the discretion of the Chairperson.

AGENDA

1. **Call to Order and Roll Call**

2. **Public Comment**

   No action may be taken on a matter raised under this item of the agenda until the matter itself has been specifically included on the agenda as an item upon which action can be taken.

3. **Administrative**

   A. **For Possible Action:** Review and approve meeting Minutes from December 3, 2015

   B. Status Update by DHCFP
      1. Public Comment

4. **Established Drug Classes**

   A. Respiratory Long-Acting Anti-muscarinic/Long-Acting Beta-Agonist Combinations
      1. Public Comment
      2. Drug Class Review Presentation – OptumRx
      3. **For Possible Action**: Committee Discussion and Action
         a. Approve Clinical/Therapeutic Equivalency of Agents in Class
         b. Identify Exclusions/Exceptions for Certain Patient Groups

4. Presentation of Recommendations for Preferred Drug List (PDL) Inclusion by OptumRx and the Division of Health Care Financing and Policy
5. **For Possible Action**: Committee Discussion and Approval of Drugs for Inclusion on the PDL

B. Acne Agents: Topical, Benzoyl Peroxide, Antibiotics and Combination Products
1. Public Comment
2. Drug Class Review Presentation – OptumRx
3. **For Possible Action**: Committee Discussion and Action
   a. Approve Clinical/Therapeutic Equivalency of Agents in Class
   b. Identify Exclusions/Exceptions for Certain Patient Groups
4. Presentation of Recommendations for Preferred Drug List (PDL) Inclusion by OptumRx and the Division of Health Care Financing and Policy
5. **For Possible Action**: Committee Discussion and Approval of Drugs for Inclusion on the PDL

5. Proposed New Drug Classes

A. Ophthalmic Anti-infective/Anti-inflammatory Combinations
1. Public Comment
2. Drug Class Review Presentation – OptumRx
3. **For Possible Action**: Committee Discussion and Action
   a. Approve Clinical/Therapeutic Equivalency of Agents in Class
   b. Identify Exclusions/Exceptions for Certain Patient Groups
4. Presentation of Recommendations for Preferred Drug List (PDL) Inclusion by OptumRx and the Division of Health Care Financing and Policy
5. **For Possible Action**: Committee Discussion and Approval of Drugs for Inclusion on the PDL

B. Injectable Long-Acting Atypical Antipsychotics
1. Public Comment
2. Drug Class Review Presentation – OptumRx
3. **For Possible Action**: Committee Discussion and Action
   a. Approve Clinical/Therapeutic Equivalency of Agents in Class
   b. Identify Exclusions/Exceptions for Certain Patient Groups

4. Presentation of Recommendations for Preferred Drug List (PDL) Inclusion by OptumRx and the Division of Health Care Financing and Policy
5. **For Possible Action**: Committee Discussion and Approval of Drugs for Inclusion on the PDL

C. Oral Non-steroidal Anti-inflammatory Drugs (NSAIDs)
1. Public Comment
2. Drug Class Review Presentation – OptumRx
3. **For Possible Action**: Committee Discussion and Action
   a. Approve Clinical/Therapeutic Equivalency of Agents in Class
   b. Identify Exclusions/Exceptions for Certain Patient Groups
4. Presentation of Recommendations for Preferred Drug List (PDL) Inclusion by OptumRx and the Division of Health Care Financing and Policy
5. **For Possible Action**: Committee Discussion and Approval of Drugs for Inclusion on the PDL

6. Report by OptumRx on New Drugs to Market, New Generic Drugs to Market, and New Line Extensions

7. Closing Discussion

A. Public comments on any subject

B. Date and location of the next meeting.

1. Discussion of the date and time of the next meeting

C. Adjournment

This notice and agenda have been posted at http://dhcfp.nv.gov and http://notice.nv.gov

Notice of this meeting will be available on or after the date of this notice at the DHCFP Web site www.dhcfp.nv.gov, Carson City Central office and Las Vegas DHCFP. The agenda posting of this meeting can be viewed at the following locations: Nevada State Library; Carson City Library; Churchill County Library; Las Vegas Library; Douglas County Library; Elko County Library; Lincoln County Library; Lyon County Library; Mineral County Library; Tonopah Public Library; Pershing County Library; Goldfield Public Library; Eureka Branch Library; Humboldt County Library; Lander County Library; Storey County Library; Washoe County Library; and White Pine County Library and may be reviewed during normal business hours.

If requested in writing, a copy of the meeting materials will be mailed to you. Requests and/or written comments may be sent to Robyn Heddy at the Division of Health Care Financing and Policy, 1100 E. William Street, Suite 101, Carson City, NV 89701, at least 3 days before the public hearing.

All persons that have requested in writing to receive the Public Hearings agenda have been duly notified by mail or e-mail.

Preferred Products	PA Criteria	Non-Preferred Products
Analgesics		
Analgesic/Miscellaneous		
Neuropathic Pain/Fibromyalgia Agents		
DULOXETINE * GABAPENTIN LYRICA® * SAVELLA® * (Fibromyalgia only)	* PA required *No PA required for drugs in this class if ICD-10 - M79.1; M60.0-M60.9, M61.1.*	CYMBALTA® * GRALISE® LIDODERM® * HORIZANT®
Tramadol and Related Drugs		
TRAMADOL TRAMADOL/APAP		CONZIPR® NUCYNTA® RYZOLT® RYBIX® ODT TRAMADOL ER ULTRACET® ULTRAM® ULTRAM® ER
Opiate Agonists		
MORPHINE SULFATE SA TABS (ALL GENERIC EXTENDED RELEASE) QL FENTANYL PATCH QL	**PA required for Fentanyl Patch** **General PA Form:** https://www.medicaid.nv.gov/Downloads/provider/FA-59.pdf	AVINZA® QL BUTRANS® DOLOPHINE® DURAGESIC® PATCHES QL EXALGO® KADIAN® QL METHADONE METHADOSE® MS CONTIN® QL NUCYNTA® ER OPANA ER® OXYCODONE SR QL OXYMORPHONE SR XARTEMIS XR® QL ZOHYDRO ER® QL
Opiate Agonists - Abuse Deterrent		
EMBEDA®		HYSINGLA ER® OXYCONTIN® QL

Preferred Products	PA Criteria	Non-Preferred Products
Antihistamines		
H1 blockers		
Non-Sedating H1 Blockers		
CETIRIZINE D OTC CETIRIZINE OTC LORATADINE D OTC LORATADINE OTC	A two week trial of one of these drugs is required before a non- preferred drug will be authorized.	ALLEGRA® CLARITIN® CLARINEX® DESLORATADINE FEXOFENADINE SEMPREX® XYZAL®
Antiinfective Agents		
Aminoglycosides		
Inhaled Aminoglycosides		
BETHKIS® KITABIS® PAK TOBI PODHALER® TOBRAMYCIN NEBULIZER		
Antivirals		
Alpha Interferons		
PEGASYS® PEGASYS® CONVENIENT PACK PEG-INTRON® and REDIPEN		
Anti-hepatitis Agents		
Polymerase Inhibitors/Combination Products		
HARVONI® SOVALDI® VIEKIRA PAK®	**PA required: (see below)** http://dhcfp.nv.gov/uploadedFiles/dhcfpnvgov/content/Resources/AdminSupport/Manuals/MSMCh1200Packet6-11-15(1).pdf https://www.medicaid.nv.gov/Downloads/provider/Pharmacy_Announcement_Viekira_2015-0721.pdf	
Protease Inhibitors		
INCIVEK® VICTRELIS® OLYSIO®	**PA required** https://www.medicaid.nv.gov/Downloads/provider/FA-75.pdf	
Ribavirins		
RIBAVIRIN		RIBASPHERE RIBAPAK® MODERIBA® REBETOL®

Preferred Products	PA Criteria	Non-Preferred Products
Anti-Herpetic Agents		
ACYCLOVIR FAMVIR® VALCYCLOVIR		
Influenza Agents		
AMANTADINE TAMIFLU® RIMANTADINE RELENZA®		
Cephalosporins		
Second-Generation Cephalosporins		
CEFACLOR CAPS and SUSP CEFACLOR ER CEFUROXIME TABS and SUSP CEFPROZIL SUSP		CEFTIN® CECLOR® CECLOR CD® CEFZIL
Third-Generation Cephalosporins		
CEFDINIR CAPS and SUSP CEFPODOXIME TABS and SUSP		CEDAX® CAPS and SUSP CEFDITOREN OMNICEF® SPECTRACEF® SUPRAX® VANTIN®
Macrolides		
AZITHROMYCIN TABS/SUSP CLARITHROMYCIN TABS/SUSP ERYTHROMYCIN BASE ERYTHROMYCIN ESTOLATE ERYTHROMYCIN ETHYLSUCCINATE ERYTHROMYCIN STEARATE		BIAXIN® DIFICID® ZITHROMAX® ZMAX®
Quinolones		
Quinolones - 2nd Generation		
CIPROFLOXACIN TABS CIPRO® SUSP		FLOXIN® OFLOXACIN
Quinolones - 3rd Generation		
AVELOX® AVELOX ABC PACK® LEVOFLOXACIN		LEVAQUIN®

Preferred Products	PA Criteria	Non-Preferred Products
Autonomic Agents		
Sympathomimetics		
Self-Injectable Epinephrine		
AUVI-Q® * EPINEPHRINE® EPIPEN® EPIPEN JR.®	* PA required	ADRENACLICK® QL
Biologic Response Modifiers		
Immunomodulators		
Disease-Modifying Antirheumatic Agents		
ENBREL® HUMIRA®	Prior authorization is required for all drugs in this class https://www.medicaid.nv.gov/Downloads/provider/FA-61.pdf	ACTEMRA® CIMZIA® KINERET® REMICADE® SIMPONI® ORENCIA®
Multiple Sclerosis Agents		
Injectable		
AVONEX® AVONEX® ADMIN PACK BETASERON® COPAXONE® QL EXTAVIA® REBIF® QL TYSABRI®	*Trial of only one agent is required before moving to a non-preferred agent*	GLATOPA® LEMTRADA® PLEGRIDY®
Oral		
AUBAGIO® TECFIDERA®		GILENYA®
Specific Symptomatic Treatment		
AMPYRA® QL	PA required	

Preferred Products	PA Criteria	Non-Preferred Products
Cardiovascular Agents		
Antihypertensive Agents		
Angiotensin II Receptor Antagonists		
DIOVAN® DIOVAN HCTZ® LOSARTAN LOSARTAN HCTZ		ATACAND® AVAPRO® BENICAR® CANDESARTAN NEW COZAAR® NEW EDARBI® EDARBYCLOR® EPROSARTAN HYZAAR® NEW IRBESARTAN MICARDIS® TELMISARTAN TEVETEN® VALSARTAN NEW
Angiotensin-Converting Enzyme Inhibitors (ACE Inhibitors)		
BENAZEPRIL BENAZEPRIL HCTZ CAPTOPRIL CAPTOPRIL HCTZ ENALAPRIL ENALAPRIL HCTZ EPANED® £ LISINOPRIL LISINOPRIL HCTZ RAMIPRIL	£ PREFERRED FOR AGES 10 AND UNDER ǂ NONPREFERRED FOR OVER 10 YEARS OLD	ACCURETIC® EPANED® ǂ FOSINOPRIL MAVIK® MOEXIPRIL QUINAPRIL QUINARETIC® TRANDOLAPRIL UNIVASC®

Preferred Products	PA Criteria	Non-Preferred Products
Beta-Blockers		
ACEBUTOLOL ATENOLOL ATENOLOL/CHLORTH BETAXOLOL BISOPROLOL BISOPROLOL/HCTZ BYSTOLIC®* CARVEDILOL LABETALOL METOPROLOL (Regular Release) NADOLOL PINDOLOL PROPRANOLOL PROPRANOLOL/HCTZ SOTALOL TIMOLOL	*Restricted to ICD-10 codes J40-J48	SOTYLIZE®
Calcium-Channel Blockers		
AFEDITAB CR® AMLODIPINE CARTIA XT® DILTIA XT® DILTIAZEM ER DILTIAZEM HCL DYNACIRC CR® EXFORGE® EXFORGE HCT® FELODIPINE ER ISRADIPINE LOTREL® NICARDIPINE NIFEDIAC CC NIFEDICAL XL NIFEDIPINE ER NISOLDIPINE ER TAZTIA XT® VERAPAMIL VERAPAMIL ER		

Preferred Products	PA Criteria	Non-Preferred Products
Direct Renin Inhibitors		
TEKAMLO® TEKTURNA® TEKTURNA HCT® VALTURNA®		AMTURNIDE®
Vasodilators		
Inhaled		
VENTAVIS® TYVASO®		
Oral		
LETAIRIS® ORENITRAM® SILDENAFIL TRACLEER®		ADCIRCA® ADEMPAS® OPSUMIT® REVATIO ®
Antilipemics		
Bile Acid Sequestrants		
COLESTIPOL CHOLESTYRAMINE WELCHOL®		QUESTRAN®
Cholesterol Absorption Inhibitors		
ZETIA®		
Fibric Acid Derivatives		
FENOFIBRATE FENOFIBRIC GEMFIBROZIL LIPOFEN®		ANTARA® FENOGLIDE® FIBRICOR® LOFIBRA® TRICOR® TRIGLIDE® TRILIPIX®
HMG-CoA Reductase Inhibitors (Statins)		
ATORVASTATIN CRESTOR® QL FLUVASTATIN LOVASTATIN PRAVASTATIN SIMVASTATIN		ADVICOR® ALTOPREV® AMLODIPINE/ATORVASTATIN CADUET® LESCOL® LESCOL XL® LIPITOR® LIPTRUZET® LIVALO® MEVACOR® PRAVACHOL® SIMCOR® VYTORIN® ZOCOR®

Preferred Products	PA Criteria	Non-Preferred Products
Niacin Agents		
NIASPAN® (Brand only) NIACIN ER (ALL GENERICS)		NIACOR®
Omega-3 Fatty Acids		
LOVAZA® VASCEPA®		OMEGA-3-ACID OMTRYG®
Dermatological Agents		
Antipsoriatic Agents		
Topical Vitamin D Analogs		
CALCIPOTRIENE		CALCITENE® DOVONEX® CREAM SORILUX® TACLONEX® VECTICAL®
Topical Analgesics		
LIDOCAINE LIDOCAINE HC LIDOCAINE VISCOUS VOLTAREN® GEL		EMLA® FLECTOR® LIDODERM® QL LIDAMANTLE® PENNSAID®
Topical Antiinfectives		
Acne Agents: Topical, Benzoyl Peroxide, Antibiotics and Combination Products		
AZELEX® 20% cream BENZACLIN® BENZOYL PEROXIDE (2.5, 5 and 10% only) CLINDAMYCIN ERYTHROMYCIN/BENZOYL PEROXIDE SODIUM SULFACETAMIDE	PA required if over 21 years old	ACANYA DUAC CS® ERYTHROMYCIN CLINDAMYCIN/BENZOYL PEROXIDE GEL SODIUM SULFACETAMIDE/SULFUR
Impetigo Agents: Topical		
MUPIROCIN OINT		ALTABAX® CENTANY® MUPIROCIN CREAM
Topical Antifungals (onychomycosis)		
CICLOPIROX SOLN TERBINAFINE TABS	PA required	JUBLIA® KERYDIN® PENLAC® ITRACONAZOLE

Preferred Products	PA Criteria	Non-Preferred Products
Topical Antivirals		
ABREVA® DENAVIR® ZOVIRAX®, OINTMENT		
Topical Scabicides		
NATROBA® * NIX® PERMETHRIN RID® SKLICE®	* PA required	EURAX® LINDANE MALATHION OVIDE® ULESFIA®
Topical Antiinflammatory Agents		
Immunomodulators: Topical		
ELIDEL® QL PROTOPIC® QL	Prior authorization is required for all drugs in this class	TACROLIMUS NEW
Topical Antineoplastics		
Topical Retinoids		
RETIN-A MICRO®(Pump and Tube) TAZORAC® ZIANA®	Payable only for recipients up to age 21.	ADAPALENE GEL AND CREAM ATRALIN® AVITA® DIFFERIN® EPIDUO® TRETINOIN TRETIN-X® VELTIN®
Electrolytic and Renal Agents		
Phosphate Binding Agents		
CALCIUM ACETATE ELIPHOS® FOSRENOL® RENAGEL® RENVELA®		AURYXIA ® PHOSLO® PHOSLYRA® SEVELAMER CARBONATE VELPHORO®
Gastrointestinal Agents		
Antiemetics		
Miscellaneous		
Diclegis® Emend®		

Preferred Products	PA Criteria	Non-Preferred Products
Serotonin-receptor antagonists/Combo		
GRANISETRON QL ONDANSETRON QL	PA required for all medication in this class	AKYNZEO® ANZEMET® QL KYTRIL® QL SANCUSO® ZOFRAN® QL ZUPLENZ® QL
Antiulcer Agents		
H2 blockers		
FAMOTIDINE RANITIDINE RANITIDINE SYRUP*	*PA not required for < 12 years	
Proton Pump Inhibitors (PPIs)		
NEXIUM® CAPSULES NEXIUM® POWDER FOR SUSP* PANTOPRAZOLE	PA required if exceeding 1 per day *for children ≤ 12 yrs.	ACIPHEX® DEXILANT® LANSOPRAZOLE OMEPRAZOLE OTC TABS PREVACID® PRILOSEC® PRILOSEC® OTC TABS PROTONIX®
Gastrointestinal Anti-inflammatory Agents		
ASACOL®SUPP BALSALAZIDE® CANASA® DELZICOL® MESALAMINE ENEMA SUSP PENTASA® SULFASALAZINE DR SULFASALAZINE IR		APRISO® ASACOL HD® COLAZAL® GIAZO® LIALDA ®
Gastrointestinal Enzymes		
CREON® ZENPEP®		PANCREAZE® PANCRELIPASE PERTZYE® ULTRESA® VIOKACE®
Genitourinary Agents		
Benign Prostatic Hyperplasia (BPH) Agents		
5-Alpha Reductase Inhibitors		
AVODART® FINASTERIDE		JALYN® PROSCAR®

Preferred Products	PA Criteria	Non-Preferred Products
Alpha-Blockers		
DOXAZOSIN TAMSULOSIN TERAZOSIN		ALFUZOSIN CARDURA® FLOMAX® MINIPRESS® PRAZOSIN RAPAFLO® UROXATRAL®
Bladder Antispasmodics		
BETHANECHOL NEW OXYBUTYNIN TABS/SYRUP/ER TOVIAZ® VESICARE®		DETROL® DETROL LA® DITROPAN XL® ENABLEX® FLAVOXATE GELNIQUE® MYRBETRIQ® NEW OXYTROL® SANCTURA® TOLTERODINE TROSPIUM
Hematological Agents		
Anticoagulants		
Oral		
COUMADIN® ELIQUIS® * JANTOVEN® PRADAXA® * QL WARFARIN XARELTO ® *	* No PA required if approved Dx code transmitted on claim	SAVAYSA®
Injectable		
ARIXTRA® ENOXAPARIN FRAGMIN®		FONDAPARINUX INNOHEP® LOVENOX®
Erythropoiesis-Stimulating Agents		
ARANESP® QL PROCRIT® QL	PA required Quantity Limit	EPOGEN® QL OMONTYS® QL
Platelet Inhibitors		
AGGRENOX® ANAGRELIDE ASPIRIN BRILINTA® * QL CILOSTAZOL® CLOPIDOGREL DIPYRIDAMOLE	* PA required	ASPIRIN/DIPYRIDAMOLE NEW DURLAZA® NEW EFFIENT® * QL PLAVIX® ZONTIVITY®

Preferred Products	PA Criteria	Non-Preferred Products
Hormones and Hormone Modifiers		
Androgens		
ANDROGEL® ANDRODERM®	**PA required** **PA Form:** https://www.medicaid.nv.gov/Downloads/provider/FA-72.pdf	AXIRON® FORTESTA® NATESTO® STRIANT® TESTIM® TESTOSTERONE GEL VOGELXO®
Antidiabetic Agents		
Alpha-Glucosidase Inhibitors/Amylin analogs/Misc.		
ACARBOSE (Precose®) GLYSET® PRECOSE® SYMLIN® (PA required)		CYCLOSET®
Biguanides		
FORTAMET® GLUCOPHAGE® GLUCOPHAGE XR® METFORMIN EXT-REL (Glucophage XR®) GLUMETZA® METFORMIN (Glucophage®) RIOMET®		
Dipeptidyl Peptidase-4 Inhibitors		
JANUMET® JANUMET XR® JANUVIA® JENTADUETO® JUVISYNC® KOMBIGLYZE XR® ONGLYZA® TRADJENTA®		KAZANO® NESINA® OSENI®
Incretin Mimetics		
BYDUREON® * BYETTA® * VICTOZA® *	* PA required	TANZEUM® TRULICITY®

Preferred Products	PA Criteria	Non-Preferred Products
Insulins (Vials, Pens and Inhaled)		
APIDRA® HUMALOG® HUMULIN® LANTUS® LEVEMIR ® NOVOLIN® NOVOLOG®		AFREZZA® HUMALOG® U-200 TOUJEO SOLO® 300 IU/ML
Meglitinides		
NATEGLINIDE (Starlix®) PRANDIMET® PRANDIN® STARLIX®		
Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors		
FARXIGA® INVOKAMET® INVOKANA® XIGDUO XR®		GLYXAMBI® JARDIANCE® SYNJARDY®
Sulfonylureas		
AMARYL® CHLORPROPAMIDE DIABETA® GLIMEPIRIDE (Amaryl®) GLIPIZIDE (Glucotrol®) GLUCOTROL® GLUCOVANCE® GLIPIZIDE EXT-REL (Glucotrol XL®) GLIPIZIDE/METFORMIN (Metaglip®) GLYBURIDE MICRONIZED (Glynase®) GLYBURIDE/METFORMIN (Glucovance®) GLUCOTROL XL® GLYBURIDE (Diabeta®) GLYNASE® METAGLIP® TOLAZAMIDE TOLBUTAMIDE		

Preferred Products	PA Criteria	Non-Preferred Products
Thiazolidinediones		
ACTOPLUS MET XR® ACTOS® ACTOPLUS MET® AVANDAMET® AVANDARYL® AVANDIA® DUETACT®		
Pituitary Hormones		
Growth hormone modifiers		
GENOTROPIN® NORDITROPIN®	**PA required for entire class** https://www.medicaid.nv.gov/Downloads/provider/FA-67.pdf	HUMATROPE® NUTROPIN AQ® OMNITROPE® NUTROPIN® SAIZEN® SEROSTIM® SOMAVERT® TEV-TROPIN® ZORBTIVE®
Progestins for Cachexia		
MEGESTROL ACETATE, SUSP		MEGACE ES®
Musculoskeletal Agents		
Antigout Agents		
ALLOPURINOL		
Bone Resorption Inhibitors		
Bisphosphonates		
ALENDRONATE TABS FOSAMAX PLUS D®		ACTONEL® ALENDRONATE SOLUTION ATELVIA® BINOSTO® BONIVA® DIDRONEL® ETIDRONATE IBANDRONATE SKELID®
Nasal Calcitonins		
MIACALCIN®		FORTICAL® NEW CALCITONIN-SALMON NEW
Restless Leg Syndrome Agents		
PRAMIPEXOLE REQUIP XL ROPINIROLE		HORIZANT® MIRAPEX® MIRAPEX® ER REQUIP

	Preferred Products	PA Criteria	Non-Preferred Products
Skeletal Muscle Relaxants			
	BACLOFEN CHLORZOXAZONE CYCLOBENZAPRINE DANTROLENE METHOCARBAMOL METHOCARBAMOL/ASPIRIN ORPHENADRINE CITRATE ORPHENADRINE COMPOUND TIZANIDINE		
Neurological Agents			
Alzheimers Agents			
	DONEPEZIL DONEPEZIL ODT EXELON® PATCH EXELON® SOLN MEMANTINE NEW NAMENDA® XR TABS RIVASTIGMINE CAPS		ARICEPT® 23mg ARICEPT® GALANTAMINE GALANTAMINE ER NAMENDA® TABS NEW NAMZARIC® NEW RAZADYNE® RAZADYNE® ER
Anticonvulsants			
	BANZEL® CARBAMAZEPINE CARBAMAZEPINE XR CARBATROL ER® CELONTIN® DEPAKENE® DEPAKOTE ER® DEPAKOTE® DIVALPROEX SODIUM DIVALPROEX SODIUM ER EPITOL® ETHOSUXIMIDE FELBATOL® GABAPENTIN GABITRIL® KEPPRA® KEPPRA XR® LAMACTAL ODT® LAMACTAL XR® LAMICTAL® LAMOTRIGINE LEVETIRACETAM LYRICA®	PA required for members under 18 years old	APTIOM® FYCOMPA® OXTELLAR XR® POTIGA® QUDEXY XR® TROKENDI XR®

			Preferred Products	PA Criteria	Non-Preferred Products
			NEURONTIN® OXCARBAZEPINE SABRIL® STAVZOR® DR TEGRETOL® TEGRETOL XR® TOPAMAX® TOPIRAGEN® TOPIRAMATE (IR AND ER) TRILEPTAL® VALPROATE ACID VIMPAT® ZARONTIN® ZONEGRAN® ZONISAMIDE		
		Barbiturates			
			LUMINAL® MEBARAL® MEPHOBARBITAL SOLFOTON® PHENOBARBITAL MYSOLINE® PRIMIDONE	PA required for members under 18 years old	
		Benzodiazepines			
			CLONAZEPAM CLORAZEPATE DIASTAT® DIAZEPAM DIAZEPAM rectal soln KLONOPIN® TRANXENE T-TAB® VALIUM®	PA required for members under 18 years old	ONFI®
		Hydantoins			
			CEREBYX® DILANTIN® ETHOTOIN FOSPHENYTOIN PEGANONE® PHENYTEK® PHENYTOIN PRODUCTS	PA required for members under 18 years old	

Preferred Products	PA Criteria	Non-Preferred Products
Anti-Migraine Agents		
Serotonin-Receptor Agonists		
RELPAX® RIZATRIPTAN ODT SUMATRIPTAN NASAL SPRAY SUMATRIPTAN INJECTION SUMATRIPTAN TABLET	PA required for exceeding Quantity Limit	AMERGE® AXERT® FROVA® IMITREX® MAXALT® TABS MAXALT® MLT NARATRIPTAN SUMAVEL® TREXIMET® ZECUITY® TRANSDERMAL ZOMIG® ZOMIG® ZMT
Antiparkinsonian Agents		
Non-ergot Dopamine Agonists		
PRAMIPEXOLE ROPINIROLE ROPINIROLE ER		MIRAPEX® MIRAPEX® ER NEUPRO® REQUIP® REQUIP XL®
Ophthalmic Agents		
Antiglaucoma Agents		
Carbonic Anhydrase Inhibitors/Beta-Blockers		
ALPHAGAN P® AZOPT® BETAXOLOL BETOPTIC S® BRIMONIDINE CARTEOLOL COMBIGAN® DORZOLAM DORZOLAM / TIMOLOL LEVOBUNOLOL METIPRANOLOL SIMBRINZA® TIMOLOL DROPS/ GEL SOLN		ALPHAGAN® BETAGAN® BETOPTIC ® COSOPT® COSOPT PF® OCUPRESS® OPTIPRANOLOL® TIMOPTIC® TIMOPTIC XE® TRUSOPT®
Ophthalmic Prostaglandins		
LATANOPROST TRAVATAN® TRAVATAN Z® ZIOPTAN®		LUMIGAN® XALATAN®

Preferred Products	PA Criteria	Non-Preferred Products
Ophthalmic Antihistamines		
ALAWAY® BEPREVE® KETOTIFEN NEW PAZEO® NEW PATADAY® ZADITOR OTC®		AZELASTINE NEW ALOMIDE NEW ALOCRIL NEW ELESTAT® EMADINE® EPINASTINE NEW LASTACRAFT® OPTIVAR® PATADAY® NEW PATANOL®
Ophthalmic Antiinfectives		
Ophthalmic Macrolides		
ERYTHROMYCIN OINTMENT		
Ophthalmic Quinolones		
BESIVANCE® CIPROFLOXACIN MOXEZA® OFLOXACIN® VIGAMOX®		CILOXAN® ZYMAXID®
Ophthalmic Anti-Inflammatory Agents		
Ophthalmic Corticosteroids		
ALREX® DEXAMETHASONE DUREZOL® FLUOROMETHOLONE LOTEMAX® PREDNISOLONE		FLAREX® FML® FML FORTE® MAXIDEX® OMNIPRED® PRED FORTE® PRED MILD® VEXOL®
Ophthalmic Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)		
DICLOFENAC FLURBIPROFEN ILEVRO® NEW KETOROLAC NEW NEVANAC®		ACULAR® NEW ACULAR LS® NEW ACUVAIL® BROMDAY® BROMFENAC® PROLENSA®
Otic Agents		
Otic Antiinfectives		
Otic Quinolones		
CIPRODEX® OFLOXACIN		

Preferred Products	PA Criteria	Non-Preferred Products
Psychotropic Agents		
ADHD Agents		
ADDERALL XR® AMPHETAMINE SALT COMBO IR DEXMETHYLPHENIDATE DEXTROAMPHETAMINE SA TAB DEXTROAMPHETAMINE TAB DEXTROSTAT® FOCALIN XR® INTUNIV® METADATE CD® METHYLIN® METHYLIN ER® METHYLPHENIDATE METHYLPHENIDATE ER (All forms generic extended release) METHYLPHENIDATE SOL PROCENTRA® QUILLIVANT® XR SUSP RITALIN LA® STRATTERA® VYVANSE®	**PA required for entire class** **Children's Form:** https://www.medicaid.nv.gov/Downloads/provider/FA-69.pdf **Adult Form:** https://www.medicaid.nv.gov/Downloads/provider/FA-68.pdf	ADDERALL® AMPHETAMINE SALT COMBO XR CONCERTA® DAYTRANA® DESOXYN® DEXEDRINE® DEXTROAMPHETAMINE SOLUTION FOCALIN® KAPVAY® METADATE ER® RITALIN®
Antidepressants		
Other		
BUPROPION BUPROPION SR BUPROPION XL DULOXETINE NEW MIRTAZAPINE MIRTAZAPINE RAPID TABS PRISTIQ® TRAZODONE VENLAFAXINE (ALL FORMS)	PA required for members under 18 years old	APLENZIN® BRINTELLIX® CYMBALTA®(PA not required for certain ICD-10) NEW DESVENLAFAXINE FUMARATE EFFEXOR® (ALL FORMS) FETZIMA® FORFIVO XL® KHEDEZLA® VIIBRYD® WELLBUTRIN®

Preferred Products	PA Criteria	Non-Preferred Products
Selective Serotonin Reuptake Inhibitors (SSRIs)		
CITALOPRAM ESCITALOPRAM FLUOXETINE PAROXETINE PEXEVA® SERTRALINE	PA required for members under 18 years old	CELEXA® FLUVOXAMINE QL LEXAPRO® LUVOX® PAXIL® PROZAC® SARAFEM® ZOLOFT®
Antipsychotics		
Atypical Antipsychotics		
ABILIFY® CLOZAPINE FANAPT® LATUDA® OLANZAPINE QUETIAPINE RISPERIDONE SAPHRIS® SEROQUEL XR® ZIPRASIDONE	**PA required for Ages under 18 years old** **PA Form:** https://www.medicaid.nv.gov/Downloads/provider/FA-70.pdf	ARIPIPRAZOLE NEW CLOZARIL® FAZACLO® GEODON® INVEGA® PALIPERIDONE NEW REXULTI® NEW RISPERDAL® SEROQUEL® ZYPREXA®
Anxiolytics, Sedatives, and Hypnotics		
ESTAZOLAM FLURAZEPAM ROZEREM® * TEMAZEPAM TRIAZOLAM ZOLPIDEM	*(PA not required for ICD-10 code G47.0 and F51.0)	AMBIEN® AMBIEN CR® BELSOMRA® DORAL® ESZOPICLONE EDLUAR® HETLIOZ® INTERMEZZO® LUNESTA® SILENOR® SOMNOTE®
	PA required for members under 18 years old	SONATA® ZALEPLON ZOLPIDEM CR ZOLPIMIST®
Psychostimulants		
Narcolepsy Agents		
Provigil® *	* (No PA required for ICD-10 code G47.4)	MODAFINIL NUVIGIL® XYREM®

Preferred Products	PA Criteria	Non-Preferred Products
Respiratory Agents		
Nasal Antihistamines		
ASTEPRO® DYMISTA® PATANASE®		AZELASTINE OLOPATADINE NEW
Respiratory Antiinflammatory Agents		
Leukotriene Receptor Antagonists		
MONTELUKAST ZAFIRLUKAST		ACCOLATE® SINGULAIR®
Respiratory Corticosteroids		
AEROSPAN HFA® ASMANEX® BUDESONIDE NEBS* FLOVENT DISKUS® QL FLOVENT HFA® QL PULMICORT FLEXHALER® QVAR®	*No PA required if < 4 years old	ALVESCO® ARNUITY ELLIPTA® PULMICORT RESPULES®*
Nasal Corticosteroids		
FLUTICASONE NASONEX®		BECONASE AQ® FLONASE® FLUNISOLIDE NASACORT AQ® OMNARIS® QNASL® RHINOCORT AQUA® TRIAMCINOLONE ACETONIDE VERAMYST® ZETONNA®
Phosphodiesterase Type 4 Inhibitors		
DALIRESP® QL	PA required	
Respiratory Antimuscarinics		
COMBIVENT RESPIMAT® IPRATROPIUM/ALBUTEROL NEBS QL IPRATROPIUM NEBS SPIRIVA®	Only one agent per 30 days is allowed	INCRUSE ELLIPTA ® SPIRIVA RESPIMAT® TUDORZA®
Respiratory Beta-Agonists		
Long-Acting Respiratory Beta-Agonist		
ARCAPTA NEOHALER® FORADIL® SEREVENT DISKUS® QL		BROVANA® PERFOROMIST NEBULIZER® STRIVERDI RESPIMAT®

Preferred Products	PA Criteria	Non-Preferred Products
Short-Acting Respiratory Beta-Agonist		
ALBUTEROL NEB/SOLN PROVENTIL® HFA PROAIR® HFA XOPENEX® HFA* QL XOPENEX® Solution* QL	* PA required	LEVALBUTEROL MAXAIR AUTOHALER® PROAIR RESPICLICK® NEW VENTOLIN HFA®
Respiratory Corticosteriod/Long-Acting Beta-Agonist Combinations		
ADVAIR DISKUS® ADVAIR HFA® DULERA® SYMBICORT®		BREO ELLIPTA®
Respiratory Long-Acting Antimuscarinic/Long-Acting Beta-Agonist Combinations		
ANORO ELLIPTA® STIOLTO RESPIMAT®		
Toxicology Agents		
Antidotes		
Opiate Antagonists		
EVZIO ® NALOXONE NARCAN® NASAL SPRAY		
Substance Abuse Agents		
Mixed Opiate Agonists/Antagonists		
BUNAVAIL® SUBOXONE® ZUBSOLV®	PA required for class	BUPRENORPHINE/NALOXONE

2. Standard Preferred Drug List Exception Criteria
Drugs that have a “non-preferred” status are a covered benefit for recipients if they meet the coverage criteria.
a. Coverage and Limitations
1. Allergy to all preferred medications within the same class;
2. Contraindication to or drug-to-drug interaction with all preferred medications within the same class;
3. History of unacceptable/toxic side effects to all preferred medications within the same class;
4. Therapeutic failure of two preferred medications within the same class.
5. If there are not two preferred medications within the same class therapeutic failure only needs to occur on the one preferred medication;
6. An indication which is unique to a non-preferred agent and is supported by peer-reviewed literature or a FDA-approved indication;
7. Antidepressant Medication – Continuity of Care.
Recipients discharged from acute mental health facilities on a nonpreferred antidepressant will be allowed to continue on that drug for up to 90 days following discharge. After 90 days, the recipient must meet one of the above five (5) PDL Exception Criteria; or
8. For atypical or typical antipsychotic, anticonvulsant and antidiabetic medications the recipient demonstrated therapeutic failure on one preferred agent.
b. Prior Authorization forms are available at:
http://www.medicaid.nv.gov/providers/rx/rxforms/aspx.

NRS 422.4025 List of preferred prescription drugs used for Medicaid program; list of drugs excluded from restrictions; role of Pharmacy and Therapeutics Committee; availability of new pharmaceutical products and products for which there is new evidence. [Effective through June 30, 2015.]

1. The Department shall, by regulation, develop a list of preferred prescription drugs to be used for the Medicaid program.

2. The Department shall, by regulation, establish a list of prescription drugs which must be excluded from any restrictions that are imposed on drugs that are on the list of preferred prescription drugs established pursuant to subsection 1. The list established pursuant to this subsection must include, without limitation:

(a) Prescription drugs that are prescribed for the treatment of the human immunodeficiency virus or acquired immunodeficiency syndrome, including, without limitation, protease inhibitors and antiretroviral medications;

(b) Antirejection medications for organ transplants;

(c) Antihemophilic medications; and

(d) Any prescription drug which the Committee identifies as appropriate for exclusion from any restrictions that are imposed on drugs that are on the list of preferred prescription drugs.

3. The regulations must provide that the Committee makes the final determination of:

(a) Whether a class of therapeutic prescription drugs is included on the list of preferred prescription drugs and is excluded from any restrictions that are imposed on drugs that are on the list of preferred prescription drugs;

(b) Which therapeutically equivalent prescription drugs will be reviewed for inclusion on the list of preferred prescription drugs and for exclusion from any restrictions that are imposed on drugs that are on the list of preferred prescription drugs;

(c) Which prescription drugs should be excluded from any restrictions that are imposed on drugs that are on the list of preferred prescription drugs based on continuity of care concerning a specific diagnosis, condition, class of therapeutic prescription drugs or medical specialty; and

(d) The criteria for prescribing an atypical or typical antipsychotic medication, anticonvulsant medication or antidiabetic medication that is not on the list of preferred drugs to a patient who experiences a therapeutic failure while taking a prescription drug that is on the list of preferred prescription drugs.

4. Except as otherwise provided in this subsection, the list of preferred prescription drugs established pursuant to subsection 1 must include, without limitation, every therapeutic prescription drug that is classified as an anticonvulsant medication or antidiabetic medication that was covered by the Medicaid program on June 30, 2010. If a therapeutic prescription drug that is included on the list of preferred prescription drugs pursuant to this subsection is prescribed for a clinical indication other than the indication for which it was approved as of June 30, 2010, the Committee shall review the new clinical indication for that drug pursuant to the provisions of subsection 5.

5. The regulations adopted pursuant to this section must provide that each new pharmaceutical product and each existing pharmaceutical product for which there is new clinical evidence supporting its inclusion on the list of preferred prescription drugs must be made available pursuant to the Medicaid program with prior authorization until the Committee reviews the product or the evidence.

6. The Medicaid program must make available without prior authorization atypical and typical antipsychotic medications that are prescribed for the treatment of a mental illness, anticonvulsant medications and antidiabetic medications for a patient who is receiving services pursuant to Medicaid if the patient:

(a) Was prescribed the prescription drug on or before June 30, 2010, and takes the prescription drug continuously, as prescribed, on and after that date;

(b) Maintains continuous eligibility for Medicaid; and

(c) Complies with all other requirements of this section and any regulations adopted pursuant thereto.

(Added to NRS by 2003, 1317; A 2010, 26th Special Session, 36; 2011, 985)

NRS 422.4025 List of preferred prescription drugs used for Medicaid program; list of drugs excluded from restrictions; role of Pharmacy and Therapeutics Committee; availability of new pharmaceutical products and products for which there is new evidence. [Effective July 1, 2015.]

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2. The Department shall, by regulation, establish a list of prescription drugs which must be excluded from any restrictions that are imposed on drugs that are on the list of preferred prescription drugs established pursuant to subsection 1. The list established pursuant to this subsection must include, without limitation:

(a) Atypical and typical antipsychotic medications that are prescribed for the treatment of a mental illness of a patient who is receiving services pursuant to Medicaid;

(b) Prescription drugs that are prescribed for the treatment of the human immunodeficiency virus or acquired immunodeficiency syndrome, including, without limitation, protease inhibitors and antiretroviral medications;

(c) Anticonvulsant medications;

(d) Antirejection medications for organ transplants;

(e) Antidiabetic medications;

(f) Antihemophilic medications; and

(g) Any prescription drug which the Committee identifies as appropriate for exclusion from any restrictions that are imposed on drugs that are on the list of preferred prescription drugs.

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(a) Whether a class of therapeutic prescription drugs is included on the list of preferred prescription drugs and is excluded from any restrictions that are imposed on drugs that are on the list of preferred prescription drugs;

(b) Which therapeutically equivalent prescription drugs will be reviewed for inclusion on the list of preferred prescription drugs and for exclusion from any restrictions that are imposed on drugs that are on the list of preferred prescription drugs; and

(c) Which prescription drugs should be excluded from any restrictions that are imposed on drugs that are on the list of preferred prescription drugs based on continuity of care concerning a specific diagnosis, condition, class of therapeutic prescription drugs or medical specialty.

4. The regulations must provide that each new pharmaceutical product and each existing pharmaceutical product for which there is new clinical evidence supporting its inclusion on the list of preferred prescription drugs must be made available pursuant to the Medicaid program with prior authorization until the Committee reviews the product or the evidence.

(Added to NRS by 2003, 1317; A 2010, 26th Special Session, 36; 2011, 985, effective July 1, 2015)

Definition of "Therapeutic Alternative"

A "Therapeutic Alternative" is defined by the AMA as: "Drug products with different chemical structures but which are of the same pharmacological and/or therapeutic class and usually can be expected to have similar therapeutic effects and adverse reaction profiles when administered to patients in therapeutically equivalent doses."

BRIAN SANDOVAL
Governor

STATE OF NEVADA
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RICHARD WHITLEY, MS
Director

MARTA JENSEN
Acting Administrator

Nevada Medicaid
Pharmacy and Therapeutics
Draft Meeting Minutes

The Division of Health Care Financing and Policy (DHCFP) Pharmacy and Therapeutics Committee held a public meeting on **December 3, 2015**, beginning at **1:00 p.m.** at the following location:

JW Marriott – Las Vegas
Marbella Room
221 N Rampart Blvd
Las Vegas, NV 89145
702-869-7777

Board Members Present:
Mark Decerbo, Pharm.D.; Shamim Nagy, MD; Weldon Havins, MD; Joseph Adashek, MD; Adam Zold, Pharm.D. Evelyn Chu, Pharm.D.; David Fluitt, RPh

Board Members Absent:
Bill Evans, MD; Mike Hautekeet, RPh

Others Present:
DHCFP:
Mary Griffith, RN, Pharmacy Services Specialist; Gabe Lither, Deputy Attorney General;

HPES:
Beth Slamowitz, Pharm.D.

Optum:
Carl Jeffery, Pharm.D., Kevin Whittington, RPh; Daniel Medina (via teleconference)

Others:
Sandy Sierawsky, Pfizer; Bret Ferguson, Pfizer; Gina Soto, Alkermes; Gergg Gittus, Alkermes; Yumi Yamamoto, Alkermes; Corinne Glock, Relypsa; Kerry Kostman Bonilla, AstraZeneca; Jin Yun, AsterZeneca;

Bob Gustafson, Lundbeck; David Kogan, Jennifer Lauper, BMS; Chriss Conner, BMS; Phil Walsh, Sunovian; Samantha Min, Otsuka; Krystal Joy, Otsuka; Melissa Walsh, Novartis; Charissa Anne, J&J; Marykay Queener, J&J; Lovel Robinson, Abbvie; Sal Lofaso, Horizon; Sean McGarr, Allergan; Aimee Redhair, UCB

Others via teleconference:
Lori Howarth, Bayer; Jean Ritter, VCG; Ron Dunbar, Prescription Alliance; Rebecca Vernon-Ritter, DHCFP; David Large, Supernus; Jeff Cameron, Dyax; Jeanette Belz; Lea Cartwright; Lisa Wilson, Biogen

AGENDA

1. Call to Order and Roll Call

Meeting called to order at 1:02 PM.

Roll Call:

David Fluitt

Evelyn Chu

Weldon Havins

Mark Decerbo

Gabe Lither, Deputy Attorney General

Shamim Nagy, Chairwoman

Mary Griffith, DHCFP

Beth Slamowitz, HPE

Adam Zold

Kevin Whittington, Optum

Carl Jeffery, Optum

2. Public Comment

Shamim Nagy, Chairwoman: Public Comment?

None.

3. Administrative

A. **For Possible Action:** Review and Approve Meeting Minutes from September 23, 2015.

Shamim Nagy, Chairwoman: We need a motion to approve the minutes from September.

David Fluitt: I make a motion to accept the minutes.

Weldon Havins: Second.

Voting: Ayes across the board – motion carries.

B. Status Update by DHCFP

1. Public Comment.

Shamim Nagy, Chairwoman: Comment from DHCFP.

Mary Griffith: We are doing this by WebEx, so more people can listen to the meeting and participate. We will be sure to mention them during our public comments. For new business, we started with the NADAC price on November 1, 2015. We are doing this because of the Affordable Care Act. We are required to reference an actual acquisition cost. This comes from CMS and we are one of the first states to use the NADAC. The dispensing fee is increased to $10.17 and the WAC price is decreased from plus 2% to plus 0%.

Shamim Nagy, Chairwoman: Any public comment?

David Fluitt: I have a question, in September we talked about changing to ICD-10.

Mary Griffith: That was effective as of October 1, 2015. It has been pretty smooth so far. Claims are denying if the claim requires a diagnosis and the ICD-9 is sent.

4. Established Drug Classes

A. Antidepressants - Other

Shamim Nagy, Chairwoman: The annual review for drug classes from September, we are going to move that to the end of the meeting.

Established drug classes, Antidepressants, Other.

Is there any public comment? None.

Carl Jeffery: This class is up for review because of the generic Cymbalta, duloxetine, we changed the fibromyalgia and neuropathic pain agents. We bring this to the Committee to make it consistent. We recommend the Committee consider these clinically and therapeutically equivalent.

David Fluitt: I make a motion that these be considered clinically and therapeutically equivalent.

Adam Zold: Second.

Mark Decerbo: Just a quick question before we vote, did the DUR Board make any changes with removing the requirement for any diagnosis?

Carl Jeffery: No, there is still a requirement for the diagnosis for the Cymbalta. It is an ICD-10 diagnosis. It should be coming up on a future meeting for the DUR Board.

Voting: Ayes across the board, the motion carries.

Carl Jeffery: The changes are presented, we are moving the generic duloxetine to preferred and the brand Cymbalta to non-preferred.

David Fluitt: I make a motion to accept the recommendation to move the duloxetine to preferred and brand Cymbalta to non-preferred.

Weldon Havins: Second.

Voting: Ayes across the board, the motion carries.

B. Nasal Antihistamines

Shamim Nagy, Chairwoman: The next class, Nasal Antihistamines.

Iis there any public comment?

Carl Jeffery: This is the nasal antihistamines. There is a new generic for the Patanase, olopatadine. This class is really second line after the nasal steroids. They have all been shown safe and effective, and head-to-head studies have not shown one product to be superior. Optum recommends these products be considered clinically and therapeutically equivalent.

Evelyn Chu: I make a motion that these be considered clinically and therapeutically equivalent

David Fluitt: Second.

Voting: Ayes across the board, the motion carries.

Carl Jeffery: Optum recommends the generic olopatadine be considered non-preferred.

Joseph Adashek: Is that something that is ever used? Why make a generic non-preferred?

Carl Jeffery: There wasn't a whole lot of usage any way. It just barely came on the market, so there are not a lot of people on it now.

Joseph Adashek: I move we accept the recommendation.

Adam Zold: Second.

Voting: Ayes across the board, the motion carries.

C. Nasal Calcitonins

Shamim Nagy, Chairwoman: The next class is Nasal Calcitonins.

Any public comment? None.

Carl Jeffery: This is another class where a generic is available, but has never been listed on the PDL. We brought this up so all the products can be listed on the PDL. The Miacalcin is synthetic where the Fortical is biological. All have been shown to build bone mass for osteoporosis. There are not any head-to-head studies. Optum recommends these be considered clinically and therapeutically equivalent.

David Fluitt: I move these be considered clinically and therapeutically equivalent.

Adam Zold: Second.

Voting: Ayes across the board, the motion carries.

Carl Jeffery: We are listing the two products that have been available for a long time as non-preferred on the PDL. Fortical and the generic calcitonin would be non-preferred and Miacalcin preferred.

David Fluitt: Is there any difference in the dosing between the Fortical and Miacalcin?

Carl Jeffery: No, they are the same, just different manufacturers.

David Fluitt: I make the motion to accept the recommendation.

Weldon Havins: Second.

Voting: Ayes across the board, the motion carries.

D. Platelet Inhibitors

Shamim Nagy, Chairwoman: The next item is Platelet Inhibitors.

Any Public comment? None.

Carl Jeffery: We have a couple things here. There is a new generic for Aggrenox, there is a new extended release aspirin product, Durlaza and ticlopidine is no longer on the market. Durlaza is an extended release aspirin product. The Pharmacist Letter had a nice write up on this product. The studies available are the studies for aspirin. There is nothing in the literature that supports the use of the product over a regular release product. Optum recommends these be considered clinically and therapeutically equivalent.

David Fluitt: Were there clinical studies that supported the extended release product with clinical outcomes?

Carl Jeffery: The only studies I saw were pharmacokinetic studies. It had a longer half-life, absorbed over 8 hours instead of the normal 2 hours, but there were no clinical outcomes.

David Fluitt: No decrease in GI bleed?

Carl Jeffery: I didn't see any studies for outcomes or side effects.

David Fluitt: I make a motion these products be considered clinically and therapeutically equivalent.

Adam Zold: Second.

Voting: Ayes across the board. The motion carries.

Carl Jeffery: Our recommendation is to make the aspirin/dipyridamole and the Durlaza as non-preferred and remove the ticlopidine from the list since it is no longer available.

Adam Zold: I make a motion to accept Optum's recommendation.

Weldon Havins: Second.

Voting: Ayes across the board, the motion carries..

E. Bladder Antispasmodics

Shamim Nagy, Chairwoman: Bladder antispasmodics.

Any public comment? None.

Carl Jeffery: There is a new drug in this class, Myrbetriq, we'll talk about that more in a minute. Sanctura XR is no longer available on the market, the generic is, but not the brand. And a DUR Board member asked we review bethanechol because it works a little differently than the others. Myrbetriq works a little differently than some of the others in this class, it is a beta-3 adrenergic receptor agonist. It relaxes the detrusor smooth muscle, so it may not have any of the other anticholinergic side effects. It was approved based on three trials. One study was compared with tolteradine as an active comparator. It was shown to be non-inferior to tolteradine. The different indications are shown here. The only one that stands out is the flavoxate, but the others

are all very similar. Optum recommends these product be considered clinically and therapeutically equivalent.

David Fluitt: I make a motion these be considered clinically and therapeutically equivalen.t

Evelyn Chu: Second,

Voting: Ayes across the board, the motion carries.

Carl Jeffery: Optum recommends bethanechol be considered preferred, remove the Sanctura XR and make Myrbetriq non-preferred.

Mark Decerbo: Was bethanechol non-preferred or was it not captured?

Carl Jeffery: It was considered non-preferred.

David Fluitt: The most restrictive aspect of this class is the anticholinergic effects, since Myrbetriq is specific to the beta-3 receptor sites, is there less incidence of dry mouth with this product?

Carl Jeffery: There are, there are some other side effects though. There were fewer anticholinergic side effects.

David Fluitt: Since there are fewer anticholinergic side effects, should the Committee consider making Myrbetriq preferred?

Carl Jeffery: We could, but there is always the argument you could use this product if you have a contraindication to one of the preferred agents. We should encourage some of the other established products first that are shown effective.

Joseph Adashek: I move we accept the recommendations.

Adam Zold: Second.

Voting: Ayes across the board, the motion carries.

F. Angiotensin II Receptor Antagonists

Shamim Nagy, Chairwoman: Angiotensin II receptor antagonists.

Any public comment? None.

Carl Jeffery: We have this class to review again because we have some new generics on the market now. The only ones on the list now are Benicar and Edarbi are the only products on the list without a generic available. The Diovan and Cozaar are higher utilized drugs. Optum recommends these be considered clinically and therapeutically equivalent.

Mark Decerbo: I make the motion these products be considered clinically and therapeutically equivalent.

Adam Zold: Second

Voting: Ayes across the board, the motion carries.

Carl Jeffery: Optum recommends candesartan, the brand Cozaar, the brand Hyzaar and valsartan be added as non-preferred. We would keep the rest of the class the same.

Adam Zold: Is the usage of the valsartan pretty low?

Carl Jeffery: Kevin, do you remember off the top of your head?

Kevin Whittington: Yes it is all in the brand.

Joseph Adashek: I move we agree with the recommendations.

Weldon Havins: Second.

Voting: Ayes across the board, the motion carries.

G. Immunomodulators: Topical

Shamim Nagy, Chairwoman: The next class is immunomodulators, topical.

Any public comment? None.

Carl Jeffery: Another class where we have a new generic on the market, Tacrolimus is the generic for Protopic. The indication is shown here on the slide. They have been shown safe and effective with the exception of the black-box warning with skin cancer possibilities. Optum recommends the products in this class be considered clinically and therapeutically equivalent.

David Fluitt: I make a motion these be considered clinically and therapeutically equivalent.

Weldon Havins: Second.

Voting: Ayes across the board, the motion carries.

Carl Jeffery: Optum recommends tacrolimus be added as non-preferred.

Joseph Adashek: I move we accept the recommendations.

Adam Zold: Second.

Voting: Ayes across the board, the motion carries..

H. Ophthalmic Nonsteroidal Antiinflammatory Drugs (NSAIDs)

Shamim Nagy, Chairwoman: Ophthalmic non-steroidal anti-inflammatory drugs.

Public comment? None.

Carl Jeffery: We have a new ketorolac generic on the market, more manufacturers giving us a chance to look at the whole class. These are used before and after surgeries and one for seasonal conjunctivitis. They are all standard NSAIDs. Optum recommends these be considered clinically and therapeutically equivalent.

Weldon Havins: I move we consider these clinically and therapeutically equivalent.

Joseph Adashek: Second.

Voting: Ayes across the board, the motion carries.

Carl Jeffery: We are going to move some things around. The Accular PF is no longer available, so that will be removed from the list. Ketorolac and Ilevero will be added as preferred and Acular and Acular LS will be added as non-preferred.

Weldon Havins: I move we accept the recommendations.

Adam Zold: Second.

Voting: Ayes across the board, the motion carries.

I. Disease-Modifying Antirheumatic Agents

Shamim Nagy, Chairwoman: Disease-modifying antirheumatic agents.

Public comment.

Carl Jeffery: Briefly, we told the Committee we would bring this back because there was some confusion about how it was named, so that is why it is coming back up. We can still open it up for public comment.

Shamim Nagy, Chairwoman: Any public comment? None.

Carl Jeffery: We did some research on this. All of them are considered DMARDs except for Cosentyx and Stelara. It makes sense to remove these two agents and keep the name the same. We are changing the class because these non-preferred agents will technically be preferred now. Gabe, so we need a vote from the committee?

Gabe Lither: Not for the changes you are proposing, no.

Joseph Adashek: All these drugs need prior authorization anyway.

Carl Jeffery: So we can just solicit some feedback if this sounds ok, but we don't need an official vote.

Joseph Adashek: So if we wanted one of these preferred for example.

Carl Jeffery: Right, the DUR Board sets the clinical criteria for these products.

Mark Decerbo: Is it one uniform process for preferred vs. non-preferred, is there any difference?

Carl Jeffery: It is essentially the same process, except the recipient must show they have tried or cannot tolerate Enbrel or Humira before getting a non-preferred, or show why they can't take these. If they had an allergy or a unique indication.

Mark Decerbo: I don't have a problem with changing the classes, we have been cleaning up a lot of these lately. The last slide you presented, the classification, is that an AHFS classification?

Carl Jeffery: Yes, exactly.

Shamim Nagy, Chairwoman: There is no vote needed.

Carl Jeffery: Right, we just wanted to let the Committee know what we are doing and solicit feedback.

5. Established Drug Classes Being Reviewed Due to the Release of New Drugs

A. Alzheimer's Agents

Shamim Nagy, Chairwoman: The next class is Alzheimer's Agents.

Any public comment? None.

Carl Jeffery: Namzaric is the new drug, a combo of Aricept and Namenda. Two well-known drugs for moderate to severe Alzheimer's disease. The combination of the two has been used together for a long time. Neither stops nor slow the progression of the disease, but they work for symptom control. The combo should only be used if they are already stabilized on the two individually. Optum recommends these products be considered clinically and therapeutically equivalent.

Joseph Adashek: So moved.

Adam Zold: Second.

Voting: Ayes across the board, the motion carries.

Carl Jeffery: The new products we recommend be non-preferred, but also switch the brand Namenda to non-preferred and the generic memantine as preferred.

Mark Decerbo: One question, wasn't there some litigation between Namenda XR and a generic manufacturer? Where they blocking a generic? Is there a memantine XR that is available?

Carl Jeffery: It didn't show on my current product list, but it might show up soon.

David Fluitt: These products are sometimes hard to take. Is there any information showing they stopped the medication less when taking the combination form?

Carl Jeffery: I don't remember seeing anything specifically addressing that.

David Fluitt: That might be the only advantage I can see with this product.

Carl Jeffery: With the criteria from the FDA indication, they have to be stable on the two products separately before moving to the combo, that will qualify them to meet the non-preferred criteria to get the Namzaric.

David Fluitt: I move to accept the recommendations.

Joseph Adashek: Second.

Voting: Ayes across the board, the motion carries.

Gabe Lither: Just to be clear, you can make an alternative motion at any time, you don't have to just accept the recommendation.

B. Oral Atypical Antipsychotics

Shamim Nagy, Chairwoman: Oral Atypical Antipsychotics, any public comment?

Samantha May: My name is Samantha May, I believe you have all had the chance to read the information about Rexulti. I have a company approved script. Covered indications, mechanism of action, efficacy of medication through studies, details of trial outcomes, and adverse effects. Please refer to the package insert. Please consider adding Rexulti to the PDL.

Carl Jeffery: We just heard about Rexulti, I won't go over all of it again. The pivotal trials were talked about. The secondary outcomes may have been more important to talk about. We have a new treatment option that works a little differently. But over all we recommend this class be considered clinically and therapeutically equivalent.

Joseph Adashek: I move we accept the recommendation that these be considered clinically and therapeutically equivalent.

Adam Zold: Second.

Voting: Ayes across the board, the motion carries.

Carl Jeffery: In addition to the new Rexulti, there are a few new generics available, aripirazole and paliperidone. We want to include both new generics and Rexulti as non-preferred.

Joseph Adashek: Are you getting a lot of requests for Rexulti.

Kevin Whittington: We didn't have any utilization.

Weldon Havins: Paliperidone is a generic?

Carl Jeffery: It is a generic for Invega.

Mark Decerbo: What is the PA process for these? We have expanded the list so much and with such a varied response to these agents. If someone is an excellent candidate for Rexulti, how hard is it to get this medication?

Carl Jeffery: They would need to show trial and failure of two preferred agents or have some good clinical justification as to why they need a non-preferred agent.

Joseph Adashek: So if someone goes to the website, how long does it take someone to answer back?

Carl Jeffery: If they send a fax, our average turnaround time is 5-6 hours for a decision, we are required to have a response back within 24 hours. A phone call is right away.

Gabe Lither: Do you have to show a failure of two?

Carl Jeffery: Unless there is justification for why they can't take two. Failure is a pretty broad term, it could be side effects, or maybe they didn't quite achieve treatment goals.

Joseph Adashek: Do you have any statistics on how many you end up denying the first time around? If someone did try one, what percentage do you have for approving it the first time around?

Carl Jeffery: I don't have those exact numbers, a ballpark, we approve about 90% of requests anyway.

Weldon Havins: Since the response is so variable, why not include the generics in the preferred category?

Carl Jeffery: To have the generics as non-preferred.

Gabe Lither: There are a host of other drugs that meet the State's needs.

Mary Griffith: I need to add, our policy for the standard preferred drug list exception policy, we only require failure of one agent for atypical antipsychotics, anticonvulsants and anti-diabetics. I just wanted to clarify that.

David Fluitt: That falls under the continuity of care that we talked about last time.

Carl Jeffery: That's right, there is only one failure, thank you.

Joseph Adashek: I move we agree with the recommendations.

Weldon Havins: Second.

Voting: Ayes across the board, the motion carries.

C. Ophthalmic Antihistamines

Shamim Nagy, Chairwoman: Ophthalmic antihistamines. Any public comment? None.

Weldon Havins: Why are we moving Pataday? For the State interest? It has been on the preferred list.

Carl Jeffery: Right, that's our recommendation. We'll move through this information first. We have a new drug Pazeo. There are three products now with olopatdine with different strengths. Patanol, Pataday and Pazeo. The indications are in line with the other products. There are several over the counter products now for the ketotifen. The prescription product is the only one indicated for allergic conjunctivitis. The Pazeo had two trials showing it was significantly better than placebo. When compared to Pataday, Pazeo was shown to be better at 24 hours. Optum recommends these be considered clinically and therapeutically equivalent.

Adam Zold: I make the motion that these are clinically and therapeutically equivalent.

David Fluitt: Second.

Voting: Ayes across the board, the motion carries.

Carl Jeffery: Optum recommends making Ketotifen and Pazeo preferred and moving Pataday to non-preferred. The other generics that have been on the market for a while will be listed as non-preferred. The reason for moving Pataday away is because there are a lot of other products on the market to treat allergic conjunctivitis. The manufacture of Pazeo is trying to drive use and has been working with use pretty well.

Weldon Havins: I move we accept the recommendations.

Joseph Adashek: Second.

Voting: Ayes across the board, the motion carries.

D. Short-Acting Respiratory Beta-Agonist

Shamim Nagy, Chairwoman: Short acting respiratory beta agonists, public comment? None

Carl Jeffery: We have a new product on the market, the Proair Respiclick, another albuterol inhaler. The slide shows what it looks like. It works by breath actuation, a big breath in gives the dose. Good delivery as long as there is good lung function. It hasn't been studied in severe lung disease. It has a dose counter and does not require a spacer. But it is just another albuterol. Optum recommends these be considered clinically and therapeutically equivalent.

Mark Decerbo: I move these products be considered clinically and therapeutically equivalent

Adam Zold: Second

Voting: Ayes across the board, the motion carries.

The same list with the addition of the Proair Respiclick as non-preferred. We still have the Proair and the Proventil as albuterol options as preferred.

Joseph Adashek: With Xopenex and a PA requirement for it. I disagree with needing a PA. I think there is such a difference in the cardiac side effects with the inhaler that I don't think we need a PA for the Xopenex. There is such a difference with side effects, and it is standard of care for the treatment of asthma. I would like the PA be removed from the Xopenex.

Carl Jeffery: It is the DUR Board that makes the clinical criteria for the Xopenex.

Mary Griffith: There are clinical criteria from the DUR Board, but it is for recipients experiencing side effects with other beta-adrenergic agonists or for patient whose cardiovascular status is considered to be in severe deteriorating condition. Those are the quantifications by the DUR Board.

Joseph Adashek: I don't understand this, who is the DUR Board?

Mary Griffith: There are two different PA's. There is a PA for non-preferred drugs. And then the clinical PA. The clinical PA is decided by the DUR Board and they make the criteria. We can bring this up to the DUR Board. We have three physicians and pharmacists on the Board.

Joseph Adashek: This is the first meeting I have heard that we cannot overrule the DUR Board.

David Fluitt: Can we make the recommendation that this no longer requires a PA?

Joseph Adashek: That is what I would like to do.

Mary Griffith: We would have to bring it back up to the DUR Board.

Gabe Lither: You can ask that the DUR Board review that and we can make sure it is on the next agenda for the meeting. You are welcome to make public comment at the meeting.

Mary Griffith: The DUR Board is a Federal requirement. The P&T is a State requirement. The DUR Board is appointed by the Director and the P&T is appointed by the Governor. The DUR Board is tasked with looking at safety and utilization and putting criteria on specific drugs.

Anyone can suggest a drug to be reviewed. Whereas the P&T Committee, you are doing the preferred vs. non-preferred.

Joseph Adashek: It just seems weird that a Board that is there for safety would have a PA for a drug with less cardiac side effects. So you think it would be the other way around. If that is more clinical.

Gabe Lither: Carl, do you know what the DUR Board was concerned about when they made this criteria?

Carl Jeffery: I think it was recently reviewed, but it is a carryover from a long time ago.

Weldon Havins: Can we make a motion to ask the DUR Board to review this drug?

Gabe Lither: You don't need a motion for that.

Joseph Adashek: How do we ask the DUR Board to review this?

Carl Jeffery: You just did, we'll get it on the next agenda for the DUR Board.

Joseph Adashek: So we have nothing to do with the clinical PA.

Carl Jeffery: Right, they look at the utilization management and this relates when Xopenex first came on the market, they wanted to make sure the utilization was appropriate. Still today, the majority of patients are going to do just fine with albuterol, from their perspective, there really isn't a reason albuterol shouldn't be considered first and then move to Xopenex.

Joseph Adashek: But that is probably because they don't know any better. They take albuterol and they are all shaky and their heart is racing, they don't know there is an alternative that doesn't have these side effects.

Gabe Lither: Can you make sure you send out an email for when the next DUR Board meeting is?

Carl Jeffery: We'll have a WebEx too.

Mary Griffith: The DUR Board is in Reno and in the evening.

Evelyn Chu: At the hospital level, we have removed Xopenex from the formulary. If the physician orders it, we auto-sub for albuterol, and we have done it for years and we have not had any issues. There have not been any difference in outcomes.

Joseph Adashek: I don't think there would be, it is the side effects, the shaky and heart rate. They don't know there is an alternative.

Evelyn Chu: But if the physician does right do not substitute for a patient with Afib or other heart problems, they can get the Xopenex, otherwise they can get albuterol.

Joseph Adashek: There are patients that just won't take albuterol because they don't like the side effects, but they don't know better that there is a drug that doesn't have the side effects.

Weldon Havins: How do we know by looking at it what kind of PA it requires?

Carl Jeffery: If it says PA on the list, then it is a clinical PA, the only other reason it would require a PA is if it is non-preferred. We added this to the PDL about a year ago to indicate what products on this list requires a PA.

Joseph Adashek: When dealing with pregnant women because it makes them shaky and they're worried about the baby. So this is something you may not see in the hospital. The levalbuterol is non-preferred and it doesn't require a PA?

Carl Jeffery: It would, it is just the nebulizer solution, and they would still need to try two preferred agents. We should have a note by that one too.

Joseph Adashek: I make a motion to agree with the recommendations.

Adam Zold: Second.

Voting: Ayes across the board, the motion carries.

6. Annual Review – Drug Classes Without Proposed Changes From September 23, 2015 Meeting

Shamim Nagy, Chairwoman: We will go back to the annual review of the September mass approval.

Public comment?

Carl Jeffery: This is here because of a technicality, we didn't have an action item on the agenda, but this is the class list where we do not recommend any changes. Every class that was not reviewed in September is on this list.

Weldon Havins: I move that we approve drugs for inclusion on the PDL as noted in our agenda item 4.C.

Adam Zold: Second.

Voting: Ayes across the board, the motion carries.

7. Closing Discussion

Shamim Nagy, Chairwoman: Any public comment? Date of the next meeting?

Carl Jeffery: March 24, 2016, here again if we can.

Meeting adjourned.

Therapeutic Class Overview
Inhaled Anticholinergics

Therapeutic Class Overview/Summary:
The inhaled anticholinergics are a class of bronchodilators primarily used in the management of chronic obstructive pulmonary disease (COPD), a condition characterized by progressive airflow restrictions that are not fully reversible.[1-3] Symptoms associated with COPD typically include dyspnea, cough, sputum production, wheezing and chest tightness. Specifically, inhaled anticholinergics work via the inhibition of acetylcholine at parasympathetic sites in bronchial smooth muscle causing bronchodilation. Meaningful increases in lung function can be achieved with the use of inhaled anticholinergics in patients with COPD.[1-3] The available single-entity inhaled anticholinergics include aclidinium (Tudorza® Pressair), glycopyrrolate (Seebri Neohaler®), ipratropium (Atrovent®, Atrovent® HFA), tiotropium (Spiriva®, Spiriva Respimat®) and umeclidinium (Incruse Ellipta®) with the combination products including glycopyrrolate/indacaterol (Utibron Neohaler®), umeclidinium/vilanterol (Anoro Ellipta®), tiotropium/olodaterol (Stiolto Respimat®) and ipratropium/albuterol, formulated as either an inhaler (Combivent Respimat®) or nebulizer solution (DuoNeb).[4-15] Ipratropium, a short-acting bronchodilator, has a duration of action of six to eight hours and requires administration four times daily. Aclidinium, glycopyrrolate, tiotropium and umeclidinium are considered long-acting bronchodilators. Aclidinium is dosed twice daily, while glycopyrrolate, tiotropium and umeclidinium are administered once daily. Ipratropium is available as a metered dose aerosol inhaler for oral inhalation as well as a solution for nebulization. Aclidinium, glycopyrrolate, tiotropium and umeclidinium are available as dry powder inhalers for oral inhalation, with tiotropium also formulated as an inhalation aerosol.[4-15]

Aclidinium, glycopyrrolate, ipratropium and tiotropium, are Food and Drug Administration (FDA)-approved for the maintenance treatment of bronchospasm associated with COPD, including chronic bronchitis and emphysema. Tiotropium is the only inhaled anticholinergic that is FDA-approved for reducing exacerbations associated with COPD. Additionally, tiotropium soft mist inhaler (Spiriva Respimat®) has been approved for the chronic management of asthma. Ipratropium/albuterol is indicated for the treatment of bronchospasms associated with COPD in patients who require more than one bronchodilator. Glycopyrrolate/indacaterol, umeclidinium, umeclidinium/vilanterol and tiotropium/olodaterol are FDA-approved for the maintenance treatment of airflow obstruction in patients with COPD.[4-15]

Table 1. Current Medications Available in the Therapeutic Class[4-16]

Generic (Trade Name)	Food and Drug Administration-Approved Indications	Dosage Form/Strength	Generic Availability
Single Entity Agents			
Aclidinium (Tudorza® Pressair)	Bronchospasm associated with COPD, maintenance treatment†	Powder for inhalation: 400 µg	-
Glycopyrrolate (Seebri Neohaler®)	Airflow obstruction in patients with COPD, maintenance treatment†	Powder for inhalation: 15.6 µg	-
Ipratropium* (Atrovent HFA®)	Bronchospasm associated with COPD, maintenance treatment	Aerosol for oral inhalation (Atrovent HFA®): 17 µg Solution for nebulization: 500 µg (0.02%)	a

Generic (Trade Name)	Food and Drug Administration-Approved Indications	Dosage Form/Strength	Generic Availability
Tiotropium (Spiriva®, Spiriva Respimat®)	Asthma, maintenance treatment (aerosol for inhalation); Bronchospasm associated with COPD, maintenance treatment†, reduce exacerbations in patients with COPD	Aerosol for inhalation (Spiriva Respimat®): 1.25 µg/actuation 2.5 µg/actuation Powder for inhalation (Spiriva HandiHaler®): 18 µg	-
Umeclidinium (Incruse Ellipta®)	Airflow obstruction in patients with COPD, maintenance treatment*	Powder for inhalation: 62.5 µg	-
Combination Products			
Glycopyrrolate/indacaterol (Utibron Neohaler®)	Airflow obstruction in patients with COPD, maintenance treatment†	Powder for inhalation: 15.6 µg/27.5 µg	-
Ipratropium/albuterol* (Combivent Respimat®)	Bronchospasm associated with COPD in patients requiring more than one bronchodilator	Inhalation spray (Combivent Respimat®): 20/100 µg‡ Solution for nebulization (DuoNeb®): 0.5/3.0 mg	a
Tiotropium/olodaterol (Stiolto Respimat®)	Airflow obstruction in patients with COPD, maintenance treatment†	Inhalation Spray 5/5 µg	-
Umeclidinium/vilanterol (Anoro Ellipta®)	Airflow obstruction in patients with COPD, maintenance treatment†	Powder for inhalation: 62.5/25 µg	-

*Generic available in at least one dosage form or strength.
†Long-term maintenance treatment.
‡Delivering 18 µg of ipratropium and 103 µg of albuterol (90 µg albuterol base).

Evidence-based Medicine

- In general, the inhaled anticholinergics have demonstrated to improve lung function and/or exercise tolerance in patients with chronic obstructive pulmonary disease (COPD).[17-79] Few head-to-head trials have noted significant differences in improvements in lung function favoring tiotropium over ipratropium.[19,42,43]
- The efficacy of glycopyrrolate is based primarily on the dose-ranging trials in 471 subjects with COPD and two placebo-controlled confirmatory trials in 867 subjects with COPD. The primary efficacy endpoint from the two placebo-controlled confirmatory trials, GEM1 and GEM2, was the change from baseline in FEV_1 $AUC_{0 \text{ to } 12 \text{ h}}$ following the morning dose at day 85 compared with placebo. In both trials, the glycopyrrolate group demonstrated a larger increase in mean change from baseline in FEV_1 $AUC_{0 \text{ to } 12 \text{ h}}$ compared to placebo.
  - In GEM1, the change from baseline least squares (LS) mean was 0.125 L in the glycopyrrolate group compared to -0.014 L in the placebo group (Treatment difference LS Mean, 0.139 L; 95% CI, 0.095 to 0.184; P values not reported).
  - For GEM2, the change from baseline LS mean was 0.115 L in the glycopyrrolate group compared to -0.008 L in the placebo group (Treatment difference LS Mean, 0.123 L; 95% CI, 0.081 to 0.165; P values not reported).[5,77,78]

- The efficacy of indacaterol/glycopyrrolate was based primarily on the results of two 12-week efficacy studies (FLIGHT1 & 2).[12,79] Both were identical, multicenter, randomized, double-blinded, placebo- and active-controlled, and parallel-group trials in subjects with COPD. A total of 2,038 individuals were randomized to indacaterol/glycopyrrolate 27.5 µg/15.6 µg twice-daily (BID), indacaterol 27.5 µg BID, glycopyrrolate 15.6 mcg BID, or placebo BID. The primary endpoint was the change from baseline in FEV_1 AUC_{0-12h} following the morning dose at Day 85 compared with placebo, glycopyrrolate 15.6 µg BID, and indacaterol 27.5 µg BID.
    - In both trials, Utibron Neohaler® (indacaterol/glycopyrrolate) demonstrated a larger increase in mean change from baseline in FEV_1 AUC_{0-12h} compared to placebo, indacaterol 27.5 µg BID, and glycopyrrolate 15.6 µg BID (treatment difference: 103 mL and 88 mL vs indacaterol and glycopyrrolate, respectively, P<0.001). In addition, both indacaterol and glycopyrrolate monotherapies had a statistically greater response than placebo at week 12 in terms of FEV_1 AUC_{0-12h} (treatment difference: 143 mL and 158 mL, respectively, P<0.001).[79]

Key Points within the Medication Class

- According to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines:[1]
    - Inhaled bronchodilators are preferred for the management of COPD. Regular use of long-acting β2-agonists or short- or long-acting anticholinergics improves health status and long-acting anticholinergics reduce the rate of COPD exacerbations and improve the effectiveness of pulmonary rehabilitation.
    - The GOLD guidelines emphasize that the use of long-acting bronchodilators is more effective and convenient than the use of short-acting bronchodilators.
- According to the National Institute for Clinical Excellence (NICE):[2]
    - Short-acting bronchodilators should be the initial empiric treatment for the relief of breathlessness and exercise limitation while long-acting bronchodilators should be used in patients who remain symptomatic with use of short-acting agents.
    - Once-daily, long-acting anticholinergic agents are preferred compared to four-times-daily short-acting anticholinergics in patients with stable COPD who remain symptomatic despite use of short-acting agents and in whom the decision has been made to begin regular maintenance therapy with an anticholinergic agent.
- Other Key Facts:
    - Ipratropium and ipratropium/albuterol solutions for nebulization are the only inhaled anticholinergic products that are currently available generically.

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Therapeutic Class Overview
Benzoyl Peroxide/Antibiotic Combinations

Therapeutic Class Overview/Summary:
This review will focus on the benzoyl peroxide/antibiotic combination products, which are approved for the topical treatment of acne vulgaris in patients 12 years of age and older.[1-6] Acne vulgaris is a chronic inflammatory dermatosis characterized by open and/or closed comedones (blackheads and whiteheads) and inflammatory lesions including papules, pustules, or nodules.[7-10] Four primary pathogenic factors interact in a complex manner to produce the different acne lesions. These four factors include sebum production by the sebaceous gland, *Propionibacterium acnes (P acnes)* follicular colonization, alteration in the keratinization process, and the release of inflammatory mediators to the skin.[7-10] Clindamycin phosphate and erythromycin are antibiotics that inhibit bacterial protein synthesis via interference at the bacterial ribosome. Benzoyl peroxide also exhibits antimicrobial effects against *P acnes*; however, it acts via release of free-radical oxygen species which oxidize bacterial proteins. In addition, benzoyl peroxide also demonstrates keratolytic activity, which produces drying and desquamative actions that contribute to its efficacy in comedone treatment.[11,12]

Several treatment options exist including topical agents, systemic antibacterial agents, hormonal agents, isotretinoin, laser and light therapies, miscellaneous therapies, complementary/alternative therapies, and dietary restrictions.[7] Traditionally, the treatment of acne vulgaris was directed toward controlling *P acnes* and centered on the use of antibiotics. However, with the knowledge of the interplay between the four different pathogenic factors, acne vulgaris treatment is now directed toward as many pathogenic factors as possible. Combination treatment has the ability to target multiple pathogenic factors, including inflammatory and noninflammatory lesions.[9] Data has shown that these agents result in faster and more complete clearing of acne vulgaris lesions compared with monotherapy.[9]

There are currently two antibiotics FDA-approved in combination with benzoyl peroxide, clindamycin phosphate and erythromycin. While both combinations are formulated as a gel, there are differences in concentrations between products.

Table 1. Current Medications Available in the Therapeutic Class[1-6]

Generic (Trade Name)	Food and Drug Administration-Approved Indications	Dosage Form/Strength	Generic Availability
Benzoyl peroxide/clindamycin phosphate (Benzamycin Pak®, Benzamycin®*)	Acne vulgaris (adults and pediatric patients ≥12 years of age)	Gel: 2.5%/1.2% 3.75%/1.2% 5%/1% 5%/1.2%	a
Benzoyl peroxide/erythromycin (Acanya®, BenzaClin®*, Duac®, Neuac®†, Onexton®)	Acne vulgaris (adults and pediatric patients ≥12 years of age)	Gel: 5%/3% Gel Pack: 5%/3%	a

*Generic available in at least one dosage form or strength.
†Branded-generic

Evidence-based Medicine
- The safety and efficacy of benzoyl peroxide/antibiotic combinations with clindamycin phosphate or erythromycin have been evaluated in a number of clinical trials.[7-10,13-19]
- Overall, current evidence suggests that benzoyl peroxide/clindamycin phosphate and benzoyl peroxide/erythromycin are more effective than placebo and also more effective than each individual agent alone.[1-6,13-19]

Key Points within the Medication Class

- According to Current Clinical Guidelines:
  - Treatment recommendations vary based upon the severity and type of acne being treated. Topical treatments are the standard of care for acne treatment.[7-10]
    - Generally, topical retinoids are the first choice treatment for most types and severities of acne (or part of the recommended regimen). Other non-retinoid topical agents include: azelaic acid, benzoyl peroxide, clindamycin phosphate, and erythromycin. Bacterial resistance is a concern when treating with systemic and topical antibiotics; therefore monotherapy is discouraged.
    - Pairing an antibiotic with benzoyl peroxide is an effective option that targets *P acnes* while minimizing the development of bacterial resistance.
  - Current guidelines strongly recommend adding benzoyl peroxide to retinoids when long-term antimicrobial use is necessary due to its efficient bactericidal properties.[7-9]
    - Overall, topical benzoyl peroxide/antibiotic combination products are indicated in patients with mild to moderate acne vulgaris.[7-9]
- Other Key Facts:
  - Benzoyl peroxide/clindamycin phosphate (BenzaClin®) and benzoyl peroxide/erythromycin (Benzamycin®) must be reconstituted prior to use, while other products are premixed.[1-6]
  - There is at least one generic formulation for each combination currently available.

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Therapeutic Class Overview
Ophthalmic Antibiotics

Therapeutic Class

- **Overview/Summary:** Ophthalmic antibiotics are used to treat ocular infections including blepharitis, conjunctivitis, keratitis and several others. There are ophthalmic antibiotics available from a variety of drug classes including aminoglycosides, macrolides, polypeptides, quinolones and sulfonamides.[1] In addition, many are available as combination products with other antibiotics or corticosteroids. A list of available ophthalmic antibiotics is available in Table 1. Blepharitis is a chronic inflammatory condition of the eyelids, often presenting with the symptoms of eye irritation and redness. Overgrowth of normal bacterial flora plays a role in the pathophysiology of blepharitis. The mainstay of blepharitis treatment is patient education regarding eye lid hygiene as well as the use of ophthalmic antibiotics.[2,3] Conjunctivitis occurs worldwide and affects all ages, social strata, and both genders.[4] Mild cases may be self limited as many cases will resolve without treatment in immunocompetent individuals although ophthalmic antibiotics are associated with earlier clinical and microbiological remission compared to placebo. All ophthalmic antibiotics, with the exception of ophthalmic levofloxacin 1.5%, are approved by the Food and Drug Administration to treat bacterial conjunctivitis.[5-37] Severe bacterial conjunctivitis is characterized by purulent discharge, pain and marked eye inflammation. In these cases, cultures and slides for gram staining should be obtained and the results of these laboratory tests should guide the choice of the antibiotic.[38] Bacterial keratitis is characterized by an inflammation of the cornea and rarely occurs in the normal eye due to the cornea's natural resistance to infection. Untreated or severe bacterial keratitis can result in corneal perforation and may develop into endophthalmitis and result in the loss of the eye. Ophthalmic antibiotics are the preferred method of treatment in many cases, and antibiotic ointments may be useful at bedtime in less severe cases or as adjunctive therapy. In severe cases, patients should be followed daily until stabilization or clinical improvement is documented.[39]

Table 1. Current Medications Available in Therapeutic Class[1,5-37]

Generic (Trade Name)	Food and Drug Administration Approved Indications	Dosage Form/Strength	Generic Availability
Single-Entity Agents			
Azithromycin ophthalmic (Azasite®)	Bacterial conjunctivitis	Ophthalmic solution: 1% (2.5 mL)	-
Bacitracin ophthalmic (Bacticin®*)	Acute meibomianitis, bacterial conjunctivitis, bacterial blepharitis, bacterial blepharoconjunctivitis, corneal ulcer, dacryocystitis, keratitis, keratoconjunctivitis	Ophthalmic ointment: 500 units/g (3.5, 3.75 g)	a
Besifloxacin ophthalmic (Besivance®)	Bacterial conjunctivitis	Ophthalmic suspension: 0.6% (5 mL)	-
Ciprofloxacin ophthalmic (Ciloxan®*)	Bacterial conjunctivitis, corneal ulcer (solution)	Ophthalmic ointment: 0.3% (3.5 g) Ophthalmic solution: 0.3% (2.5, 5, 10 mL)	a (solution)
Erythromycin ophthalmic (Ilotycin®*, Romycin®*)	Bacterial conjunctivitis, corneal ulcer†, prophylaxis of ophthalmia neonatorum*	Ophthalmic ointment: 0.5% (3.5 g)	a
Gatifloxacin ophthalmic (Zymaxid®)	Bacterial conjunctivitis	Ophthalmic solution: 0.5% (2.5 mL)	-
Gentamicin sulfate ophthalmic (Genoptic®*, Gentak®*)	Acute meibomianitis, bacterial blepharitis, bacterial blepharo-conjunctivitis, corneal ulcer,	Ophthalmic ointment: 0.3% (3.5 g)	a

Generic (Trade Name)	Food and Drug Administration Approved Indications	Dosage Form/Strength	Generic Availability
	dacryocystitis, keratitis, kerato-conjunctivitis	Solution: 0.3% (5, 15 mL)	
Levofloxacin ophthalmic (Iquix®, Quixin®)	Bacterial conjunctivitis (Quixin®), corneal ulcer (Iquix®)	Ophthalmic solution: 0.5% (5 mL) (Quixin®) 1.5% (5 mL) (Iquix®)	a (0.5% solution)
Moxifloxacin hydrochloride ophthalmic (Moxeza®, Vigamox®)	Bacterial conjunctivitis	Ophthalmic solution: 0.5% (3 mL)	-
Ofloxacin ophthalmic (Ocuflox®*)	Bacterial conjunctivitis, corneal ulcer	Ophthalmic solution: 0.3% (1, 5, 10 mL)	a
Sulfacetamide sodium ophthalmic (AKSulf®*, Bleph-10®*, Ocusulf®*, Sturzsulf®*, Sulster®*)	Bacterial conjunctivitis, bacterial blepharitis‡, bacterial blepharo-conjunctivitis‡, keratitis‡, kerato-conjunctivitis‡, treatment of trachoma (adjunct therapy)‡	Ophthalmic ointment: 10% (3.5 g) Ophthalmic solution: 1% (5, 10 mL) 10% (2, 2.5, 5, 15 mL) 30% (15 mL)	a
Tobramycin ophthalmic (AKTob®*, Tobrex®)	Bacterial conjunctivitis§, bacterial blepharitis§, bacterial blepharo-conjunctivitis§, keratitis§, kerato-conjunctivitis§	Ophthalmic ointment: 0.3% (3.5 g) Ophthalmic solution: 0.3% (5 mL)	a
Combination Products			
Bacitracin zinc/ polymyxin B sulfate ophthalmic (AK-Poly-Bac®*, Polysporin®*)	Bacterial conjunctivitis, bacterial blepharoconjunctivitis, keratitis, keratoconjunctivitis	Ophthalmic ointment: 500 units/g/10,000 units/g (3.5 g)	a
Gentamicin sulfate/ prednisolone acetate ophthalmic (Pred G®)	Bacterial conjunctivitis‖, corneal ulcer‖	Ophthalmic ointment: 0.3%/0.6% (3.5 g) Ophthalmic suspension: 0.3%/1.0% (5, 10 mL)	-
Polymyxin B sulfate/ trimethoprim ophthalmic (Polytrim®*)	Bacterial conjunctivitis, bacterial blepharo-conjunctivitis	Ophthalmic solution: 10,000 units/mL/0.1% (10 mL)	a
Sulfacetamide sodium/ prednisolone acetate ophthalmic (Blephamide®*)	Bacterial conjunctivitis‖, corneal ulcer‖	Ophthalmic ointment: 10%/0.2% (3.5 g) Ophthalmic suspension: 10%/0.2% (5, 10 mL)	a
Sulfacetamide sodium/ prednisolone sodium phosphate ophthalmic (Vasocidin®*)	Bacterial conjunctivitis‖, corneal ulcer‖	Ophthalmic solution: 10%/0.23% (5, 10 mL)	a
Tobramycin/ dexamethasone ophthalmic (Tobradex®*, Tobradex® ST)	Bacterial conjunctivitis‖, corneal ulcer‖	Ophthalmic ointment: 0.3%/0.1% (3.5 g) Ophthalmic suspension:	a (suspension)

Generic (Trade Name)	Food and Drug Administration Approved Indications	Dosage Form/Strength	Generic Availability
		0.3%/0.1% (2.5, 10 mL) 0.3%/0.05% (2.5, 5, 10 mL)	
Tobramycin/loteprednol etabonate ophthalmic (Zylet®)	Bacterial conjunctivitis¶, corneal ulcer	Ophthalmic suspension: 0.3%/0.5% (2.5, 5, 10 mL)	-
Neomycin sulfate/ polymyxin B sulfate/ bacitracin zinc ophthalmic (Neosporin®*)	Bacterial conjunctivitis, bacterial blepharitis, bacterial blepharo-conjunctivitis, keratitis, kerato-conjunctivitis	Ophthalmic ointment: 0.35%/10,000 units/g/ 400 units/g (3.5 g)	a
Neomycin sulfate/ polymyxin B sulfate/ dexamethasone ophthalmic (Maxitrol®*)	Bacterial conjunctivitis‖, corneal ulcer‖	Ophthalmic ointment: 0.35%/10,000 units/g/ 0.1% (3.5 g) Ophthalmic suspension: 3.5mg/mL/10,000 units /mL/0.1% (5 mL)	a
Neomycin sulfate/ polymyxin B sulfate/ gramicidin ophthalmic (Neosporin®*)	Bacterial conjunctivitis, bacterial blepharitis, bacterial blepharo-conjunctivitis, keratitis, kerato-conjunctivitis	Ophthalmic solution: 1.75 mg/mL/10,000 units/mL/0.025 mg/mL (10 mL)	a
Neomycin sulfate/ polymyxin B sulfate/ hydrocortisone ophthalmic	Bacterial conjunctivitis‖, corneal ulcer‖	Ophthalmic suspension: 0.35%/10,000 units/mL/ 1% (7.5 mL)	a
Neomycin sulfate/ polymyxin B sulfate/ prednisolone acetate sulfate ophthalmic (Poly-Pred®)	Bacterial conjunctivitis‖, corneal ulcer‖	Ophthalmic suspension: 0.35%/10,000 units/mL/ 0.5% (5 mL)	-
Neomycin sulfate/ polymyxin B sulfate/ bacitracin zinc/ hydrocortisone ophthalmic	Bacterial conjunctivitis‖, corneal ulcer‖	Ophthalmic ointment: 0.35%/10,000 units/g/ 400 units/g/1% (3.5 g)	a

* Due to Neisseria gonorrhoeae or Chlamydia trachomatis.
† Indicated for the treatment of superficial ocular infections involving the conjunctiva and/or cornea caused by organisms susceptible to erythromycin.
‡ Indicated for the treatment of conjunctivitis and other superficial ocular infections due to susceptible microorganisms, and as an adjunctive in systemic sulfonamide therapy of trachoma.
§ Indicated in the treatment of external infections of the eye and its adnexa caused by susceptible bacteria.
‖ Indicated for steroid-responsive inflammatory ocular conditions for which a corticosteroid is indicated and where superficial bacterial ocular infection or a risk of bacterial ocular infection exists, inflammatory conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe where the inherent risk of corticosteroid use in certain infective conjunctivitides is accepted to obtain diminution in edema and inflammation as well as use in chronic anterior uveitis and corneal injury from chemical, radiation or thermal burns or penetration of foreign bodies.
¶Indicated for steroid-responsive inflammatory ocular conditions for which a corticosteroid is indicated and where superficial bacterial ocular infection or a risk of bacterial ocular infection exists, inflammatory conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe such as allergic conjunctivitis, acne rosacea, superficial punctuate keratitis, herpes zoster keratitis, iritis, cyclitis, and where the inherent risk of steroid use in certain infective conjunctivides is accepted to obtain a diminution in edema and inflammation, as well as use in chronic anterior uveitis and corneal injury from chemical, radiation or thermal burns or penetration of foreign bodies.

Evidence-based Medicine

- Results from clinical trials have demonstrated that ophthalmic antibiotics are effective in treating and providing relief of conjunctivitis in pediatric and adult patients.[40-62] Several studies comparing ophthalmic antibiotics such as azithromycin, besifloxacin, levofloxacin, moxifloxacin and polymyxin B sulfate/bacitracin zinc to either placebo or vehicle have concluded that these medications resulted in significantly higher clinical resolution rates at days one through five.
- Head-to-head trials evaluating the efficacy of ophthalmic antibiotics for the treatment of bacterial conjunctivitis have found that no one medication was inferior to another. In one trial, significantly more patients treated with ophthalmic moxifloxacin had complete resolution of ocular signs and symptoms at 48 hours compared to treatment with ophthalmic polymyxin B sulfate/trimethoprim.[48] In a small meta-analysis, moxifloxacin was found to be associated with fewer drop-outs for treatment failure (*P*=0.002) compared to ofloxacin.[61] In a seven day trial, a higher percentage of patients receiving levofloxacin had microbial eradication at the final visit compared to patients receiving ofloxacin (*P*=0.034); however, clinical cure rates were similar between the two treatments (*P* value not reported).[63]
- In patients with a diagnosis of corneal ulcer, ophthalmic ciprofloxacin was shown to be an efficacious treatment option.[64-66] Specifically, in one trial of patients with a diagnosis of infectious keratitis ophthalmic ciprofloxacin had a shorter average time to healing as compared to ophthalmic cefazolin sodium fortified with gentamicin sulfate, although this was not found to be significant *(P* value not reported).[65]

Key Points within the Medication Class

- According to Current Clinical Guidelines:
  - There is insufficient evidence to recommend treatment for blepharitis, and due to the self-limiting nature of the condition, a cure is not possible in most cases. An ophthalmic antibiotic ointment may be prescribed and applied on the eyelid margins one or more times daily or at bedtime for one or more weeks. The combination of tobramycin/dexamethasone ophthalmic suspension and azithromycin in a sustained-release system appear to reduce some of the symptoms of blepharitis, but are not approved for this indication.[3]
  - Bacterial conjunctivitis may be self-limiting and resolve spontaneously without treatment in immunocompetent adults. Ophthalmic antibacterial therapy is associated with earlier clinical and microbiological remission compared to placebo at days two to five of treatment. The choice of ophthalmic antibiotic is usually empirical and a five to seven day course of ophthalmic broad-spectrum antibiotic is usually effective. The most convenient or least expensive option can be selected. For severe bacterial conjunctivitis, the choice of ophthalmic antibiotic is guided by the results of laboratory tests.[38]
  - Ophthalmic broad-spectrum antibiotics are used initially for empiric treatment of bacterial keratitis. Therapy with an ophthalmic fluoroquinolones has been shown to be as effective as combination therapy with fortified ophthalmic antibiotics. Ciprofloxacin 0.3%, ofloxacin 0.3% and levofloxacin 1.5% are Food and Drug Administration-approved for this indication. The fourth generation fluoroquinolones have not been approved for the treatment of bacteria keratitis, however, both agents have performed at least as well as standard therapy and potentially better than ciprofloxacin.[39]
  - Some pathogens (e.g., *Streptococci*, anaerobes) reportedly have variable susceptibility to ophthalmic fluoroquinolones and the prevalence of resistance to fluoroquinolones appears to be increasing. The initial therapeutic regimen should be modified (change in type, concentration or frequency of antibiotic) when the eye shows a lack of improvement or stabilization within 48 hours.[39]
- Other Key Facts:
  - There is at least one generic product available for treating each of the conditions outlined in outlined in Table 1.[1]
  - With the approval of gatifloxacin 0.5% ophthalmic solution (Zymaxid®) in 2010, Allergan discontinued manufacturing of the 0.3% strength (Zymar®) in January 2011. Both agents have the same indications and administration schedule.[1]

- Both ophthalmic moxifloxacin formulations (Moxeza® and Vigamox®) are 0.5% solutions. Moxeza® may be administered twice daily while Vigamox® is to be administered three times daily for seven days.[15,16]
- Ciprofloxacin and ofloxacin are considered second-generation fluoroquinolones, with levofloxacin being a third-generation fluoroquinolone. The fourth-generation fluoroquinolones include gatifloxacin, moxifloxacin and the newest fluoroquinolone, besifloxacin.[67,68]

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Therapeutic Class Overview
Extended-Release Injectable Atypical (Second-Generation) Antipsychotics

Therapeutic Class Overview/Summary:
This review will focus on the extended-release (ER) injectable atypical antipsychotics and will not cover oral or immediate-release injectable formulations. Collectively, all of the ER injectable atypical antipsychotic agents are Food and Drug Administration (FDA)-approved for the maintenance treatment of schizophrenia in adult patients.[1-6] Additionally, risperidone microspheres (Risperdal Consta®) is approved for the treatment of bipolar I disorder and paliperidone palmitate (Invega Sustenna®) is approved for the treatment of schizoaffective disorder.[4,6] Other ER injectable atypical antipsychotic products include aripiprazole (Abilify Maintena®), aripiprazole lauroxil (Aristada®), olanzapine pamoate (Zyprexa Relprevv®), and paliperidone palmitate (Invega Trinza®). Partial or total nonadherence with oral antipsychotics in the treatment of schizophrenia has been associated with significant increases in the risk of relapse and rehospitalization.[7] Long-acting injectable (LAI) antipsychotics were developed to ensure drug delivery through decreased dosing frequency, improved bioavailability, and more stable concentrations of drug. These attributes, coupled with the regular monitoring that is attendant to injectable treatment regimens, presumably can enhance medication adherence in patients with schizophrenia, thereby reducing the risk of relapse and improving the long-term prognosis of the illness.

Antipsychotic medications have been used for over fifty years to treat schizophrenia and a variety of other psychiatric disorders.[8] Schizophrenia is believed to be caused by an increase in the cerebral activity of dopamine D2 in the mesolimbic and/or mesocortical regions of the brain. Antipsychotic medications exert their effect in part by blocking D2 receptors. It is the blockade of these receptors in the mesolimbic pathway that is believed to contribute to desired antipsychotic effects, especially improvement of positive symptoms associated with the disorder.[9] As a class, atypical antipsychotics, or second-generation antipsychotics are more selective in targeting the mesolimbic D_2 pathway compared with older first-generation antipsychotics. They also block or partially block serotonin $(5\text{-HT})_{2A}$ and 5-HT_{1A} receptors and have a greater affinity for 5-HT_2 receptors than D_2 receptors.[9,10] The neuropharmacology of aripiprazole differs from other atypical antipsychotics, as it is a partial D_2 and 5-HT_{1A} agonist and a 5-HT_{2A} and 5-HT_{2C} antagonist. It is referred to as a D_2-serotonin system stabilizer since the partial agonist activity allows for blockade of an overstimulated receptor and stimulation of a receptor when activity is needed.[16] These differences in neuropharmacologic activity are associated with a lower risk of EPS and tardive dyskinesia; the risks vary with the specificity of each agent for D_2 and serotonin receptors.[9,10]

The ER injectable atypical antipsychotics are all administered via intramuscular administration. The location where the injection can be made varies by drug and also sometimes varies by strength. The acceptable locations may include the gluteus or deltoid muscles.[1-6] During maintenance therapy, aripiprazole, aripiprazole lauroxil, and paliperidone palmitate are dosed once a month. Additionally, aripiprazole lauroxil may be given once every six weeks in some cases. Risperidone microsphere is dosed every two weeks, olanzapine pamoate is dosed every two or four weeks, and paliperidone palmitate is dosed once every three months. Prior to initiating therapy with paliperidone palmitate (Invega Trinza®), the patient should be stabilized on once-monthly paliperidone palmitate (Invega Sustenna®) for at least four months.[1-6]

Table 1. Current Medications Available in the Therapeutic Class[1-6]

Generic (Trade Name)	FDA-Approved Indications	Dosage Form/Strength	Generic Availability
Aripiprazole (Abilify Maintena®)	Schizophrenia	ER Suspension for Injection (pre-filled dual chamber syringe): 300 mg 400 mg ER Suspension for Injection (single-use vial): 300 mg 400 mg Administer only via the deltoid or gluteal muscle. Must be administered by a health care professional.	-
Aripiprazole Lauroxil (Aristada®)	Schizophrenia	ER Suspension for Injection (pre-filled syringe): 441 mg/1.6 mL 662 mg/2.4 mL 882 mg/3.2 mL Administer via the deltoid (441 mg only) or gluteal muscles (all doses). Must be administered by a health care professional.	-
Olanzapine pamoate (Zyprexa Relprevv®)	Schizophrenia	ER Suspension for Injection (single-use vial): 210 mg 300 mg 405 mg Administer via the gluteal muscles. Must be administered by a health care professional.	-
Paliperidone palmitate (Invega Sustenna®, Invega Trinza®)	Schizoaffective disorder* (Invega Sustenna), Schizophrenia	ER Suspension for Injection (pre-filled syringe [Invega Sustenna®]): 39 mg/0.25 mL 78 mg/0.5 mL 117 mg/0.75 mL 156 mg/1 mL 234 mg/1.5 mL Administer via the deltoid or gluteal muscles. Must be administered by a health care professional. ER Suspension for Injection (pre-filled syringe [Invega Trinza®]): 273 mg/ 0.875 mL	-

Generic (Trade Name)	FDA-Approved Indications	Dosage Form/Strength	Generic Availability
		410 mg/1.315 mL 546 mg/1.75 mL 819 mg/2.625 mL	
Risperidone microsphere (Risperdal Consta®)	Bipolar I Disorder†, Schizophrenia	ER Suspension for Injection (single-use vials): 12.5 mg 25 mg 37.5 mg 50 mg	-

*Monotherapy and as an adjunct to mood stabilizers or antidepressants
†Monotherapy or as adjunctive therapy to lithium or valproate for the maintenance treatment

Evidence-based Medicine

- Numerus Clinical trials evaluating the safety and efficacy of the ER injectable atypical antipsychotics have been conducted.[11-49]
  - Safety and efficacy of these agents has been established in numerous clinical trials, mostly comparing each ER injectable to placebo.[1-6,11-49]
- Risperidone microsphere was compared to paliperidone palmitate (Invega Sustenna®) in two open-label studies. Results suggest there is a slight benefit in favor of paliperidone palmitate (Invega Sustenna®); however, the difference was not statistically significant in either trial.[41,42]
- In another study, after 12 months of treatment with risperidone microsphere or a typical antipsychotic, the time to all-cause treatment discontinuation was significantly shorter for individuals assigned to switch to risperidone than for individuals assigned to stay on a first generation injectable antipsychotic (P=0.01).[43]

Key Points within the Medication Class

- According to Current Clinical Guidelines:
  - The National Institute for Health and Clinical Excellence 2014 practice guideline for psychosis and schizophrenia in adults identifies candidates for injectable antipsychotic formulations as patients who prefer an injectable formulation after an acute episode or if the clinical treatment priority is to avoid non-adherence.[50]
  - Similarly, the American Psychiatric Association 2004 practice guidelines for schizophrenia state long-acting injectable antipsychotics may include patients have compliance issues.[51]
  - Clinical guidelines do not note a preference among the ER injectable antipsychotic agents.
- Other Key Facts:
  - There are no generic products currently available.
  - Dosing and injection site vary by drug and/or strength
    - The acceptable locations may include the gluteus or deltoid muscles.[1-6]
    - During maintenance therapy, aripiprazole, aripiprazole lauroxil, and paliperidone palmitate are dosed once a month. Additionally, aripiprazole lauroxil may be given once every six weeks in some cases. Risperidone microsphere is dosed every two weeks, olanzapine pamoate is dosed every two or four weeks, and paliperidone palmitate is dosed once every three months.
  - Prior to initiating therapy with paliperidone palmitate (Invega Trinza®), the patient should be stabilized on once-monthly paliperidone palmitate (Invega Sustenna®) for at least four months.[1-6]

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Therapeutic Class Overview
Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)

Therapeutic Class Overview/Summary:
This review encompasses the single-entity oral and injectable nonsteroidal anti-inflammatory drugs (NSAIDs).[1-37] NSAIDs are among the most commonly prescribed drugs worldwide to treat common pain and inflammatory conditions.[38] Some of the conditions NSAIDS have been Food and Drug Administration (FDA)-approved to treat include acute pain and inflammation, osteoarthritis (OA), rheumatoid arthritis (RA), ankylosing spondylitis (AS), painful shoulder (bursitis and/or tendonitis), acute gouty arthritis, and postoperative pain. Additionally several agents are indicated for the treatment of primary dysmenorrhea, clinically significant patent ductus arterioles, or fever reduction. Each year, approximately 60 million NSAID prescriptions are written, with the number of prescriptions for older patients approximately 3.6-fold higher than that for younger patients. NSAIDs have been prescribed for decades and a number are available generically and/or over-the-counter.[38] Salicylates, over-the-counter formulations of ibuprofen and naproxen, any topical and ophthalmic preparations of NSAIDs or combination products will not be included in this review. A list of medications reviewed is summarized in Table 1 and includes various salt formulations for the NSAIDs.

The primary mechanism of action of all NSAIDs is through the inhibition of cyclooxygenase (COX), resulting in impaired transformation of arachidonic acid to prostaglandins, prostacyclin, and thromboxanes.[39] The COX enzyme can be subdivided into related isoforms, including COX-1 and COX-2; however, important differences in the regulation and expression of these two enzymes in various tissues exist which are relevant to the mechanism of action of NSAIDs and their associated adverse effect profile. Specifically, the COX-2 enzyme is typically undetectable in most tissue except during states of inflammation; therefore, the anti-inflammatory properties of NSAIDs are associated with the inhibition of COX-2.[39] In contrast, COX-1 is expressed variably in most tissues and regulates normal cell processes including gastric cytoprotection, vascular homeostasis, platelet aggregation and kidney function. The inhibition of COX-1 by NSAIDs is thought to be associated with the well-established gastrointestinal adverse reaction profile of these agents, which includes dyspepsia, peptic ulcer disease and bleeding.[40]

All NSAID-containing agents are associated with a Black Box Warning regarding the increased risk of serious gastrointestinal adverse reactions including bleeding, ulceration and perforation of the stomach and intestines, which can be fatal.[1-37] Additionally, ketorolac tromethamine, a potent NSAID, is also contraindicated in renal impairment, patients at risk of bleeding (i.e., before surgery), and during labor, delivery, breast-feeding and coadministration with other NSAIDs.[15-17] Due to these risks, ketorolac should only be administered for acute pain (≤5 days).[15-17]

NSAIDs have traditionally been grouped by their chemical characteristics. Currently available products have been derived from acetic acid, anthranilic acid, enolic acid, or propionic acid. However, with the development of products selective to COX-2, classification has begun to shift towards selectivity, rather than chemical structure.[41] There is only one selective COX-2 inhibitor currently available, celecoxib (Celebrex®). In addition, recent evidence suggests that some of the older NSAIDs such as diclofenac and meloxicam show some selectivity towards the COX-2 enzyme.[41] Due to the variability in NSAID half-life ($t_{1/2}$), a classification system has also been developed to group NSAIDs by half-life. Some NSAIDs such as ibuprofen and diclofenac are eliminated rapidly ($t_{1/2}$ of one to four hours), while other agents have a much greater half-life. Agents with $t_{1/2}$ greater than 10 hours include: celecoxib, naproxen, meloxicam, nabumetone, oxaprozin and piroxicam. Piroxicam has an estimated $t_{1/2}$ of 50 hours.[41-43] Agents with longer half-lives are generally given once per day.

Table 1. Current Medications Available in the Therapeutic Class[1-34]

Generic (Trade Name)	Food and Drug Administration-Approved Indications	Dosage Form/Strength	Generic Availability
Acetic Acid Derivatives			
Diclofenac (Zorvolex®)	Mild to Moderate Pain, Osteoarthritis	Capsule: 18 mg 35 mg	-
Diclofenac potassium (Cataflam®*, Zipsor®)	Acute Pain, Mild to Moderate Pain, Primary Dysmenorrhea, Osteoarthritis, Rheumatoid Arthritis	Capsule, liquid filled (Zipsor®): 25 mg Tablet, sugar coated (Cataflam®): 50 mg	a
Diclofenac sodium* (Dyloject®, Voltaren XR®*)	Acute Pain, Ankylosing Spondylitis, Osteoarthritis, Rheumatoid Arthritis	Tablet, DR: 25 mg 50 mg 75 mg Tablet, film coated ER (Voltaren XR®): 100 mg Solution, injection (Dyloject®) 37.5 mg/mL	a
Etodolac*	Acute Pain, Osteoarthritis, Rheumatoid Arthritis, Juvenile Rheumatoid Arthritis (age six and older)	Capsule: 200 mg 300 mg Tablet, ER: 400 mg 500 mg 600 mg Tablet, film coated: 400 mg 500 mg	a
Indomethacin* (Indocin®, Tivorbex®)	Acute Pain, Acute Gouty Arthritis, Acute Shoulder Pain, Ankylosing Spondylitis, Rheumatoid Arthritis, Osteoarthritis	Capsule: 20 mg (Tivorbex®) 25 mg 40 mg (Tivorbex®) 50 mg Capsule, ER: 75 mg Suppository: 50 mg (Indocin®) Suspension, oral: 25 mg/5 mL (Indocin®)	a
Indomethacin sodium	Closure of Patent Ductus Arteriosus (Neonatal patients)	Solution, lyophilized powder for injection: 1 mg/vial	-

Generic (Trade Name)	Food and Drug Administration-Approved Indications	Dosage Form/Strength	Generic Availability
Ketorolac tromethamine* (Sprix®)	Moderate to severe acute pain:	Nasal Spray, metered: 15.75 mg/spray Solution, injection (vial): 15 mg/mL 30 mg/mL 60 mg/2 mL 300 mg/10 mL Tablet, film coated: 10 mg	a
Nabumetone*	Osteoarthritis, Rheumatoid Arthritis	Tablet: 500 mg 750 mg	a
Sulindac*	Acute Gouty Arthritis, Acute Shoulder Pain, Ankylosing Spondylitis, Osteoarthritis, Rheumatoid Arthritis	Tablet: 150 mg 200 mg	a
Tolmetin sodium*	Osteoarthritis, Rheumatoid Arthritis, Juvenile Rheumatoid Arthritis (age 2 or older)	Capsule: 400 mg Tablet: 200 mg 600 mg	a
Anthranilic Acid (Fenamate) Derivatives			
Meclofenamate sodium	Fever Reduction, Mild to moderate pain, Primary dysmenorrhea, Rheumatoid arthritis, osteoarthritis	Capsule: 50 mg 100 mg	-
Mefenamic acid (Ponstel®*)	Mild to moderate pain, Primary dysmenorrhea	Capsule: 250 mg	a
Enolic Acid Derivatives			
Meloxicam (Mobic®*, Vivlodex®)	Osteoarthritis, Rheumatoid Arthritis, Juvenile Rheumatoid Arthritis (age 2 and older)	Capsule (Vivlodex®): 5 mg 10 mg Suspension, oral (Mobic®): 7.5 mg/5 mL Tablet (Mobic®): 7.5 mg 15 mg	a
Piroxicam (Feldene®*)	Osteoarthritis, Rheumatoid Arthritis	Capsule: 10 mg 20 mg	a
Propionic Acid Derivatives			
Fenoprofen calcium* (Nalfon®*)	Mild to Moderate Pain, Osteoarthritis, Rheumatoid Arthritis	Capsule: 200 mg 400 mg Tablet, film coated:	a

Generic (Trade Name)	Food and Drug Administration-Approved Indications	Dosage Form/Strength	Generic Availability
		600 mg	
Flurbiprofen*	Osteoarthritis, Rheumatoid Arthritis	Tablet: 50 mg 100 mg	a
Ibuprofen* (Caldolor®)	Fever Reduction, Mild to Moderate Pain, Moderate to Severe Pain, Osteoarthritis, Rheumatoid Arthritis, Primary Dysmenorrhea:	Injection (Caldolor®): 400 mg/mL 800 mg/mL Tablet, film coated: 400 mg 600 mg 800 mg	a
Ibuprofen Lysine (Neoprofen®)	Closure of Patent Ductus Arteriosus (Neonatal patients)	Solution, injection: 10 mg/mL	-
Ketoprofen*	Acute Pain, Primary Dysmenorrhea, Osteoarthritis, Rheumatoid Arthritis	Capsule: 50 mg 75 mg	a
Naproxen (EC-Naprosyn®*, Naprosyn®*)	Ankylosing Spondylitis, Osteoarthritis, Rheumatoid Arthritis, Acute Gouty Arthritis, Juvenile rheumatoid arthritis (5 years of age and older)	DR Tablet (EC-Naprosyn®): 375 mg Suspension, oral: 125 mg/5 mL Tablet (Naprosyn®): 250 mg 375 mg 500 mg	a
Naproxen sodium (Anaprox®*, Anaprox DS®*, Naprelan®*)	Ankylosing Spondylitis, Osteoarthritis, Rheumatoid Arthritis, Acute Gouty Arthritis, Acute Pain, Acute Shoulder Pain, Primary Dysmenorrhea	Tablet: 275 mg (Anaprox®) 550 mg (Anaprox DS®) ER tablet: 375 mg 500 mg 750 mg	a
Oxaprozin (Daypro®*)	Osteoarthritis, Rheumatoid arthritis, Juvenile Rheumatoid Arthritis (6 years of age and older)	Tablet: 600 mg	a
Selective COX-2 Inhibitors			
Celecoxib (Celebrex®*)	Acute Pain, Primary Dysmenorrhea, Juvenile Rheumatoid Arthritis (2 years of age and older)	Capsule: 50 mg 100 mg 200 mg 400 mg	a

*Generic available in at least one dosage form or strength.

Evidence-based Medicine

- Clinical trials have demonstrated NSAIDs to be more efficacious compared to placebo in the treatment of pain and inflammatory conditions. Although there are many head to head trials comparing various NSAIDs, there is no single agent that has been continuously found to be more efficacious or safe than the others.[44-75]

Key Points within the Medication Class

- According to Current Clinical Guidelines:[76-82]
  - Although the efficacy of NSAIDs appears to be similar at equipotent doses, there is a wide variability of response between individual patients, which is believed to be associated with non-prostaglandin-mediated NSAID-induced mechanisms of action.
  - It is suggested that if a patient fails an NSAID of one class, an NSAID from a different class may be effective and is a reasonable option.[38]
- Other Key Facts:
  - There are many generic and over-the-counter (OTC) NSAIDs available.
  - In recent years, newer formulations of NSAIDs have been developed. Recently approved products include: enteric-coated tablets, liquid filled capsules, nasal spray, suppositories, oral suspensions, and injections.
  - Several NSAIDs have recently been formulated using the SoluMatrix Fine Particle Technology™.[83]
    - SoluMatrix™ is a patented dry milling technology, which grinds the drug particles into a superfine powder and protects those submicron particles from subsequent agglomeration (clumping together into big particles).
    - SoluMatrix Fine Particle Technology™ produces NSAIDs as submicron particles that are approximately 20 times smaller than their original size.
    - The reduction in particle size provides an increased surface area, leading to faster dissolution.
    - It may also allow the NSAID to be given at a lower dose than a standard-formulation.
    - Products currently approved that utilize the SoluMatrix™ technology include Zorvolex® (diclofenac capsules), Tivorbex® (indomethacin capsules), and Vivlodex® (meloxicam capsules).[83]

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OPTUMRx®

RxOutlook®

1st Quarter 2016

Pending drug approvals

Drug name	Manufacturer	Indication/use	Expected FDA decision date
dronabinol	Insys Therapeutics	• AIDS-associated anorexia • Chemotherapy-associated nausea and vomiting	4/2016
methylnaltrexone (Relistor®)	Valeant/Progenics	Opioid-induced constipation	4/2016
venetoclax	AbbVie/Genentech	Chronic lymphocytic leukemia	4/2016–5/2016
pimavanserin (Nuplazid™)	Acadia	Parkinson's psychosis	5/2016
sodium zirconium cyclosilicate	ZS Pharma	Hyperkalemia	5/26/2016
arbaclofen extended-release (Ontinua™ ER)	Osmotica	Spasticity associated with multiple sclerosis	5/2016–6/2016
benzhydrocodone/ acetaminophen	KemPharm	Pain management	6/9/2016
testosterone undecanoate	Lipocine/AbbVie	Hypogonadism	6/28/2016
sofosbuvir/velpatasvir	Gilead	Hepatitis C	6/28/2016
lixisenatide (Lyxumia®)	Sanofi/Alkermes/Zealand	Type 2 diabetes mellitus	6/2016–7/2016
lixisenatide/insulin glargine (LixiLan™)	Sanofi/Alkermes/Zealand	Type 2 diabetes mellitus	6/2016–7/2016
glycopyrrolate/formoterol	AstraZeneca	Chronic obstructive pulmonary disease (COPD)	2Q2016

dronabinol

Manufacturer: Insys Therapeutics

Therapeutic use
Insys Therapeutics' dronabinol is an oral solution. It is being pursued for two indications: (1) treatment of anorexia associated with weight loss in patients with acquired immune deficiency syndrome (AIDS); (2) nausea and vomiting associated with chemotherapy in patients who have failed on conventional antiemetic treatments.

Currently, brand and generic dronabinol capsules are available for the same indications as the pending oral solution.

- Treatment of anorexia associated with weight loss in AIDS patients
- Treatment of chemotherapy-associated nausea and vomiting

Clinical profile
Dronabinol is a cannabinoid receptor agonist.

Dronabinol is one of the psychoactive compounds present in cannabis and has abuse potential. Thus, similar to Marinol® (dronabinol) capsules, it is expected to be listed as a Schedule III (C-III) controlled substance.

Dronabinol oral solution is supported by bioequivalency data, demonstrating bioequivalence to Marinol capsules.

The safety concerns are expected to be similar to Marinol capsules. Significant adverse events may include depersonalization, euphoria, hallucinations, paranoia, and abnormal reactions.

Similar to Marinol, the dose of dronabinol oral solution is expected to vary by the specific indication.

- Cannabinoid receptor agonist
- Controlled substance (C-III)
- Oral solution
- Bioequivalent to Marinol capsules
- Common adverse events: similar to Marinol capsules

Competitive environment
Dronabinol oral solution is a new formulation and may be useful for patients with difficulty swallowing.

However, there is no compelling clinical advantage over dronabinol capsules, which are generically available.

- Advantages: new formulation, possible use in those unable to swallow
- Disadvantages: similar product is available (ie, dronabinol capsules), controlled substance

Expected FDA decision date
An FDA decision regarding the approval of Insys Therapeutics' dronabinol oral solution is expected in April 2016.

- PDUFA: 4/2016

methylnaltrexone (Relistor)

Manufacturer: Valeant/Progenics

Therapeutic use

Valeant, in partnership with Progenics, is developing a new oral formulation of methylnaltrexone, for the treatment of opioid-induced constipation in adults with chronic non-cancer pain.

Methylnaltrexone is currently available as Relistor for subcutaneous injection. The injection is approved for opioid-induced constipation in adults with chronic non-cancer pain and for opioid-induced constipation in adults with advanced illness.

- Treatment of opioid-induced constipation in chronic non-cancer pain

Clinical profile

Methylnaltrexone is a peripheral opioid receptor antagonist.

In a clinical trial, less patients in the oral methylnaltrexone group required rescue therapy to achieve laxation vs. the placebo group ($p < 0.05$). In addition, more patients achieved laxation within 4 hours of the first dose vs. placebo.

The most common adverse events with oral methylnaltrexone use were abdominal pain, nausea, flatulence, and diarrhea. However, the overall incidence of adverse events was comparable to placebo.

Based on trial information, oral methylnaltrexone will be dosed once daily.

- Opioid receptor antagonist
- Improved rescue-free laxation vs. placebo
- Common adverse events: abdominal pain, nausea, flatulence, diarrhea

Competitive environment

This formulation of methylnaltrexone has two primary benefits — it is orally administered and dosed once daily.

However, methylnaltrexone is not a unique product. It is already available as an injection. Moreover, other oral treatment options are available for treating opioid-induced constipation in adults with chronic non-cancer pain (ie, Amitiza®, Movantik™).

The projected annual U.S. sales for oral methylnaltrexone are $225 million by 2020.

- Advantages: oral formulation, once daily dosing
- Disadvantages: related product is available (ie, Relistor injection), other oral therapeutic alternatives are available (eg, Amitiza, Movantik)

Expected FDA decision date

An FDA decision regarding the approval of oral methylnaltrexone is expected in April 2016.

- PDUFAs: 4/2016

venetoclax

Manufacturer: AbbVie/Genentech

Therapeutic use
Venetoclax is in development for the treatment of chronic lymphocytic leukemia (CLL) in adults who have received at least 1 prior therapy, including patients with 17p deletion.

The 17p deletion is associated with rapid disease progression and short survival. An estimated 3%–10% of CLL patients have this deletion at diagnosis, and 30%–50% of relapsed or refractory CLL patients have this deletion.

- Treatment of CLL in adults who received ≥ 1 prior therapy, including patients with 17p deletion

Clinical profile
Venetoclax is an oral apoptosis stimulator. It works by targeting the B-cell lymphoma-2 (BCL-2) family of proteins, which regulate apoptosis.

Currently, trial data are only available for one single-arm phase 2 trial, in which patients received venetoclax as monotherapy. The objective response rate (ORR) was 79.4%.

Significant safety concerns associated with venetoclax include pulmonary embolism, febrile neutropenia, infection, anemia, thrombocytopenia, and tumor lysis syndrome (TLS). However, the clinical risk for TLS may be reduced or eliminated by ramping-up the dose over several weeks.

Other trials are still in progress, including active-controlled trials comparing venetoclax as part of combination treatment regimens.

Based on trial information, the oral dose of venetoclax will be once daily.

- Apoptosis stimulator
- Oral formulation
- ORR = 79.4%
- Safety concerns: pulmonary embolism, febrile neutropenia, infection, anemia, thrombocytopenia, and TLS

Competitive environment
Venetoclax is an oral, orphan drug that employs a novel mechanism for treating CLL patients. In addition, it is dosed once daily and may benefit patients with the 17p deletion.

However, venetoclax is not expected to be a first-line agent. Moreover, late-stage trial data are still lacking, and there are no overall survival data at this time.

The projected annual U.S. sales for venetoclax are over $1 billion by 2020.

- Advantages: novel mechanism, oral formulation, once daily dosing, orphan drug status, benefit in CLL 17p deletion
- Disadvantages: not first-line, late-stage trial results or overall survival data are not available

Expected FDA decision date
An FDA decision regarding the approval of venetoclax is expected by April or May 2016.

- PDUFA: 4/2016–5/2016

pimavanserin (Nuplazid)

Manufacturer: Acadia

Therapeutic use
Pimavanserin is in development for the treatment of psychosis associated with Parkinson's disease (PD).

- Treatment of psychosis associated with PD

Clinical profile
Pimavanserin is an oral selective serotonin inverse agonist. It works by stabilizing the inactive conformation of the target receptor, thus, inhibiting the spontaneous conversion of the receptor to its active conformation in the absence of a ligand.

Trial results have been inconsistent for pimavanserin. While one trial did show greater improvement from baseline in psychotic symptoms compared to placebo (p = 0.001), two other trials failed to demonstrate a statistically significant difference.

Common adverse events reported in trials include urinary tract infections, falls, drowsiness, headache, and dizziness.

Based on trial information, pimavanserin will be dosed once daily.

- Selective serotonin inverse agonist
- Oral formulation
- Inconsistent trial results
- Common adverse events: urinary tract infections, falls, drowsiness, headache, and dizziness

Competitive environment
Currently, there are no FDA-approved drugs for the treatment of psychosis associated with PD. Thus, if approved, pimavanserin would be the first drug to hold this indication.

Unfortunately, the trial data are mixed, with two trials failing to achieve their primary endpoints.

The projected annual U.S. sales for pimavanserin are $201 million by 2020.

- Advantage: no FDA-approved drugs for psychosis associated with PD
- Disadvantage: some trials failed to achieve their key endpoints

Expected FDA decision date
The FDA's Psychopharmacologic Drugs Advisory Committee (AdCom) is scheduled to meet on March 29, 2016 to discuss the risks and benefits of pimavanserin in psychosis associated with PD.

An FDA decision regarding the approval of pimavanserin is expected in May 2016.

- FDA AdCom: 3/29/2016
- PDUFA: 5/2016

sodium zirconium cyclosilicate

Manufacturer: ZS Pharma

Therapeutic use
Sodium zirconium cyclosilicate is in development for the treatment of hyperkalemia.

- Treatment of hyperkalemia

Clinical profile
Sodium zirconium cyclosilicate is an oral, non-absorbable potassium binder. In the gastrointestinal tract, this product preferentially traps potassium ions over other ions.

Sodium zirconium cyclosilicate is being developed as an odorless and tasteless powder or oral tablet.

In pivotal trials, sodium zirconium cyclosilicate normalized potassium levels in 84% of hyperkalemic patients within 24 hours and 98% of patients within 48 hours. In patients who were switched from the active drug to placebo, 46% of patients remained normal vs. 80%–94% of patients who continued on sodium zirconium cyclosilicate.

The most common adverse event reported in trials was diarrhea.

Based on trial information, the dose of sodium zirconium cyclosilicate may vary depending on its use for acute or maintenance therapy.

- Potassium binder
- Oral formulation
- 84% of patients achieved normal potassium levels within 24 hours
- More patients maintain normal potassium levels vs. placebo
- Common adverse event: diarrhea

Competitive environment
Kayexalate® (sodium polystyrene sulfonate) is the primary oral drug used to treat hyperkalemia. However, Kayexalate is poorly tolerated. Gastrointestinal complaints are common, and its approval was not based on clinical trial data.

Nonetheless, Kayexalate is generically available. In addition, Veltassa™ (patiromer), another oral potassium binder, was recently approved for the same indication. But due to the absence of head-to-head trials, it is unclear whether sodium zirconium cyclosilicate offers a compelling clinical advantage over its competition.

The projected annual U.S. sales for sodium zirconium cyclosilicate are $721 million by 2020.

- Advantages: Kayexalate is poorly tolerated and lacks clinical trial data
- Disadvantages: other options are available (ie, Kayexalate, Veltassa), no head-to-head trial data

Expected FDA decision date
An FDA decision regarding the approval of sodium zirconium cyclosilicate is expected by May 26, 2016.

- PDUFA: 5/26/2016

arbaclofen extended-release (Ontinua ER)

Manufacturer: Osmotica

Therapeutic use
Arbaclofen extended-release (ER) is in development for the treatment of spasticity in adults with multiple sclerosis (MS).

- Treatment of spasticity in adults with MS

Clinical profile
Arbaclofen is an oral derivative of baclofen, a gamma aminobutyric acid (GABA) receptor agonist and antispasmodic agent. GABA reduces neuronal excitability and is also responsible for the regulation of muscle tone.

In a clinical trial, arbaclofen ER was compared to baclofen and placebo. Muscle tone was measured using the Modified Ashworth Scale (MAS). In addition, symptom response and severity were measured using the Clinical Global Impression of Change (CGIC). Arbaclofen met its co-primary endpoints for MAS and CGIC.

Due to limited data, the degree of clinical improvement and safety concerns are not known at this time.

Based on trial information, arbaclofen ER will be dosed twice daily.

- GABA receptor agonist
- Oral formulation
- Arbaclofen ER met its co-primary endpoints vs. baclofen
- Approximately 50%–80% of MS patients will suffer from spasticity

Competitive environment
Arbaclofen ER is an oral drug dosed twice daily. In contrast, baclofen may require three to four doses per day to manage spasticity.

However, baclofen is a similar product that is generically available. Thus, arbaclofen is not a unique clinical treatment.

Currently, various products are available to manage spasticity in MS patients including tizanidine, diazepam, dantrolene, clonidine, and onabotulinumtoxin A.

An estimated 50%–80% of MS patients will suffer from spasticity at some point during the course of their disease.

- Advantages: oral, twice daily dosing
- Disadvantages: not a clinically unique offering, related product is available (ie, baclofen)

Expected FDA decision date
An FDA decision regarding the approval of arbaclofen extended-release is expected by May or June 2016.

- PDUFA: 5/2016–6/2016

benzhydrocodone/acetaminophen

Manufacturer: KemPharm

Therapeutic use

Benzhydrocodone/acetaminophen (APAP) is a fixed-dose combination (FDC) product in development for the management of pain where the use of an opioid analgesic is appropriate.

- Management of pain where the use of an opioid analgesic is appropriate

Clinical profile

The product combines an opioid receptor agonist, benzhydrocodone, with a non-opioid analgesic, APAP.

In a bioequivalency study, benzhydrocodone/APAP was compared to Norco® (hydrocodone/APAP), a commonly prescribed opioid combination agent. When given as a single dose, the plasma concentrations of hydrocodone, hydromorphone, and APAP were comparable to an equimolar dose of Norco.

Because benzhydrocodone is a prodrug of hydrocodone, a drug with high potential for abuse and diversion, benzhydrocodone/APAP will likely be classified as a Schedule II (C-II) controlled substance similar to other hydrocodone combination products.

- Opioid agonist/analgesic combination
- C-II controlled substance
- Oral formulation
- Bioequivalent to Norco
- Common adverse events: similar to other products containing hydrocodone and APAP

However, benzhydrocodone/APAP is being developed as a tamper-resistant, abuse-deterrent product to prevent the release of the opioid by crushing, physical manipulation, or other extraction techniques.

In an intranasal human abuse liability trial, benzhydrocodone reduced the overall exposure to hydrocodone vs. hydrocodone bitartrate when both were administered intranasally. Moreover, benzhydrocodone showed reduced abuse potential, including lower drug liking scores vs. hydrocodone ($p < 0.0001$). But in a second trial evaluating the FDC vs. Norco, drug liking scores were similar for all treatments, which KemPharm believes was due to the APAP component.

The common adverse events are expected to be similar to other related products containing hydrocodone and APAP.

The dosing frequency of benzhydrocodone/APAP is expected to be comparable to other immediate-release opioid-combination products.

Continued…

benzhydrocodone/acetaminophen (Continued…)

Manufacturer: KemPharm

Competitive environment

If approved, benzhydrocodone/APAP would be the first immediate-release, abuse-deterrent opioid combination product. It would offer another pain management option to patients and add to the growing list of abuse-deterrent opioid agents.

However, there are many opioid options currently available on the market. Moreover, it is unclear whether existing abuse-deterrent opioids have significantly reduced the incidence of opioid abuse and dependence.

- Advantage: first immediate-release, abuse-deterrent opioid combination
- Disadvantage: many opioid alternatives are available

Expected FDA decision date

The FDA has granted priority review for benzhydrocodone/APAP. Thus, a decision regarding the approval of benzhydrocodone/APAP is expected by June 9, 2016.

- PDUFA: 6/9/2016

testosterone undecanoate

Manufacturer: Lipocine/AbbVie

Therapeutic use
Lipocine and AbbVie's testosterone undecanoate is an oral prodrug of testosterone in development for the treatment of hypogonadism in adult male patients.

- Treatment of hypogonadism in adult male patients

Clinical profile
Testosterone is an androgenic hormone.

Because oral testosterone is heavily metabolized by the liver, existing testosterone products are formulated for either transdermal or intramuscular delivery.

However, testosterone undecanoate is an oral prodrug designed to bypass the first-pass hepatic effect, thus, allowing for more active drug to reach systemic circulation before being significantly metabolized.

In trials, 88% of patients were able to achieve normal testosterone levels with oral testosterone undecanoate, and 85% of subjects were able to achieve these levels with only 1 dose titration.

Common adverse events reported in trials include upper respiratory tract infection (URTI), fatigue, headaches, weight increase, hypertension, and acne. Less than or equal to 1% of patients experienced peripheral edema, polycythemia, and thrombocytopenia.

Similar to other testosterone products, oral testosterone undecanoate is expected to be listed as a Schedule III (C-III) controlled substance.

Based on trial information, testosterone undecanoate will be dosed twice daily.

- Androgen hormone
- Oral formulation
- 88% of patients achieved normal testosterone levels
- Common adverse events: URTI, fatigue, headaches, weight increase, hypertension, and acne

Competitive environment
Testosterone undecanoate is an oral agent formulated to bypass the first-pass hepatic effect. If approved, it may provide a convenient way for patients to treat their condition.

Furthermore, available testosterone products carry boxed warnings. The transdermal agents warn about the risks for secondary exposure to testosterone. The injectables warn about the risk for pulmonary microembolism and anaphylaxis. Oral testosterone undecanoate is expected to avoid these concerns and the need for a boxed warning.

However, testosterone undecanoate will still be a controlled substance. Moreover, its long-term adverse effects remain uncertain.

In 2015, an estimated 500,000 prescriptions per month were dispensed for testosterone products.

- Advantages: oral formulation, bypass first-pass hepatic effect, possibly no boxed warning
- Disadvantages: controlled substance, long-term effects uncertain

Expected FDA decision date
An FDA decision regarding the approval of oral testosterone undecanoate is expected by June 28, 2016.

- PDUFA: 6/28/2016

sofosbuvir/velpatasvir

Manufacturer: Gilead

Therapeutic use

Sofosbuvir/velpatasvir is a FDC product for the treatment of chronic hepatitis C virus (HCV) infection in patients with genotypes 1–6.

- Treatment of HCV genotypes 1–6 infection

Clinical profile

Sofosbuvir is an NS5B polymerase inhibitor. Velpatasvir is an NS5A inhibitor. Together these agents work by different mechanisms to eradicate HCV.

There are multiple clinical trials that evaluated sofosbuvir/velpatasvir across different genotypes, including treatment-naïve, treatment-experienced, cirrhotic, and non-cirrhotic patients. The overall sustained virologic response 12 weeks after treatment (SVR12) were 97%–100%. Among genotype 2, genotype 3, and decompensated cirrhotics, the SVR12 rates were greater than 90%.

- NS5B polymerase inhibitor/ NS5A inhibitor combination
- Targets all HCV genotypes
- Overall SVR12 rates were 97%–100%

Common adverse events include fatigue, nausea, and headache. In the trials that evaluated sofosbuvir/velpatasvir in combination with ribavirin, anemia was a common and anticipated adverse event due to the addition of ribavirin.

- Common adverse events: fatigue, nausea, headache

Based on trial information, sofosbuvir/velpatasvir will be dosed as 1 pill orally once daily for 12 weeks, regardless of genotype.

Competitive environment

If approved, sofosbuvir/velpatasvir would be the first pan-genotypic agent for HCV. In addition, it may have high efficacy in underserved and difficult-to-treat populations, including decompensated cirrhotic patients.

- Advantages: first pan-genotypic HCV drug, may benefit other genotypes and difficult-to-treat populations

However, sofosbuvir/velpatasvir is entering an increasingly competitive market. Examples of all-oral HCV regimens include Harvoni®, Viekira Pak™, Technivie™, and Zepatier™. Sofosbuvir is also used in combination with other agents (eg, Daklinza™) for treating specific genotypes.

- Disadvantage: other all-oral regimens are available

The projected peak U.S. sales for sofosbuvir/velpatasvir are $5.1 billion by 2018.

Expected FDA decision date

An FDA decision regarding the approval of sofosbuvir/velpatasvir is expected by June 28, 2016.

- PDUFA: 6/28/2016

lixisenatide (Lyxumia) and lixisenatide/insulin glargine (LixiLan)

Manufacturer: Sanofi/Alkermes/Zealand

Therapeutic use
Both lixisenatide and lixisenatide/insulin glargine are in development as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus (T2DM).

- Adjunct to diet and exercise to improve glycemic control in T2DM

Clinical profile
Lixisenatide is a glucagon-like peptide-1 (GLP-1) receptor agonist. Insulin glargine is a long-acting insulin. These agents work by different mechanisms to improve glycemic control.

In clinical trials, lixisenatide was non-inferior to Byetta® (exenatide) at lowering average blood glucose levels (ie, hemoglobin A1c) and achieved lower hemoglobin A1c values than insulin glargine. In addition, there was a 6-fold lower risk for hypoglycemia with lixisenatide vs. exenatide.

- GLP-1 agonist with or without long-acting insulin
- Superior reductions in hemoglobin A1c vs. insulin glargine

Similarly, the combination of lixisenatide and insulin glargine achieved lower hemoglobin A1c levels than either lixisenatide or insulin glargine alone. Moreover, some trials suggest that the risk of hypoglycemia with lixisenatide plus insulin glargine may be no greater than with insulin glargine.

- Common adverse events: nausea, vomiting, diarrhea, and hypoglycemia

Common adverse events reported in trials with lixisenatide use were nausea, vomiting, diarrhea, and hypoglycemia.

Based on trial information, both lixisenatide and lixisenatide/insulin glargine will be dosed once daily by subcutaneous injection.

Competitive environment
Lixisenatide is another GLP-1 agonist, similar to agents such as Byetta, Victoza®, Trulicity®, and Tanzeum®.

Some trials suggest that lixisenatide plus insulin glargine may have no greater risk for hypoglycemia than insulin glargine; nonetheless, GLP-1 agonists and long-acting insulin products are already available. Thus, the main benefit to patients may be the convenience of the combination product, which reduces the number of injections needed in those who require both a GLP-1 agonist and a long-acting insulin product.

- Advantages: another treatment option, combination product, possibly no greater hypoglycemic risk vs. insulin glargine
- Disadvantages: other GLP-1 agonists are available, crowded market

The projected annual U.S. sales for lixisenatide are $146–$249 million by 2020.

The projected annual U.S. sales for lixisenatide/insulin glargine are $283–$500 million by 2020.

Expected FDA decision date
An FDA decision regarding the approval of lixisenatide and lixisenatide/insulin glargine is expected by June or July 2016.

- PDUFA: 6/2016–7/2016

glycopyrrolate/formoterol

Manufacturer: AstraZeneca

Therapeutic use
Glycopyrrolate/formoterol is a FDC product in development for the treatment of chronic obstructive pulmonary disease (COPD).

- Treatment of COPD

Clinical profile
Glycopyrrolate is a long-acting muscarinic antagonist (LAMA) combined with formoterol, a long-acting beta agonist (LABA).

This FDC product is being formulated as a hydrofluoroalkane metered-dose inhaler. Hydrofluoroalkane is a propellant, which is replacing the chlorofluorocarbon propellants due to environmental concerns.

In clinical trials, the FDC product showed greater improvement in lung function compared to glycopyrrolate or formoterol alone.

Common adverse events are expected to be similar to the individual components, which may include nasopharyngitis, hypertension, and URTI.

- LAMA/LABA combination
- Inhaled formulation
- Greater improvement in lung function vs. individual components
- Common adverse events: nasopharyngitis, hypertension, and URTI

Competitive environment
Overall, glycopyrrolate/formoterol offers another treatment option for patients and may provide a convenient alternative to the individual agents, which are marketed as Seebri™ Neohaler® (glycopyrrolate) and Foradil® (formoterol).

However, there are many treatment options available for COPD, including other LAMA/LABA combinations (eg, Utibron™ Neohaler®, Anoro® Ellipta®). Thus, glycopyrrolate/formoterol is not a unique clinical offering.

The projected annual U.S. sales for glycopyrrolate/formoterol are $432 million by 2020.

- Advantages: another treatment option, may offer convenience as a combination product
- Disadvantage: other treatment options are available (eg, Utibron Neohaler, Anoro Ellipta)

Expected FDA decision date
An FDA decision regarding the approval of glycopyrrolate/formoterol is expected in the second quarter of 2016.

- PDUFA: 2Q2016

OptumRx brand pipeline forecast

OptumRx closely monitors and evaluates the pipeline landscape for upcoming brand drug approvals, including both traditional and specialty medications. This report provides a summary of developmental drugs that may be approved in the upcoming two years.

Read more

OptumRx generic pipeline forecast

OptumRx closely monitors and evaluates the pipeline landscape for upcoming first-time generics and biosimilars. This report provides a summary of upcoming first-time generic drugs and biosimilars that may be approved in the upcoming two years.

Read more

Getting acquainted with pipeline forecast terms

Clinical trial phases

Phase I trials	Researchers test an experimental drug or treatment in a small group of people for the first time to evaluate its safety, determine a safe dosage range, and identify side effects.
Phase II trials	The experimental study drug or treatment is given to a larger group of people to see if it is effective and to further evaluate its safety.
Phase III trials	The experimental study drug or treatment is given to large groups of people to confirm its effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will allow the experimental drug or treatment to be used safely.
Phase IV trials	Post marketing studies delineate additional information including the drug's risks, benefits, and optimal use.

Pipeline acronyms

ANDA	Abbreviated New Drug Application
BLA	Biologic License Application
CRL	Complete Response Letter
FDA	Food and Drug Administration
NME	New Molecular Entity
NDA	New Drug Application
sBLA	Supplemental Biologic License Application
sNDA	Supplemental New Drug Application
OTC Drugs	Over-the-Counter Drugs
PDUFA	Prescription Drug User Fee Act
REMS	Risk Evaluation and Mitigation Strategy

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