AHCCCS
Arizona Health Care Cost Containment System

AHCCCS Pharmacy and Therapeutics Committee

July 10, 2017

Introductions & Minutes Approval

- April 13, 2017 Meeting Minutes
- Review and Amend
- Vote

P&T Meeting Dates

- **2017 Next Meeting Date:**
  - Thursday October 12, 2017
- **2018 Meeting Dates:**
  - January 16, 2018
  - April 17, 2018
  - July 17, 2018
  - October 16, 2018

Magellan Drug Class Reviews

Richard L. Pope, R.Ph., Pharm.D.

Magellan Class Reviews

Therapeutic Classes

- Oral Atypical (2nd Generation) Antipsychotics
- Long-Acting Atypical Injectable Antipsychotics
- Stimulants
- Pancreatic Enzymes
- Anticoagulants
- Hemophilia Factor

Oral Atypical Second Generation Antipsychotics

Rick Pope, PharmD

Magellan

Antipsychotics

Class Overview - Product indications include*:

- Schizophrenia, Bipolar disorder, major depressive order, schizoaffective disorder, irritability associated with autism, Tourette's disorder, Parkinson's disease psychosis

Not inclusive of all product indications, all products differ in indication

Antipsychotics, Oral

Agents in Class

- Abilify (aripiprazole)
- Saphris (asenapine)
- Rexulti (brexpiprazole)
- Vraylar (cariprazine)
- Clozaril (clozapine)
- Fazaclo (clozapine)
- Versacloz (clozapine)
- Seroquel (quetiapine)
- Seroquel XR (quetiapine XR)
- Risperdal (risperidone)
- Geodon (ziprasidone)
- Fanapt (iloperidone)
- Latuda (lurasidone)
- Zyprexa (olanzapine)
- Symbyax (olanzapine/fluoxetine)
- Invega (paliperidone ER)
- Nuplazid (pimavanserin)

Antipsychotics - Oral

Drug	Manufacturer	Other Indications	Schizophrenia	Bipolar Disorder			
				Acute Manic Episodes	Depressive Episodes	Acute Mixed Episodes	Maintenance
Second Generation Antipsychotics – Oral							
aripiprazole (Abilify®)	generic	Major depressive disorder (adjunct); Irritability associated with autistic disorder (ages 6 to 17 years); Tourette's disorder (ages 6 to 18 years)	X (ages ≥ 13 years)	X (ages ≥ 10 years for acute treatment as monotherapy and in combination with lithium or valproate)	--	X (ages ≥ 10 years for acute treatment as monotherapy and in combination with lithium or valproate)	X (monotherapy and in combination with lithium or valproate for ages ≥ 10 years)
asenapine (Saphris®)	Schering	--	X	X (ages ≥ 10 years for acute treatment as monotherapy; adults in combination with lithium or valproate)	--	X (ages ≥ 10 years for acute treatment as monotherapy; adults in combination with lithium or valproate)	X (monotherapy; adults only)
brexpiprazole (Rexulti®)		Major depressive disorder (adjunct)	X	--	--	--	--
cariprazine (Vraylar™)	Actavis	--	X	X (acute treatment)	--	X (acute treatment)	--

Antipsychotics - Oral

Drug	Manufacturer	Other Indications	Schizophrenia	Bipolar Disorder			
				Acute Manic Episodes	Depressive Episodes	Acute Mixed Episodes	Maintenance
Second Generation Antipsychotics – Oral							
clozapine (Clozaril®)	generic	--	X (treatment-resistant schizophrenia; reducing suicidal behavior in schizophrenia or schizoaffective disorder	--	--	--	--
clozapine (Fazaclo®)	generic						
clozapine (Versacloz®)	Jazz						

Antipsychotics - Oral

Drug	Manufacturer	Other Indications	Schizophrenia	Bipolar Disorder			
				Acute Manic Episodes	Depressive Episodes	Acute Mixed Episodes	Maintenance
Second Generation Antipsychotics – Oral							
iloperidone (Fanapt®)	Novartis	--	X	--	--	--	--
lurasidone (Latuda®)	Sunovion	--	X	--	X (monotherapy and in combination with lithium or valproate)	--	--
olanzapine (Zyprexa®)	generic	Treatment-resistant depression (in combination with fluoxetine);	X (ages ≥ 13 years; second-line in adolescents due to metabolic effects)	X (ages ≥ 13 years as monotherapy and in combination with lithium or valproate; second-line in adolescents due to metabolic effects)	X (ages ≥ 10 years; in combination with fluoxetine)	X (ages ≥ 13 years as monotherapy and in combination with lithium or valproate; second-line in adolescents due to metabolic effects)	X (ages ≥ 13 years)

Antipsychotics - Oral

Drug	Manufacturer	Other Indications	Schizophrenia	Bipolar Disorder			
				Acute Manic Episodes	Depressive Episodes	Acute Mixed Episodes	Maintenance
Second Generation Antipsychotics – Oral							
olanzapine/ fluoxetine (Symbyax®)	generic	Treatment-resistant depression	--	--	X (ages ≥ 10 years for acute episodes)	--	--
paliperidone ER (Invega®)	generic	Schizoaffective disorder (monotherapy or adjunct with mood stabilizers and/or antidepressants)	X (ages ≥ 12 years)	--	--	--	--
pimavanserin (Nuplazid™)	Acadia	Hallucinations and delusions associated with Parkinson's disease (PD) psychosis	--	--	--	--	--

Antipsychotics - Oral

Drug			Manufacturer	Other Indications	Schizophrenia	Bipolar Disorder			
						Acute Manic Episodes	Depressive Episodes	Acute Mixed Episodes	Maintenance
Second Generation Antipsychotics – Oral									
quetiapine (Seroquel®)		generic	--	X (ages ≥ 13 years)	X (ages ≥ 10 years as monotherapy; adults in combination with lithium or valproate)	X	--	X (in combination with lithium or divalproex)	
quetiapine ER (Seroquel XR®)		generic	Major depressive disorder (adjunct)	X (ages ≥ 13 years)	X (ages ≥ 10 years as monotherapy; adults in combination with lithium or valproate)	X	X (ages ≥ 10 years as monotherapy; adults in combination with lithium or valproate)	X (in combination with lithium or divalproex)	

Antipsychotics - Oral

Drug	Manufacturer	Other Indications	Schizophrenia	Bipolar Disorder			
				Acute Manic Episodes	Depressive Episodes	Acute Mixed Episodes	Maintenance
Second Generation Antipsychotics – Oral							
risperidone (Risperdal®)	generic	Irritability associated with autistic disorder (ages 5-17 years)	X (ages ≥ 13years)	X (ages ≥ 10 years as monotherapy; adults in combination with lithium or valproate)	--	X (ages ≥ 10 years as monotherapy; adults in combination with lithium or valproate)	--
ziprasidone (Geodon®)	generic	--	X	X (acute episodes)	--	X (acute episodes)	X (in combination with lithium or divalproex)

Antipsychotics

Class Summary:

- While there remains inconclusive evidence regarding the overall effectiveness of second generation antipsychotics being better than first generation agents in terms of primary outcomes as seen in changes in rating scale scores, particularly when considering the length of many clinical studies, second generation antipsychotics are associated with less extrapyramidal symptoms (EPS) than first generation antipsychotics.
- The question of long-term adverse events with second generation antipsychotic use remains unresolved, particularly related to metabolic disorders.
- Second generation antipsychotics have largely replaced first generation antipsychotics in the treatment of psychotic disorders, but the long-term effectiveness and adverse event profiles of these products have not been shown to be definitively better

Antipsychotics

Class Summary:

- Inconclusive data exists to definitively indicate which second generation antipsychotic agent to use first
- Clozapine is used for patients with treatment-resistant schizophrenia and in patients with recurrent suicidal behavior at high risk of suicide
- Clozapine is reserved for refractory patients due to reports of severe neutropenia and seizures occurring, patients taking it must have regular white blood cell and absolute neutrophil counts closely monitored
- Various guidelines exist to help in choosing the best individualized treatment for schizophrenia, bipolar disorder, or major depressive disorder
- Relative occurrences of adverse events may also be considered in product selection

Antipsychotics

Current Preferred Products

- Oral Agents
  - aripiprazole ODT, solution & tablets
  - clozapine ODT & tablets
  - Latuda
  - olanzapine ODT & tablets
  - quetiapine tablets
  - risperdone ODT, solution & tablets
  - Saphris
  - ziprasidone tablets

Long-Acting Atypical Injectable Antipsychotics

Rick Pope, PharmD

Antipsychotics

Class Overview - Product indications include*:

- Schizophrenia, Bipolar disorder, major depressive order, schizoaffective disorder, irritability associated with autism, Tourette's disorder, Parkinson's disease psychosis

Not inclusive of all product indications, all products differ in indication

Antipsychotics – Long-Acting Injectable

Drug	Manufacturer	Other Indications	Schizophrenia	Bipolar Disorder
Second Generation Antipsychotics – Long Acting Injectable				
aripiprazole ER (Abilify Maintena®)	Otsuka	--	X	--
aripiprazole lauroxil ER (Aristada™)	Alkermes	--	X	--
olanzapine (Zyprexa® Relprevv)	Eli Lilly	--	X	--
paliperidone palmitate (Invega Sustenna®)	Janssen	Schizoaffective disorder (monotherapy and as an adjunct to mood stabilizers or antidepressants)	X	--
paliperidone palmitate (Invega Trinza®)	Janssen	--	X (treatment in patients after they have been adequately treated with Invega Sustenna for ≥ 4 months)	--
risperidone microspheres (Risperdal Consta®)	Janssen	--	X	X (maintenance treatment as monotherapy or in combination with lithium or valproate)

Antipsychotics

Long-Acting Injectable Agents (Long-Acting)

- Abilify Maintena (aripiprazole ER), monthly
- Aristada (aripiprazole lauroxil ER), monthly or 6 weeks
- Risperdal Consta (risperidone microspheres), 2 weeks
- Zyprexa Relprevv (olanzapine), 2-4 weeks
- Invega Sustenna (paliperidone palmitate), monthly
- Invega Trinza (paliperidone palmitate), 3 months

Antipsychotics

Class Summary:

- There are not enough comparative data to support distinctions among the injectable second generation antipsychotics
- A meta-analysis evaluated the impact of long-acting injectable antipsychotic frequency on efficacy and other outcomes
- No differences were found in psychotic symptoms or quality of life between injectables dosed every 2 or 4 weeks
- Safety analyses were also very similar, with the exception of injection-site pain, which was lower with every 2 week formulations compared to every 4 week formulations
- Overall, data were very limited.

Antipsychotics

Product/Guideline Updates:

- Class wide labeling revision now to include a warning that antipsychotics may cause somnolence, postural hypotension and motor/sensory instability which can lead to falls. (March 2017)
- FDA has approved a new formulation of Aristada (1,064 mg suspension in a single-use prefilled syringe) for every 2 month intramuscular administration for the treatment of schizophrenia. (June 2017)

Antipsychotics

Current Preferred Products

- Long-Acting Injectable Agents
  - Abilify Maintena
  - Aristada
  - Invega Sustenna
  - Invega Trinza
  - Risperdal Consta

Stimulants and Related Agents

Rick Pope, PharmD

Stimulants and Related Agents

Class Overview: Product Indications

- ADHD (attention deficit hyperactivity disorder), narcolepsy
- Other: exogenous obesity, binge eating disorder

Stimulants and Related Agents

Class Overview: Immediate Release Products

- Amphetamine sulfate (Evekeo)
- Dexmethylphenidate IR (Focalin)
- Dextroamphetamine IR (Zenzedi)
- Dextroamphetamine solution (ProCentra)
- Methamphetamine (Desoxyn)
- Methylphenidate IR (Methylin, Ritalin)
- Mixed amphetamine salts IR (Adderall)

Stimulants and Related Agents

Drug	Manufacturer	ADHD			Narcolepsy (Age ≥6 years)	Other Indications
		Age 3–5 years	Age ≥ 6 years	Adults		
Stimulants: Immediate-Release						
amphetamine sulfate (Evekeo™)	Arbor	X	X	--	X	Exogenous obesity age ≥12 years
armodafinil (Nuvigil®)	generic, Cephalon	--	--	--	--	Excessive sleepiness associated with narcolepsy, OSA, and SWD for age ≥ 17 years
dexmethylphenidate IR (Focalin™)	generic, Novartis	--	X	--	--	--
dextroamphetamine IR (Zenzedi™)	generic, Arbor	X	X (≤ 16 years)	--	X	--
dextroamphetamine solution (ProCentra™)	generic	X	X (≤ 16 years)	--	X	--

Stimulants and Related Agents

Drug	Manufacturer	ADHD			Narcolepsy (Age ≥6 years)	Other Indications
		Age 3–5 years	Age ≥ 6 years	Adults		
Stimulants: Immediate-Release						
methamphetamine (Desoxyn®)	generic	--	X	--	--	Exogenous obesity in adults and adolescents ≥ 12 years of age
methylphenidate IR (Methylin®, Ritalin®)	generic, Shionogi	--	X	--	X	--
mixed amphetamine salts IR (Adderall®)	generic	X	X	--	X	--
modafinil (Provigil®)	generic, Cephalon	--	--	--	--	Excessive sleepiness associated with narcolepsy, OSA, and SWD for age ≥ 17 years

Stimulants and Related Agents

Class Overview: Extended Release Products

- Amphetamine ER (Adzenys XR-ODT, Dyanavel XR)
- Dexmethylphenidate ER (Focalin XR)
- Dextroamphetamine ER (Dexedrine)
- Lisdexamfetamine dimesylate (Vyvanse)
- Methylphenidate ER OROS (Concerta)
- Methylphenidate SR (Metadate ER)

Stimulants and Related Agents

Class Overview: Extended Release Products continued

- Methylphenidate ER (Metadate CD, Quillichew ER, Quillivant XR, Ritalin LA, Aptensio XR)
- Methylphenidate transdermal (Daytrana)
- Mixed amphetamine salts ER (Adderall XR)

Stimulants and Related Agents

Drug	Manufacturer	ADHD			Narcolepsy (Age ≥6 years)	Other Indications
		Age 3–5 years	Age ≥ 6 years	Adults		
Stimulants: Extended-Release						
amphetamine ER (Adzenys XR-ODT™)	Neos	--	X	X	--	--
amphetamine ER (Dyanavel™ XR)	Tris	--	X	X	--	--
dexmethylphenidate ER (Focalin XR™)	generic (5, 10, 15, 20, 30, 40 mg), Novartis	--	X	X	--	--
dextroamphetamine ER (Dexedrine®)	generic	X	X (≤ 16 years)	--	X	--
lisdexamfetamine dimesylate (Vyvanse™)	Shire	--	X	X	--	Moderate to severe binge eating disorder in adults

Stimulants and Related Agents

Drug	Manufacturer	ADHD			Narcolepsy (Age ≥6 years)	Other Indications
		Age 3–5 years	Age ≥ 6 years	Adults		
Stimulants: Extended-Release						
methylphenidate ER OROS (Concerta®)	generic, OMJPI	--	X	X	--	--
methylphenidate SR (Metadate ER®)‚	generic	--	X	--	X	--
methylphenidate ER† (Metadate CD®)	generic, UCB	--	X	--	--	--
methylphenidate ER (QuilliChew™ ER)	Tris/Pfizer	--	X	X	--	--
methylphenidate ER (Quillivant XR®)	NextWave/Pfizer	--	X	X	--	--

Stimulants and Related Agents

Drug		Manufacturer	ADHD			Narcolepsy (Age ≥6 years)	Other Indications
			Age 3–5 years	Age ≥ 6 years	Adults		
Stimulants: Extended-Release							
methylphenidate ER (Ritalin LA®)		generic, Novartis	--	X	--	--	--
methylphenidate ER (Aptensio XR®)		Rhodes	--	X	X	--	--
methylphenidate transdermal (Daytrana™)		Noven	--	X	--	--	--
mixed amphetamine salts ER (Adderall XR®)		generic, Shire	--	X	X	--	--

Stimulants and Related Agents

Class Overview: Non stimulants

- Atomoxetine (Strattera)
- Clonidine ER (Kapvay)
- Guanfacine ER (Intuniv)

Stimulants and Related Agents

Drug	Manufacturer	ADHD			Narcolepsy (Age ≥6 years)	Other Indications
		Age 3–5 years	Age ≥ 6 years	Adults		
Non-Stimulants						
atomoxetine (Strattera®)	generic, Eli Lilly	--	X	X	--	--
clonidine ER (Kapvay™)	generic, Shionogi	--	X	--	--	Treatment of ADHD as adjunct to stimulants
guanfacine ER (Intuniv™)	generic, Shire	--	X	--	--	Treatment of ADHD as adjunct to stimulants

Stimulants and Related Agents

Class Summary:

- Meta-analyses and reviews confirm the short-term efficacy of stimulant medications in reducing the core symptoms of ADHD: *inattention, hyperactivity, and impulsivity*
- Studies have not shown clear advantages of any one stimulant medication over another or between dosage forms of a given agent
- The AAP states that stimulants are equally effective for ADHD
- Children who fail to respond to one medication may have a positive response to an alternative
- Agents used for the treatment of ADHD are associated with different contraindications and precautions for use and this may influence the selection of appropriate therapy in specific patients

Stimulants and Related Agents

Product/Guideline Updates:

- Nuvigil is now available as a generic. (June 2016)
- Vyvanse now available as a chewable tablet that may be substituted (1mg: 1mg basis) with the already approved capsule formulation. (February 2017).
- All strengths of Metadate CD have been discontinued by UCB. (April 2017)
- Strattera is now available as a generic. (June 2017)

Stimulants & Related Agents

Current Preferred Products

- Adderall XR
- amphetamine salt combination
- Daytrana
- dextroamphetamine capsule ER
- dextroamphetamine tablet
- Focalin
- Focalin XR
- guanfacine ER
- Kapvay
- Metadate CD

Stimulants & Related Agents (continued)

Current Preferred Products

- Methylin Chewable Tablets & Solution
- methylphenidate
- methylphenidate ER (gen. Concerta)
- methylphenidate ER (gen. Ritalin LA)
- Quillichew ER
- Quillivant XR
- Ritalin LA 10mg capsule
- Strattera
- Vyvanse Capsule

Pancreatic Enzymes

Rick Pope, PharmD

Pancreatic Enzymes

Class Overview: Products

- Zenpep
- Creon
- Viokace
- Pancreaze
- Pertzye
- Ultresa

Pancreatic Enzymes

Class Overview: Product Indications

- Viokace is indicated for the treatment of exocrine pancreatic insufficiency due to chronic pancreatitis or pancreatectomy in combination with a proton pump inhibitor in adults only

Pancreatic Enzymes

Class Overview: Product Indications

- Pancreaze, Pertzye, Ultresa, and Zenpep are indicated for the treatment of exocrine pancreatic insufficiency due to cystic fibrosis or other conditions in both adults and children
- Creon is indicated for these conditions, as well as exocrine pancreatic insufficiency due to chronic pancreatitis and pancreatectomy
- Other conditions that may result in exocrine pancreatic insufficiency include ductal obstruction from a neoplasm and gastrointestinal bypass surgery

Pancreatic Enzymes

Product	Manufacturer	Formulation	Amylase (Units)	Lipase (Units)	Protease (Units)	Notes
Creon® 3,000	AbbVie	Capsule (EC, DR)	15,000	3,000	9,500	For infants, capsule contents may be administered directly to the mouth or with a small amount of applesauce Capsule can be opened for patients unable to swallow
Creon 6,000			30,000	6,000	19,000	
Creon 12,000			60,000	12,000	38,000	
Creon 24,000			120,000	24,000	76,000	
Creon 36,000			180,000	36,000	114,000	

Pancreatic Enzymes

Product	Manufacturer	Formulation	Amylase (Units)	Lipase (Units)	Protease (Units)	Notes
Pancreaze®	Janssen	Capsule (DR)	10,850	2,600	6,200	Capsule can be opened for patients unable to swallow
			24,600	4,200	14,200	
			61,500	10,500	35,500	For infants, capsule contents may be administered directly to the mouth or with a small amount of acidic food such as applesauce. Contents should be followed by breast milk or formula but may not be administered directly into breast milk or formula.
			98,400	,16,800	56,800	
			83,900	21,000	54,700	

Pancreatic Enzymes

Product	Manufacturer	Formulation	Amylase (Units)	Lipase (Units)	Protease (Units)	Notes
pancrelipase 5,000 (authorized generic for Zenpep® by Aptalis)*	X-GEN	Capsule (EC)	27,000	5,000	17,000	Capsule can be opened for patients unable to swallow

Pancreatic Enzymes

Product	Manufacturer	Formulation	Amylase (Units)	Lipase (Units)	Protease (Units)	Notes
Pertzye™ 4,000	Digestive Care	Capsule (DR)	15,125	4,000	14,375	Only pancreatic enzyme containing bicarbonate-buffered enteric-coated microspheres Capsule can be opened for patients unable to swallow Pertzye 400 (infants up to 12 months): For infants, capsule contents may be administered directly to the mouth or with a small amount of acidic food with a pH ≤ 4.5, such as applesauce. Contents should be followed by breast milk or formula but may not be administered directly into breast milk or formula.
Pertzye™ 8,000			30,250	8,000	28,750	
Pertzye 16,000			60,500	16,000	57,500	

Pancreatic Enzymes

Product	Manufacturer	Formulation	Amylase (Units)	Lipase (Units)	Protease (Units)	Notes
Viokace™ 10,440	Aptalis	Tablet	39,150	10,440	39,150	Tablets should be swallowed whole and not crushed Should not be used in pediatric patients; may result in tablet degradation in the gastric environment which may result in suboptimal growth
Viokace 20,880			78,300	20,880	78,300	

Pancreatic Enzymes

Product	Manufacturer	Formulation	Amylase (Units)	Lipase (Units)	Protease (Units)	Notes
Zenpep 3	Aptalis	Capsule (EC,DR)	16,000	3,000	10,000	For infants, capsule contents may be administered directly to the mouth or with a small amount of acidic food with a PH greater than 4.5 such as applesauce Capsule can be opened for patients unable to swallow
Zenpep 5			27,000	5,000	17,000	
Zenpep 10			55,000	10,000	34,000	
Zenpep 15			82,000	15,000	51,000	
Zenpep 20			109,000	20,000	68,000	
Zenpep 25			136,000	25,000	85,000	
Zenpep 40			218,000	40,000	136,000	

Pancreatic Enzymes

Class Summary:

- Pancreatic enzyme supplements differ in enzyme content and bioavailability
- These products have demonstrated favorable risk-benefit profiles in the treatment of exocrine pancreatic insufficiency due to cystic fibrosis and other conditions
- Dosing of these products should be individualized in accordance with the individual products prescribing information and the Cystic Fibrosis Foundation (CFF) Consensus Guidelines

Pancreatic Enzymes

Product/Guideline Updates:

- There is no recent clinical information or product specific news of significance for this class.

Pancreatic Enzymes

Currently Preferred Products

- Creon
- Zenpep

Anticoagulants

Rick Pope, PharmD

Anticoagulants

Class Overview

- **Injectable Agents**
  - Fragmin (dalteparin)
  - Lovenox (enoxaparin)
  - Arixtra (fondaparinux)
- **Oral Agents**
  - Eliquis (apixaban)
  - Pradaxa (dabigatran)
  - Savaysa (edoxaban)
  - Xarelto (rivaroxaban)
  - Coumadin (warfarin)

Anticoagulants

Class Overview - Product indications include*:

- DVT and PE prophylaxis and treatment
- Prophylaxis of ischemic complications of unstable angina and non-Q-wave myocardial infarction
- Treatment of acute ST-segment elevation myocardial infarction managed medically or with subsequent percutaneous coronary intervention
- To reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation

Not inclusive of all product indications, all products differ in indication

Anticoagulants

Class Overview (Product indications include)*:

- Prophylaxis and/or treatment of the thromboembolic complications associated with atrial fibrillation and/or cardiac valve replacement
- Reduce the risk of death, recurrent myocardial infarction, and thromboembolic events, such as stroke or systemic embolization after myocardial infarction

***Not inclusive of all product indications, all products differ in indication**

Anticoagulants

Drug	Manufacturer	DVT prophylaxis				DVT Treatment
		Hip Replacement	Knee Replacement	Hip Fracture surgery	Abdominal Surgery	
Injectable						
dalteparin (Fragmin®)	Eisai	X	-	-	X	-
enoxaparin (Lovenox®)	generic, Sanofi-Aventis	X	X	-	X	X (without PE in outpatient setting, with or without PE in inpatient setting)
fondaparinux (Arixtra®)	generic, GSK	X	X	X	X	X

Anticoagulants

Drug	Manufacturer	DVT prophylaxis				DVT Treatment
		Hip Replacement	Knee Replacement	Hip Fracture surgery	Abdominal Surgery	
Oral						
apixaban (Eliquis®)	Bristol-Myers Squibb	X	X	-	-	X
dabigatran (Pradaxa®)	Boehringer Ingelheim	X	-	-	-	X*
edoxaban (Savaysa®)	Daiichi Sankyo	-	-	-	-	X*
rivaroxaban (Xarelto®)	Janssen	X	X	-	-	X
warfarin (Coumadin®)	generic, Bristol-Myers Squibb	X	X	X	X**	X

Anticoagulants

Class Summary:

- Low molecular weight heparins (LMWHs) are important treatment options in DVT and PE management with advantages over unfractionated heparin (UFH)
- LMWHs have been shown to reduce mortality rates after acute deep vein thrombosis (DVT) and provide similar efficacy as UFH
- While subcutaneous (SC) anticoagulants have subtle differences in methods of preparation, pharmacokinetic parameters, and anti-Xa activity, the clinical characteristics are similar
- The newer oral anticoagulants show comparable efficacy and superiority or non-inferiority to warfarin for stroke prevention in NVAF with similar to lower overall rates of major bleeding

Anticoagulants

Class Summary:

- The newer oral agents do not require laboratory monitoring and the associated dose adjustments required with warfarin therapy
- Except for dabigatran, however, none of these new anticoagulants have an antidote currently available
- Dabigatran does has corresponding reversal agent (idarucizumab [Praxbind])
- Meta-analysis found the newer oral anticoagulants to have an approximately 10% reduction in all-cause mortality compared to warfarin in patients with avalvular atrial fibrillation
- A network meta-analysis reported statistically similar reductions in the risk of VTE or VTE-related death for all newer oral anticoagulants

Anticoagulants

Current Preferred Products

- Oral Agents
  - Eliquis
  - Pradaxa
  - Xarelto
  - warfarin
- Injectable Agents
  - Fragmin Vial
  - Lovenox Syringe
  - Lovenox Vial

Hemophilia Class Review

Rick Pope, PharmD

Executive Session

AHCCCS
Arizona Health Care Cost Containment System

AHCCCS Pharmacy and Therapeutics Committee

Mental Health Parity and Addiction Equity Act (MHPAEA)

Presented by Michelle Cavner, PharmD
Mercy Maricopa Pharmacy Director

Mental Health Parity

Many Americans suffer from health care inequities in behavioral health (BH) care

- Health care inequities are defined as the inequalities that occur in the access to, provision and delivery of health care across different racial, ethnic and socioeconomic groups
- While stigma continues to play a significant role in accessing BH services, one of the primary causes listed for BH care inequities is the lack of parity in benefit structure and benefit management practices

Mental Health Parity for Medicaid Benefits

- The purpose of MH Parity is to improve access to behavioral health (BH) services (MH and substance use disorder) under health insurance or benefit plans that manage & provide both physical health (PH) and BH benefits
- The overarching requirement of Parity is that BH services cannot have greater benefit management restrictions or limitations than what they are for comparable PH services = Non-quantitative treatment limitations (NQTLs)
- CMS has given a deadline of October 2, 2017 to become Parity compliant.

Mental Health Parity for Medicaid Benefits

- AHCCCS currently manages two formularies:
  - ✓ Acute/Long Term Care Drug List
  - ✓ Behavioral Health Drug List
- Both formularies contain BH drugs
- Formulary edits on the BH drugs are not consistent between the two formularies
- Full review completed to identify the inconsistencies

Mental Health Parity for Medicaid Benefits

- RBHA Pharmacy Directors collaborated on proposed changes to align the formularies
- Proposed recommendations bring parity and alignment across both AHCCCS formularies, as well as, across the RBHA Plans.
- Recommendations include:
  - ✓ Prior authorization
  - ✓ Quantity Limits: based on FDA maximum daily dose
  - ✓ Age
  - ✓ Addition of drugs not listed
- Any Questions?

Biosimilar Update

Suzi Berman, RPh

BIOSIMILAR UPDATE

- Renflexis (Infliximab-abda) - Pfizer
- Inflectra (infliximab-dyyb) – Biogen
- Both are biosimilars for Remicade
- Remicade is an infused drug and is currently available for AHCCCS members unable to use our preferred agents listed on the AHCCCS Drug List:
  - Humira
  - Enbrel

Renflexis (Infliximab-abda)
Inflectra (infliximab-dyyb)

- Per AHCCCS Policy 310-V: AHCCCS Contractors shall not transition to a biosimilar drug until AHCCCS has determined that the biosimilar drug is overall more cost-effective to the state than the continued use of the brand name drug.
- The recommendation is to continue use only Remicade as the preferred infliximab product because it is the most cost effective infliximab product to the State.

AHCCCS
Arizona Health Care Cost Containment System

New Drug Reviews

Suzi Berman, RPh

Seven New Products

- Austedo – Deutetrabenazine
- Dupixent – Dupiluma
- Rhofade - Oxymetazoline HCl 1% Cream
- Symproic – Naldemedine
- Xadago – Safinamide
- Ingrezza – Valbenazine
- Emflaza – Deflazcort

Austedo – Deutetrabenazine

- Indicated for treatment of chorea associated with Huntington disease.
- Chorea is an abnormal involuntary movement disorder.
- Black Box Warning for Depression and Suicide risk.
- Dosage – 6mg daily up to a maximum of 48mg/day

Austedo – Deutetrabenazine

- Adverse reactions > 10%: drowsiness
- A double-blinded placebo controlled trial
  - 90 patients – 87 patients completed the study
  - Median age - 54 years
  - Dose titration was completed over 8 weeks and then maintenance was for 4 weeks
  - Primary efficacy endpoint was based on evaluations using the United Huntington's Disease Rating Scale which has a maximum score of 60.

Austedo – Deutetrabenazine

Clinical Trial Results was the rating scale score reduction.

- Average change was a reduction of 4.4 points for the Austedo participants and 1.9 for the placebo group.
  - This is <10% change, although considered statistically significant, the clinical significance is questionable.
  - 51% of the Austedo control group and 20% of the placebo group rated their symptoms as "much" or "very much" improved.

Austedo – Deutetrabenazine

- Recommendation is to not add Austedo to the AHCCCS drug list due to the lack of evidence to support the clinical efficacy.
- Austedo is available through prior authorization based on medical necessity.

Dupixent – Dupiluma

- A monoclonal antibody indicated to treat moderate-to-severe atopic dermatitis that is not controlled with topical therapies.
- No Black Box Warnings
- Initial dosage is a 600mg subcutaneous injection then 300mg SQ every other week.
- Adverse Reactions ≥ 10%
  - Conjunctivitis,
  - Herpes Simplex Virus Infection, &
  - Injection site reactions

Dupixent – Dupiluma

- Clinical trials –
  - 3 Double Blinded - Placebo Controlled Trials
    - 2119 participants
    - Two trials were for 16 weeks & one for 52 weeks
  - Participants were 18 years or older with moderate to severe atopic dermatitis.
  - Primary endpoint was an evaluation of 0 (clear) or 1 (almost clear) in accordance with the Investigators Global Assessment Scale.

Dupixent – Dupiluma

Clinical Trial Results used Investors Global Assessment Score of zero or one - 40% of the participants met the primary end point

- Trial 1: Dupixent 38% vs. 10% for placebo
- Trial 2 Dupixent 36% vs. 9% for placebo
- Trial 3 Dupixent 39% vs. 12% for placebo

- Recommendation is to not add Dupixent to the AHCCCS Drug List because the use of Dupixent is indicated when the atopic dermatitis is not controlled by topical steroids. There are many steroids and other products available for the treatment of atopic dermatitis on the AHCCCS Drug List.
- Dupixent is available through prior authorization based on medical necessity.

Rhofade - Oxymetazoline HCl 1% Cream

- Indicated for the treatment of redness on the face caused by Rosacea.
- Oxymetazoline is the same drug used in Afrin nasal spray
- Black Box Warnings: None
- Apply a pea size amount to the entire face once daily.
- Adverse reactions ≥ 1-10%:
  - Exacerbation of Rosacea;
  - Application site dermatitis, erythema & pain.

Rhofade - Oxymetazoline HCl 1% Cream

- Drug Interactions: Caution with antihypertensives
- Two double blinded - vehicle controlled trials
- 885 subjects- 90% caucasian and 79% female
- Participants applied Rhofade or a vehicle once daily for 29 days.
- Severity was graded on a 5-point clinician erythema assessment scale (CEA) by the clinician, and the participant completed a 5-point self assessment scale (SSA).

Rhofade - Oxymetazoline HCl 1% Cream

- Clinical Trial Results
  - The primary efficacy endpoint was defined as the proportion of subjects with at least a 2-grade reduction in erythema (improvement) from baseline (pre-testing on Day 1) on both the CEA and SSA measured at hours 3, 6, 9, and 12 on Day 29.
  - In both trials the percent of patients meeting the endpoint on day 29 was:
    - 14.5% using Rhofade, and
    - 6.6% for subjects using a vehicle.

Rhofade - Oxymetazoline HCl 1% Cream

- It should be noted that there were less participants responding at hour 12 than at hour 9.
- Recommendation is to not add this medication to the AHCCCS Drug List because there are many other topical medications on the AHCCCS Drug List which are efficacious and more cost effective.
- Rhofade is available through prior authorization based on medical necessity.

Symproic – Naldemedine

- A Schedule II opioid antagonist indicated for the treatment of opioid- induced constipation (OIC) in adult patients with chronic non-cancer pain.
- Black Box Warning: None
- Dosage: 0.2mg once daily with or without food.
- Adverse reactions $\geq$ 5%
  - Abdominal pain, nausea & diarrhea
- Two 12-week double blinded placebo controlled randomized 1:1 studies with approximately 1100 participants

Symproic – Naldemedine

- Endpoints were subjects who had at least 3 bowel movements per week and a baseline change of at least 1 bowel movement per week for 9 of the 12 weeks.
- Reporting was by the responding participant
- Results:
  - Study 1: 48% of Symproic participants responded vs. 35% of participants on placebo
  - Study 2: 53% of Symproic participants responded vs. 35% of participants on placebo

Symproic – Naldemedine

- Results were statistically significant but it is difficult to determine whether they were clinically significant.
- Recommendation is to not add Symproic to the AHCCCS Drug List because there are many alternatives available that are more cost effective to treat constipation.
- Symproic is available through prior authorization based on medical necessity.

Xadago – Safinamide

- An MAO Inhibitor indicated as adjunctive therapy in addition to levodopa/carbidopa in patients with Parkinson disease experiencing “Off time" episodes.
- Off-time" refers to periods of the day when the medication is not working well, causing worsening of Parkinsonian symptoms.
- Use Limitation – Xadago has not been shown to be effective as monotherapy for the treatment of Parkinson disease.
- Black Box Warning: None

Xadago – Safinamide

- Dosage: 50 – 100 mg daily
- Adverse reactions occurring in ≥ 5%
  - Dyskinesia
  - Hypertension
  - Falling
  - Increased liver function tests
  - Serotonin syndrome

Xadago – Safinamide

Clinical Trials

- 2 double-blind, placebo controlled 24 weeks studies:
  - Study 1 – 645 patients randomized to Xadago 50mg/day
  - Study 2 – 216 patients randomized to Xadago 100mg/day
  - Studies were completed in patients who were on "OFF" time with treatment of carbidopa/levodopa and other Parkinson's medications.
  - Primary endpoint was the measurement of efficacy by evaluating the change from baseline in total daily "ON" Time without any or without problematic dyskinesia based on 18-hour diaries completed by participants. "ON" time refers to periods of adequate control of the Parkinson's symptoms.

Xadago – Safinamide

- Results were based on the increase in "ON" time without troublesome dyskinesia.
  - Placebo: 9.3 hours ± 2.2 standard deviation
  - Xadago 50mg: 9.4 hours ± 2.2 standard deviation
  - Xadago 100mg: 9.6 hours ± 2.2 standard deviation
- Changes in the Uniform Parkinson's Disease Rating Scale Part III Motor Examination
  - Placebo: 28.6 ± 12.0 standard deviation
  - Xadago 50mg: 27.3 ± 12.8 standard deviation
  - Xadago 100mg: 28.4 ± 13.5 standard deviation

Xadago – Safinamide

- Recommendation is to not add Xadago to the AHCCCS Drug List because the primary endpoint outcomes of Xadago were very similar to placebo.
- Xadago is available through prior authorization based on medical necessity.

Ingrezza – Valbenazine

- Indicated for the treatment of Tardive Dyskinesia (TD)
- First FDA approved drug to treat TD, although there have been older medications used.
- Black Box Warnings: None
  - Warning: QTC prolongation, Depression & Suicidal Ideation
- Dosage: 40-80mg once daily with or without food
- Adverse reactions ≥ 5%
  - Somnolence, Fatigue, Sedation
  - Dry mouth, Constipation, Blurred Vision, Urinary Retention and attention disturbances

Ingrezza – Valbenazine

- Clinical Trial was a Double-blinded,placebo controlled study
  - Participants had an underlying diagnosis of schizophrenia, schizoaffective disorder or a mood disorder.
  - Moderate to severe TD based on clinical observation
  - Primary endpoint measured by the Abnormal Involuntary Movement Scale (AIMS) items 1-7 scored 0 to 4 for each item with zero = no TD and 4 = maximum severity. Score range was 0 – 28.
  - Compared the mean change from baseline at week 6 of patients assigned, 40mg, 80mg and placebo.

Ingrezza – Valbenazine

- Clinical Trial Results
- 234 subjects enrolled with a 12% dropout rate
- Mean age 56
- Participants were randomized to 40mg, 80 mg and placebo
- Antipsychotic Use
  - 70% Atypicals, 14% Typicals & 16% No antipsychotics
- Primary endpoint at 6 weeks:
  - Mean change AIMS score changes
  - 7 items were evaluated to asses the severity of involuntary movements. Maximum score = 28

Ingrezza – Valbenazine

- The change from baseline in the AIMS total dyskinesia score in the 80 mg INGREZZA group was statistically significantly different from the change in the placebo group.
- 40mg tablets did not indicate statistically significant changes and scored similar to placebo.
- Subgroup analyses by gender, age, racial subgroup, underlying psychiatric diagnostic category, and concomitant antipsychotic medication did not suggest any clear evidence of differential responsiveness.

Ingrezza – Valbenazine

- Ingrezza 80mg had a mean baseline score of 10.4 with a standard deviation of 3.6
  - Slightly better than participants taking Ingrezza 40mg: For the 80 mg participants:

Endpoint	Treatment Group	AIMS Mean Baseline Score (SD)	AMS LS Mean Change from Baseline
AIMS Dyskinesia Total Score	Ingrezza 40mg	9.8 (4.1)	-1.9
	Ingrezza 80mg	10.4 (3.6)	-3.2
	Placebo	9.3 (4.3)	-0.1

Ingrezza – Valbenazine

- Recommendation is to not add Ingrezza to the AHCCCS Behavioral Health Drug List because there is minimal benefit as evidenced by the endpoints of the study.
- Ingrezza is available through prior authorization based on medical necessity.

Emflaza - Deflazacort

- Indicated for the treatment for Duchenne Muscular Dystrophy in patients 5 years of age and older. Its use is expected to improve muscle strength in patients.
- Emflaza is an internationally used corticosteroid treatment that no longer carries patent protections or market exclusivity in the U.S., but the FDA granted the therapy seven years of exclusivity as an orphan drug which the FDA has been asked to explain by a couple of US Senators.
- Black Box Warnings: None
- Dosage – weight based - 0.9mg/kg take with grapefruit juice
  - When 0.9mg/kg was compared to 1.2mg/kg, the 1.2mg/kg had a higher incidence of side effects and is not recommended.

Emflaza - Deflazacort

- Adverse reactions ≥ 10% Similar to other steroids
  - Erythema (skin redness due to capillary dilation) 8-28%
  - Cushingoid appearance (facial puffiness) - 33-60%
  - Hirsutism (excessive hair growth) - 10-35%
  - Abdominal pain – 18%
  - Increased appetite – 14%
  - Pollakiuria (frequent small voids) – 12-15%
  - Cough and upper respiratory tract infection – 12%
  - Irritability – 8-10%
  - Constipation – 10%
  - Nasopharyngitis – 10%

Emflaza - Deflazacort

- Multicenter, randomized, double-blind, placebo-controlled, 52-week study, n=196 male pediatric patients, documented dystrophin gene mutation, EMFLAZA vs. placebo at 12 weeks; vs. active comparator at additional 40 weeks.
- Primary Endpoint: Change in Baseline at Week 12 in average strength of 18 muscle groups using Medical Research Council (MRC) 11-point scale
- The Emflaza participants had significantly greater scores vs. placebo (p=0.017) at week 12.
- Additional randomized, double-blind, placebo-controlled 104 week trial of Emflaza vs. placebo;
  - **N= 29 patients 6-12 years of age**
- **Average muscle strength score at 2 years was not statistically significant; patients on EMFLAZA appeared to lose the walking ability later than placebo.**

Emflaza - Deflazacort

- Recommendation is to not add Emflaza to the AHCCCS Drug List.
- The AHCCCS Drug List does contain other corticosteroids.
- Emflaza is available through prior authorization based on medical necessity.

Questions?

Agenda Items For The Next Meeting Thursday 12 October 2017

Please send agenda items to:

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Thank You