AHCCCS
Arizona Health Care Cost Containment System

AHCCCS Pharmacy and Therapeutics Committee

July 17, 2018

Introductions & Minutes Approval

- April 17, 2018 Meeting Minutes
  - Review and Amend
  - Vote
- P&T Purpose and Operational Policy

Magellan Drug Class Reviews

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

Magellan Class Reviews

Classes for Review: Supplemental Rebate Classes

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

Magellan Class Reviews

Classes for Review: ***Non-Supplemental Rebate Classes***

- Antifungals, Oral
- Antifungals, Topical
- Beta Blockers
- BPH Treatments
- Calcium Channel Blockers
- Topical Steroids - Low, Medium, High & Very High Potency

Oral Atypical Second Generation Antipsychotics

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

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

- aripiprazole - (Abilify Discmelt, Abilify MyCite, solution, tablets; aripiprazole ODT, solution, tablets)
- asenapine - (Saphris SL)
- brexpiprazole - (Rexulti)
- cariprazine - (Vraylar)
- clozapine - (clozapine ODT, tablets; Clozaril; Fazaclo; Versacloz)
- iloperidone - (Fanapt tablets, Titration Pack)
- lurasidone - (Latuda)
- olanzapine - (olanzapine ODT, tablets; Zyprexa tablets, Zydis)

Antipsychotics, Oral

Agents in Class

- olanzapine/fluoxetine - (olanzapine/fluoxetine; Symbyax)
- paliperidone ER - (Invega; paliperidone)
- pimavanserin - (Nuplazid)
- quetiapine - (quetiapine, Seroquel)
- quetiapine ER - (quetiapine ER, Seroquel XR)
- risperidone - (Risperdal ODT, solution, tablets; risperidone ODT, solution, tablets)
- ziprasidone - (Geodon, ziprasidone)

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

Product/Guideline Updates:

- Latuda is now indicated for use as monotherapy to treat pediatric patients aged 10-17 years with depressive episodes associated with bipolar I disorder. It was already approved for the treatment of patients 13 years and older with schizophrenia and for depressive episodes associated with bipolar I disorder in adults as monotherapy or as adjunctive therapy with lithium or valproate.

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

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

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 Agents (Long-Acting)

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

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

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 is very limited.

Antipsychotics

New Product: Aristada Initio (aripiprazole lauroxil)

- Aristada Initio is a an injection of aripiprazole lauroxil used in combination with oral aripiprazole when used in the initiation of Aristada for the treatment of schizophrenia in adults
- Aristada Initio is only to be used as a single dose to initiate Aristada therapy or in re-initiating therapy following a missed dose
- Aristada Initio is not for repeated dosing
- It is administered IM by a healthcare professional
- Dosage is one 675mg extended-release injection and one 30mg dose or oral aripiprazole
- Patients naïve to aripiprazole must still establish tolerance prior to beginning treatment with Aristada Initio
- Not interchangeable with Aristada as there are pharmacokinetic differences

Antipsychotics

New Product: Aristada Initio (aripiprazole lauroxil)

- Adverse effects, warnings and contraindications are similar to those seen in Aristada and oral aripiprazole as well as other antipsychotic agents
- Effectiveness and safety for Aristada Initio were established in previous studies of oral aripiprazole and Aristada
- Additionally a pharmacokinetic bridging study was performed that demonstrated Aristada Initio plus oral aripiprazole produced concentrations comparable to Aristada started with 21 days of oral therapy

Antipsychotics

Product/Guideline Updates:

- FDA has approved Abilify Maintena for maintenance monotherapy of bipolar I disorder in adults. Recommended maintenance dose is 400 mg IM once monthly (no sooner than 26 days after last dose). Tolerability to oral aripiprazole should be established prior to initiating Abilify Maintena.

Antipsychotics

Current Preferred Products

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

Stimulants and Related Agents

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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 - (dexmethylphenidate IR, Focalin)
- dextroamphetamine IR - (dextroamphetamine IR, Zenzedi)
- dextroamphetamine solution - (dextroamphetamine solution, ProCentra)
- methamphetamine - (methamphetamine, Desoxyn)
- methylphenidate IR - (methylphenidate IR, Ritalin)
- mixed amphetamine salts IR - (Adderall, mixed amphetamine salts IR)

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 (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 ER, Adzenys XR-ODT, Dyanavel XR)
- dexmethylphenidate ER - (dexmethylphenidate ER, Focalin XR)
- dextroamphetamine ER - (Dexedrine, dextroamphetamine ER)
- lisdexamfetamine dimesylate - (Vyvanse)
- methylphenidate ER OROS - (Concerta, methylphenidate ER OROS)
- methylphenidate ER - (methylphenidate ER)
- methylphenidate ER - (Aptensio XR, Cotempla XR-ODT, Quillichew ER, Quillivant XR, Ritalin LA)

Stimulants and Related Agents

Class Overview: Extended Release Products continued

- methylphenidate transdermal - (Daytrana)
- mixed amphetamine salts ER - (Adderall XR, mixed amphetamine salts ER, Mydayis)

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 ER, 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† (Cotempla XR-ODT®)	Neos	--	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®, Mydayis®)		generic, Shire	--	X	X (Mydais ≥ 13 years)	--	--

Stimulants and Related Agents

Class Overview: Non-Stimulants

- atomoxetine - (atomoxetine, Strattera)
- clonidine ER - (clonidine ER, Kapvay)
- guanfacine ER - (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:

- Cotempla XR-ODT (methylphenidate ER), is approved for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in pediatric patients 6 to 17 years of age
- Approved as an extended-release orally disintegrating tablet in 8.6mg, 17.3mg, and 25.9mg strengths
- Contains approximately ¼ immediate-release and ¾ extended-release methylphenidate
- Recommended starting dose is 17.3mg given orally once daily in the morning. Dosage may be increased weekly in increments of 8.6mg to 17.3mg per day; maximum daily dosage is 51.8mg
- Should be taken consistently either with or without food

Stimulants and Related Agents

Product/Guideline Updates:

- Contraindications, warnings and adverse reactions are similar to other methylphenidate products
- No comparative clinical data available
- Mydayis (mixed salts amphetamine product), is approved for the treatment of ADHD in patients 13 years of age and older
- Approved as an extended-release capsule in 12.5mg, 25mg, 37.5mg and 50mg strengths
- Recommended starting dose for patients 13 years and older (including adults) is 12.5mg once daily upon awakening

Stimulants and Related Agents

Product/Guideline Updates:

- Titration schedule is 12.5mg weekly with a maximum daily dose of 25mg and 50mg for patients 13 to 17 years of age and adults, respectively
- Contraindications, warnings and adverse reactions are similar to other amphetamine products in the class
- No comparative clinical data are available
- Shionogi has discontinued Methylin chewable tablets
- Adzenys ER oral suspension now approved for treatment of ADHD in patients ≥ 6 years of age

Stimulants and Related Agents

Product/Guideline Updates:

- Administered once daily in the morning
- Starting dose varies by age
- Refrigeration and reconstitution are not required
- Adzenys XR-ODT and Adzenys ER oral suspension are bioequivalent to Adderall XR

Stimulants & Related Agents

Current Preferred Products

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

Stimulants & Related Agents (continued)

Current Preferred Products

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

Pancreatic Enzymes

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Pancreatic Enzymes

Class Overview: Products

- Creon
- Pancreaze
- Pertzye
- Viokace
- Pancreaze

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

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

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
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

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Anticoagulants

Class Overview

- **Injectable Agents**
  - dalteparin - (Fragmin syringes & vials)
  - enoxaparin - (enoxaparin syringes & vials; Lovenox syringes & vials
  - fondaparinux - (Arixtra syringes & fondaparinux syringes)

Anticoagulants

Class Overview

- **Oral Agents**
  - apixaban - (Eliquis & Dose Pack)
  - betrixaban - (Bevyxxa)
  - dabigatran - (Pradaxa)
  - edoxaban - (Savaysa)
  - rivaroxaban - (Xarelto & Dose Pack)
  - warfarin - (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

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

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
betrixaban (Bevyxxa®)	Portola	-	-	-	-	-
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

Product Updates:

- Safety and efficacy of Praxbind (idarucizumab) as a reversal agent for Pradaxa in emergency situations was confirmed in the phase 3 RE-VERSE AD trial
- FDA has revised Xarelto's indication and dosing for secondary prevention of DVT/PE based on their review of EINSTEIN CHOICE trial
- Now states, "for the reduction in the risk of recurrence of DVT and/or PE in patients at continued risk for recurrent DVT and/or PE after completion of initial treatment lasting at least 6 months"
- Dosing for this indication now states 10 mg once daily after ≥ 6 months of standard anticoagulation treatment, (previously 20 mg once daily with food)

Anticoagulants

Product Updates:

- Eliquis is now available as a starter pack to support the transition of dosing from 10 mg twice daily (for the first 7 days) to 5 mg twice daily.

Anticoagulants

Guideline Updates:

- The American College of Cardiology (ACC) published guidelines on managing acute bleeding in patients taking direct oral anticoagulants and warfarin, including a decision trees and guidance on the clinical use of anticoagulant reversal agents and when to restart anticoagulation therapy.

Anticoagulants

Current Preferred Products

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

Antifungals, Oral

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

Antifungals, Oral

Class Overview - Product indications include*:

- Candidiasis, (esophageal, oropharyngeal,vaginal), Candida Infections, Cryptococcal Infections, Tinea Topical Infections, Onychomycosis, Invasive Aspergillosis

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

Antifungals, Oral

Class Overview: Single Agents

- clotrimazole troche - (clotrimazole troche)
- fluconazole - (Diflucan, fluconazole)
- flucytosine - (Ancobon, flucytosine)
- griseofluvin suspension - (griseofluvin suspension)
- griseofluvin microsized - (griseofluvin microsized)
- griseofluvin ultramicrosized - (Gris-Peg, griseofluvin ultramicrosized)
- isavuconazonium - (Cresmba)
- itraconazole - (itraconazole, Onmel, Sporanox)
- ketoconazole - (ketoconazole)

Antifungals, Oral

Class Overview: Single Agents

- miconazole - (Oravig)
- nystatin - (nystatin)
- posaconazole - (Noxafil)
- terbinafine - (Lamisil, Lamisil Granules, terbinafine)
- voriconazole - (Vfend, voriconazole)

Antifungals, Oral

- Antifungal agents have different spectrums of activity and are FDA-approved to treat a variety of infections
- Oral antifungal agents are useful in the treatment of a variety of infections in both the immunocompetent and immunocompromised patient
- Few trials have been performed to compare safety and efficacy profiles of the drugs
- Many of the agents carry boxed warnings related to adverse events and/or drug interactions

Antifungals, Oral

Product Updates:

- Novartis made a business decision to permanently discontinue Lamisil 250 mg tablets. They will remain available until approximately April 2018

Antifungals, Topical

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

Antifungals, Topical

Class Overview - Product indications include*:

- Cutaneous Candida Infections, Tinea Topical Infections, Topical Onychomycosis Treatment, Seborrheic Dermatitis

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

Antifungals, Topical

Class Overview: Single Agents

- butenafine - (Mentax)
- butenafine OTC - (butenafine OTC, Lotrimin Ultra OTC)
- ciclopirox 0.77% - (Ciclodan Cream, Kit; ciclopirox cream; Loprox Cream, Suspension)
- ciclopirox 8% - (Ciclodan Solution, ciclopirox 8%, Penlac)
- clotrimazole OTC - (Alevazol OTC, clotrimazole OTC, Desenex OTC Lotrimin AF OTC)
- clotrimazole/betamethasone - (clotrimazole/betamethasone, DermacinRx Pak, Lotrisone)
- econazole - (econazole)
- econazole foam - (Ecoza)

Antifungals, Topical

Class Overview: Single Agents

- Efinaconazole - (Jublia)
- Ketoconazole - (Extina, ketoconazole, Nizoral A-D Shampoo, Nizoral Shampoo, Xolegel)
- luliconazole - (Luzu)
- miconazole OTC - (Azolen, Fungoid, Lotrimin Spray, miconazole, Zeasorb)
- miconazole/zinc oxide/white petrolatum - (Vusion)
- naftifine - (naftifine, Naftin)
- nystatin - (nystatin)
- nystatin/triamcinolone - (nystatin/triamcinolone)

Antifungals, Topical

Class Overview: Single Agents

- oxiconazole - (oxiconazole, Oxistat)
- sertaconazole - (Ertazco)
- sulconazole - (Exelderm)
- tavaborole - (Kerydin)
- terbinafine OTC - (Lamisil OTC, Lamisil AT OTC, terbinafine OTC)
- tolnaftate OTC - (Fungoid-D OTC, Lamisil AF OTC, Tinactin OTC, tolnaftate OTC)
- undecylenic acid solution OTC - (Hongo Cura OTC, Sponix Anti-Fungal OTC)
- undecylenic acid/zinc undecylenic - (Fungi-nail OTC, Hongo Cura OTC)

Antifungals, Topical

- Topical antifungal agents have different spectrums of activity and are FDA-approved to treat a variety of infections
- Topical agents may be formulated as creams, foams, gels, lacquers, lotions, ointments, powders, solutions and sprays
- Many topical antifungal preparations are available as prescription medications and over-the-counter (OTC) products
- Few trials have been performed to compare safety and efficacy profiles of the drugs in treating topical fungal infections
- Based on limited efficacy data, choice of therapy is mainly based on clinical judgment with regard to prior treatments and complicating conditions, such as bacterial growth or intense inflammation

Antifungals, Topical

Product Updates:

- Luzu is now indicated for treatment of interdigital tinea pedis, tinea cruris, and tinea corporis caused by the organisms Trichophyton rubrum and Epidermophyton floccosum in pediatric patients. Luzu was previously only approved in adults

Beta Blockers

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

Beta Blockers

Class Overview - Product indications include*:

- Hypertension, Heart Failure, Angina, Myocardial Infarction, Cardiac Arrhythmias, Migraine Prophylaxis

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

Beta Blockers

Class Overview: Single Agents

- acebutolol - (acebutolol, Sectral)
- atenolol - (atenolol, Tenormin)
- betaxolol - (betaxolol)
- bisoprolol - (bisoprolol)
- carvedilol - (carvedilol, Coreg)
- carvedilol extended-release - (carvedilol ER, Coreg CR)
- labetalol - (labetalol)
- metoprolol succinate ER - (metoprolol succinate ER, Toprol XL)
- metoprolol tartrate - (Lopressor, metoprolol tartrate)

Beta Blockers

Class Overview: Single Agents

- nadolol - (Corgard, nadolol)
- nebivolol - (Bystolic)
- pindolol - (pindolol)
- propranolol - (propranolol)
- propranolol hydrochloride - (Hemangeol)
- propranolol ER - (Inderal XL, InnoPran XL)
- propranolol LA - (Inderal LA, propranolol LA)
- propranolol - (propranolol)
- sotalol - (Betapace, sotalol)

Beta Blockers

Class Overview: Single Agents

- sotalol AF - (Betapace AF, sotalol AF)
- sotalol - (Sotylize)
- timolol - (timolol)

Class Overview: Beta-Blocker/Diuretic Combinations

- atenolol/chlorthalidone - (atenolol/chlorthalidone, Tenoretic)
- bisoprolol/HCTZ - (bisoprolol/HCTZ , Ziac)
- metoprolol succinate/HCTZ - (Dutoprol, metoprolol succinate/HCTZ)
- metoprolol tartrate/HCTZ - (metoprolol tartrate/HCTZ)

Beta Blockers

Class Overview: Beta-Blocker/Diuretic Combinations

- nadolol/bendroflumethiazide - (Corzide, nadolol/bendroflumethiazide)
- propranolol/HCTZ - (propranolol/HCTZ)

Beta Blockers

- Approximately 75 million (32%) of adults in the United States have hypertension
- Highest prevalence is among African American men and women at 43% and 45.7%, respectively
- Estimated that hypertension is controlled in only 54% of patients with the condition
- Hypertension is an independent risk factor for the development of cardiovascular disease (CVD)
- Beta-blockers are one of the classes suggested as first-line therapy in patients with coronary artery disease, post-MI, HF, and diabetes
- Beta-blockers have similar efficacy for the treatment of hypertension (HTN). The role of beta-blockers in primary prevention for hypertension has been questioned

Beta Blockers

- Beta-blockers are generally not appropriate as first-line agents and are recommended only if a compelling indication such as stable heart failure, myocardial infarction (MI), angina, and tachyarrhythmias exists
- All beta-blockers are equally effective in treating stable angina
- Beta-blockers reduce morbidity and mortality and are considered the standard of care in patients with a prior MI
- Hemangeol is only indicated for proliferating infantile hemangioma requiring systemic therapy

Beta Blockers

Product Updates:

- In February 2018 the FDA approved 25, 50, 100, and 200 mg extended release capsules of metoprolol succinate via the 505(b)(2) pathway. The tablets can be opened and mixed with soft foods for patients unable to swallow the intact capsule. Previous formulations of metoprolol succinate available as tablets

Beta Blockers

Guideline Updates:

- American College of Cardiology published its first guidelines on syncope management. If no contraindications, beta-blockers are recommended as first-line therapy for long QT syndrome (LQTS) and suspected arrhythmic syncope
- Beta-blockers that lack intrinsic sympathomimetic activity are recommended for catecholaminergic polymorphic ventricular tachycardia (CPVT) and stress-induced syncope

BPH Treatments

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

BPH Treatments

Class Overview: Alpha-Blockers

- alfuzosin ER - (alfuzosin ER, Uroxatral)
- doxazosin - (Cardura, doxazosin)
- doxazosin ER - (Cardura XL)
- silodosin - (Rapaflo)
- tamsulosin - (Flomax, tamsulosin)
- terazosin - (terazosin)

BPH Treatments

Class Overview: 5-Alpha Reductase Inhibitors (5AR)

- dutasteride - (Avodart, dutasteride)
- finasteride - (finasteride, Proscar)

Class Overview: 5-Alpha Reductase Inhibitor (5AR)/Alpha Blocker Combinations

- dutasteride/tamsulosin - (dutasteride/tamsulosin, Jalyn)

Class Overview: Phosphodiesterase 5 (PDE5) Inhibitors

- tadalafil - (Cialis)

BPH Treatments

- Benign prostatic hyperplasia (BPH) is one of the most common conditions in aging men
- Symptoms are induced by hyperplastic changes in prostate tissue, leading to prostatic enlargement. The resulting obstruction increases urinary outflow resistance and results in an impaired detrusor muscle response
- Drugs used in BPH treatment relieve lower urinary tract symptoms (LUTS) and prevent complications
- They may be an alternative to surgical intervention
- All products are indicated for the treatment of symptomatic BPH but none are indicated for prevention of prostate cancer
- Various products carry other non-BPH indications

BPH Treatments

- The American Urological Association (AUA) 2010 standards were reaffirmed in 2014 and state patients with mild symptoms of BPH (AUA Symptom Score < 8) and patients with moderate or severe disease (AUA Symptom Score > 8) not bothered by their symptoms generally do not require pharmacologic intervention
- Alpha-adrenergic blocker therapy is an appropriate treatment option for patients with moderate to severe LUTS secondary to BPH
- The AUA states that all four agents have equal clinical effectiveness. Silodosin (Rapaflo) did not have published peer-reviewed studies prior to the guideline update
- Guidelines state the 5ARs are appropriate and effective treatments for patients with LUTS associated with demonstrable prostatic enlargement, but not men with LUTS no evidence of prostatic enlargement

BPH Treatments

- The 5α-reductase inhibitors may be used to prevent progression of LUTS secondary to BPH and to reduce the risk of urinary retention and future prostate-related surgery
- Combination therapy utilizing an alpha blocker and a 5α-reductase inhibitor is an appropriate and effective treatment for patients who exhibit LUTS symptoms and have definitive prostatic enlargement
- 5ARs are not to be administered to women or children. Additionally, women who are pregnant or who may become pregnant should not handle dutasteride capsules or finasteride tablets
- The NIH-funded Medical Therapy of Prostatic Symptoms (MTOPS) and CombaT studies indicate that combination therapy is likely to be more effective at inhibiting disease progression than monotherapy

BPH Treatments

- Combination therapy is most appropriate for men at highest risk for disease progression and those experiencing symptoms of LUTS with demonstrable or indicated prostate enlargement
- While combination therapy has demonstrated greater effectiveness than monotherapy, the combination product available has not proven more effective than co-administration of the individual products in treating disease progression and symptom relief

Calcium Channel Blockers

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

Calcium Channel Blockers

Class Overview - Product indications include*:

- Hypertension, Angina, Vasospastic Angina, Ventricular Rate Control, Unstable Angina, Coronary Artery Disease

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

Calcium Channel Blockers

Class Overview: Dihydropyridines

- amlodipine - (amlodipine, Norvasc)
- felodipine ER - (felodipine ER, Plendil)
- isradipine - (isradipine)
- nicardipine - (Cardene, nicardipine)
- nicardipine ER - (Cardene SR)
- nifedipine - (nifedipine, Procardia)
- nifedipine ER, SA, SR - (Adalat CC; Afeditab CR; Nifediac CC; Nifedical XL; nifedipine ER, SA, SR; Procardia XL)
- nimodipine - (nimodipine)

Calcium Channel Blockers

Class Overview: Dihydropyridines

- nimodipine solution - (Nymalize)
- nisoldipine - (nisoldipine, Sular)

Class Overview: Non-dihydropyridines

- diltiazem - (Cardizem, diltiazem)
- diltiazem ER - (Cardizem LA, diltiazem ER, Matzim LA)
- diltiazem ER - (Cardizem CD; Cartia XT; diltiazem CD, ER; Dilacor XR; Dilt CD; Taztia XT; Tiazac)

Calcium Channel Blockers

Class Overview: Non-dihydropyridines

- diltiazem ER - (Dilt XR, Dilt XT)
- verapamil - (Calan, verapamil)
- verapamil ER - (Covera-HS)
- verapamil ER - (verapamil ER, Verelan PM)
- verapamil SR - (Calan SR, Isoptin SR, verapamil ER, Verelan)

Calcium Channel Blockers

- Hypertension affects approximately one-third of adult Americans and only half of this population have their hypertension under control
- Hypertension is an independent risk factor for the development of cardiovascular disease
- Calcium channel blockers (CCBs) are widely used in the treatment of hypertension and angina pectoris
- The American Diabetes Association (ADA) 2013 guidelines recommend that dihydropyridine (DHP) CCBs be used as second-line drugs for patients with diabetes and hypertension who cannot tolerate the other preferred antihypertensive agents or require additional therapy to achieve the target blood pressure

Calcium Channel Blockers

- The benefits of CCBs in controlling angina and hypertension have been clearly documented in clinical use
- No CCB has demonstrated a clinical advantage over other CCBs in the treatment of hypertension
- Dihydropyridine CCBs may cause a baroreceptor-mediated reflex increase in heart rate because of their potent peripheral vasodilating effects
- Nimodipine (Nymalize) oral solution is only indicated for use in subarachnoid hemorrhage

Calcium Channel Blockers

Product/Guideline Updates:

- Nymalize ready-to-use oral solution (30mg/10mL) is approved for the treatment of subarachnoid hemorrhage. It is designed for patients who require a dosage that is lower than the standard 20mL (60mg) dose

Steroids, Topical

Steroids, Topical

Class Overview: Low Potency Topical Steroid Products

- alclometasone dipropionate – (alclometasone dipropionate cream & ointment)
- desonide – (Desonate Gel; desonide cream, lotion & ointment; Tridesilon)
- fluocinolone acetonide – (Capex Shampoo; Dema-Smoothe-FS; fluocinolone 0.01% oil)
- hydrocortisone/white petrolatum – (hydrocortisone/min oil/pet ointment)
- hydrocortisone - (Ala-Scalp HP; hydrocortisone cream, gel, lotion & ointment; Texacort)

Steroids, Topical

Class Overview: Low Potency Topical Steroid Products

- hydrocortisone acetate - (MiCort HC)
- Hydrocortisone/skin cleansers - (Aqua Glycolic HC; Dermasorb HC)

Steroids, Topical

Class Overview: Medium Potency Topical Steroid Products

- betamethasone valerate - (betamethasone valerate foam; Luxiq)
- clocortolone pivalate - (clocortolone cream (AG); Cloderm)
- fluocinolone acetonide - (fluocinolone acetonide cream, ointment & solution; Synalar Ointment & Solution)
- fluocinolone acetonide/emollient - (Synalar Cream Kit & Ointment Kit)
- fluocinolone acetonide/skin cleansers - (Synalar TS Kit)
- flurandrenolide - (Cordran Tape; flurandrenolide cream, lotion, lotion (AG) & ointment)
- fluticasone propionate - (Cutivate Cream & Lotion; fluticasone cream, lotion & ointment)

Steroids, Topical

Class Overview: Medium Potency Topical Steroid Products

- hydrocortisone butyrate - (hydrocortisone butyrate cream, cream (AG), lotion, ointment, ointment (AG), solution & solution (AG))
- hydrocortisone butyrate/emollient - (hydrocortisone butyrate/emollient & emollient (AG))
- hydrocortisone probutate - (Pandel)
- hydrocortisone valerate - (hydrocortisone valerate cream & ointment)
- mometasone furoate - (Elocon Cream & Ointment; mometasone furoate cream, ointment & solution)
- prednicarbate - (prednicarbate cream & ointment)

Steroids, Topical

Class Overview: High Potency Topical Steroid Products

- amcinonide - (amcinonide cream & lotion)
- betamethasone dipropionate - (betamethasone dipropionate cream, gel, lotion & ointment; Sernivo Spray)
- betamethasone valerate - (betamethasone valerate cream & ointment)
- betamethasone/propylene glyc - (betamet diprop/prop gly cream, lotion & ointment; Diprolene Ointment)
- desoximetasone - (desoximetasone cream, gel & ointment; Topicort Ointment & Spray)
- diflorasone diacetate - (diflorasone diacetate cream & ointment)
- fluocinonide - (fluocinonide cream, gel, ointment & solution)

Steroids, Topical

Class Overview: High Potency Topical Steroid Products

- fluocinonide/emollient - (fluocinonide emollient)
- halcinonide - (Halog Cream & Ointment)
- triamcinolone acetonide/dimethicone - (Ellzia Pak)
- triamcinolone acetonide/silicones - (DermacinRx Silazone; Silazone-II)
- triamcinolone acetonide - (Kenalog Aerosol; triamcinolone acetonide aerosol, cream, lotion & ointment; Trianex Ointment)
- triamcinolone acetonide/dimethicone/silicones - (DermacinRx Silapak; triamcinolone acetonide/dimethicone)
- triamcinolone/emollient - (Dermasorb TA)

Steroids, Topical

Class Overview: Very High Potency Topical Steroid Products

- clobetasol propionate - (clobetasol lotion; clobetasol propionate cream, gel, ointment, solution, spray & spray (AG); clobetasol shampoo; Clobex Lotion, Shampoo & Spray; Olux; Temovate Cream)
- clobetasol propionate/clobetasol propionate/emollient - (clobetasol propionate foam)
- clobetasol propionate/emollient - (clobetasol propionate/emollient)
- clobetasol propionate/skin cleanser - (Clodan Kit)
- diflorasone diacetate/emollient - (Apexicon E)
- halobetasol propionate - (halobetasol propionate cream & ointment; Ultravate Lotion)
- halobetasol/lactic acid - (Ultravate X Pac Cream & Ointment)

Steroids, Topical

Class Overview: Very High Potency Topical Steroid Products

- fluocinonide/emollient - (fluocinonide emollient)
- halcinonide - (Halog Cream & Ointment)
- triamcinolone acetonide/dimethicone - (Ellzia Pak)
- triamcinolone acetonide/silicones - (DermacinRx Silazone; Silazone-II)
- triamcinolone acetonide - (Kenalog Aerosol; triamcinolone acetonide aerosol, cream, lotion & ointment; Trianex Ointment)
- triamcinolone acetonide/dimethicone/silicones - (DermacinRx Silapak; triamcinolone acetonide/dimethicone)
- triamcinolone/emollient - (Dermasorb TA)

Steroids, Topical

- Topical corticosteroids are used for a variety of inflammatory skin conditions, including:
- Atopic dermatitis (AD) is a chronic, inflammatory dermatologic condition and is often referred to as “eczema.” Commonly occurs in patients affected by asthma and/or allergic rhinitis and is associated with elevated serum IgE levels. AD can occur at any age, but occurs most frequently in children
- Psoriasis is another inflammatory skin condition. Plaque psoriasis is the most common type frequently forming on the elbows, knees, lower back, and scalp. Controlling symptoms typically requires lifelong therapy
- Seborrheic dermatitis is an inflammatory disorder affecting areas of the head and trunk, where sebaceous glands are most prominent

Steroids, Topical

- Pharmacotherapy choices for these conditions include emollients and topical corticosteroids
- Emollients remain the cornerstone of any AD pharmacotherapeutic regimen
- Topical corticosteroids are the standard of care to which other treatments are compared
- The selection of medication and potency should depend on medication efficacy then severity of disease, location and surface area of affected skin, intended duration of treatment, medication vehicle, patient preference, and the age of the patient.
- In short-term durations of treatment, high potency medications have greater efficacy when compared to less potent medications, but with an increased risk in side effects

Steroids, Topical

- Increased incidences of adverse dermatologic effects are positively correlated with the medication's frequency and duration of use
- True efficacy and risk of long-term topical corticosteroid use is unknown due to most clinical trials only involving short-term studies
- Recommended in the guidelines of care from the American Academy of Dermatology that continued therapy be supervised and, once a clinical response is demonstrated, a gradual reduction in utilization is appropriate
- There are differing compendia listings for corticosteroid potencies
- Efficacy of the topical corticosteroids is relative to their potency, but individual agents within a potency category are not distinguishable from each other

Executive Session

AHCCCS Drug Lists

- Dr. Salek, MD Chief Medical Officer AHCCCS

Biktarvy Review

- Julie DiTucci-Reiter, PharmD
  Clinical Policy and Programs
  Steward Health Choice

Biosimilar Update

Suzi Berman, RPh

BIOSIMILAR UPDATE

- Retacrit: epoetin alfa-epbx – Epogen/Procrit
- Glatopa: glatiramer acetate – Copaxone
- Fulphilia: pegfilgrastim – Neulasta

- *As a reminder – 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.*

BIOSIMILAR UPDATE

- **Procrit, Epogen, & Retacrit**
  - The net cost of Procrit and Epogen are less costly to the State. Contractors shall not transition to Retacrit and continue to cover Procrit and Epogen as the preferred epoetin products.
- **Copaxone & Glatopa**
  - The net cost of Copaxone 20mg is must less costly to the State. Contractors shall continue to utilize and/or transition to Copaxone as the preferred glatiramer acetate 20mg.
  - The net cost of Glatopa 40mg is less costly to the State. Contractors shall transition to Glatopa 40mg as the preferred glatiramer acetate 40mg product.

BIOSIMILAR UPDATE

- **Neulasta & Fulphilia**
  - AHCCCS is evaluating the costs of both drugs and will communicate which pegfilgrastim will be the preferred product in the Contractor P&T Memo.
  - The Contractor P&T Memo will also be posted on the AHCCCS website.

New Drug Reviews

Non-PDL Classes

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

Two New Products

- Steglatro, (*Segluromet, Steglujan*) - ertugliflozin, (*ertugliflozin/metformin, ertugliflozin/sitagliptin*)
- Zypitamag - pitavastatin magnesium

Steglatro (ertugliflozin) [Segluromet - ertugluflozin/metformin; Steglujan – ertugliflozin/sitagliptan]

- Ertugliflozin, (Steglatro) - a sodium-glucose co-transporter 2 (SGLT2) inhibitor, indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (T2DM)
- Ertugliflozin/metformin (Segluromet) is a fixed-ratio combination SGLT2/biguanide indicated as an adjunct to diet and exercise to improve glycemic control in adults with T2DM not adequately controlled on a regimen with ertugliflozin or metformin, or in patients who are already treated with both agents
- Ertugliflozin/sitagliptan (Steglujan) is a fixed-ratio combination SGLT2/DPP-4 inhibitor indicated as an adjunct to diet and exercise to improve glycemic control in adults with T2DM when treatment with both ertugliflozin and sitagliptin is appropriate

Steglatro (ertugliflozin) [Segluromet - ertugluflozin/metformin; Steglujan – ertugliflozin/sitagliptan]

- None of the agents are indicated for use in type 1 diabetes (T1DM) or diabetic ketoacidosis
- Ertugliflozin/sitagliptin has not been studied in patients with a history of pancreatitis
- All products are contraindicated in patients with severe renal impairment (eGFR < 30 mL/min/1.73 m^2), end stage renal disease (ESRD), and patients on dialysis
- Use in patients with a history of serious hypersensitivity reactions to any component of the product is contraindicated
- There is a boxed warning for lactic acidosis associated with Segluromet due to the metformin component; use in patients with metabolic acidosis is contraindicated

Steglatro (ertugliflozin) [Segluromet - ertugluflozin/metformin; Steglujan – ertugliflozin/sitagliptan]

- Symptomatic hypotension can occur with ertugliflozin. This may occur more in patients with impaired renal function, elderly patients, patients with low systolic blood pressure and on a diuretic
- Ertugliflozin can cause ketoacidosis. Consider risk factors before initiating therapy and discontinue promptly if ketoacidosis is suspected
- Ertugliflozin may cause renal impairment. Renal function should be evaluated prior to therapy and thereafter. Regularly assess renal function and monitor for signs and symptoms of acute kidney injury
- Ertugliflozin use is associated with an increased risk of urosepsis and pyelonephritis. Monitor for signs and symptoms of urinary tract infections and treat if indicated

Steglatro (ertugliflozin) [Segluromet - ertugluflozin/metformin; Steglujan – ertugliflozin/sitagliptan]

- An increased risk of lower limb amputation has been reported with another SGLT2 inhibitor. Prior to use, consider predisposing factors of amputations such as smoking, prior amputation, and peripheral artery disease. Discontinue if patients develop infections or ulcers of lower limbs
- Insulin or insulin secretagogue dosages may require lowering to reduce the risk of hypoglycemia when used with ertugliflozin
- Ertugliflozin can increase the risk of genital mycotic infections
- Ertugliflozin may cause dose-related increases in LDL-C
- No clinical studies have established a benefit of ertugliflozin on macrovascular risk

Steglatro (ertugliflozin) [Segluromet - ertugluflozin/metformin; Steglujan – ertugliflozin/sitagliptan]

- Other DPP-4 inhibitors have been associated with an increased risk of heart failure. Evaluate the risks and benefits in patients taking ertugliflozin/sitagliptin with known risk factors for heart failure and monitor for signs and symptoms
- Ertugliflozin is a substrate of P-glycoprotein (P-gp), breast cancer resistance protein (BCRP) and a weak inhibitor of UGT1A1 and UGT1A4. No dose adjustments are necessary with concomitant medications
- Co-administration with other blood sugar lowering medications may increase the risk of hypoglycemia

Steglatro (ertugliflozin) [Segluromet - ertugluflozin/metformin; Steglujan – ertugliflozin/sitagliptan]

- The most common adverse reactions reported during clinical trials in ≥ 3% of patients were female genital mycotic infections (9.1% to 12.2%), male genital mycotic infections (3.7% to 4.2%), urinary tract infections (4% to 4.1%), and headache (2.9% to 3.5%)
- The most common adverse reactions reported in ≥ 5% of patients associated with metformin were diarrhea, nausea, vomiting, flatulence, abdominal discomfort, indigestion, asthenia, and headache
- The most common adverse reactions reported in ≥ 5% of patients associated with sitagliptin were upper respiratory tract infection, nasopharyngitis, and headache
- No agents are recommended for use in pregnancy during the second and third trimesters. Data on ertugliflozin in pregnant women are not sufficient to determine a drug-associated risk

Steglatro (ertugliflozin) [Segluromet - ertugluflozin/metformin; Steglujan – ertugliflozin/sitagliptan]

- No information is available regarding the efficacy or safety of any of these ertugliflozin-containing products in patients under 18 years old
- No dosage adjustments recommended for patients with mild or moderate hepatic impairment (Child-Pugh classes A and B)
- Ertugliflozin is not recommended in patients with moderate renal impairment
- Steglatro is supplied as 5mg and 15mg tablets
- Segluromet as 2.5 mg/500mg, 2.5 mg/1,000mg, 7.5 mg/500mg, and 7.5 mg/1,000mg tablets
- Steglujan as 5 mg/100mg and 15 mg/100mg tablets

Steglatro (ertugliflozin) [Segluromet - ertugluflozin/metformin; Steglujan – ertugliflozin/sitagliptan]

- Starting dosage for ertugliflozin is 5mg daily without regard to food. Dose may be increased to the maximum recommended dose (15 mg) if tolerated the current dose
- Dosing of ertugliflozin/metformin is twice daily with meals and may be gradually titrated to the maximum dose of 7.5mg/1,000mg
- Dosing of ertugliflozin/sitagliptin is once daily
- Safety and efficacy for ertugliflozin were demonstrated in the **Vertis Mono** Trial, a 26-week, double-blind, placebo-controlled study in 461 patients with T2DM not controlled by diet and exercise (HbA1C, 7% to 10.5%)
- Patients were either treatment naïve or ≥ 8 weeks without antihyperglycemic treatment and entered a 2-week, single-blind, placebo run-in period

Steglatro (ertugliflozin) [Segluromet - ertugluflozin/metformin; Steglujan – ertugliflozin/sitagliptan]

- Patients were randomized to ertugliflozin 5 mg, ertugliflozin 15 mg, or placebo once daily. The primary endpoint, a change from baseline HbA1C at week 26, was significantly higher the ertugliflozin groups compared to the placebo group. Patients treated with ertugliflozin 5 mg and 15 mg once daily also had greater reductions in body weight compared to placebo
- The **VERTIS MET** trial evaluated the safety and efficacy of ertugliflozin as add-on combination therapy with metformin. It was a 26-week, double-blind, placebo-controlled study in 621 patients with T2DM not adequately controlled (HbA1C, 7% to 10.5%) on metformin monotherapy (≥ 1,500 mg/day for ≥ 8 weeks)

Steglatro (ertugliflozin) [Segluromet - ertugluflozin/metformin; Steglujan – ertugliflozin/sitagliptan]

- Patients were randomized to similar to the Vertis Mono trial and again the primary endpoint, a change from baseline HbA1C at week 26, was significantly higher the ertugliflozin groups compared to the placebo group. Patients treated with ertugliflozin 5 mg and 15 mg once daily also had greater reductions in body weight compared to placebo
- Similar results were seen in the **Vertis Sita** trial with sitagliptan, the **Vertis Sita2** trial with metformin and sitagliptan and the **Vertis Factorial** trial with sitagliptan and sitagliptan/metformin combinations. All trials had a similar construct as the **Vertis Mono** trial
- Ertugliflozin demonstrated non-inferiority to glimepiride as add on with metformin in the **Vertis SU** trial

Zypitamag (pitavastatin magnesium)

- An HMG-CoA reductase inhibitor (Statin) indicated for patients with primary hyperlipidemia or mixed dyslipidemia as adjunctive to diet/exercise to reduce elevated total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), apolipoprotein B (Apo B), triglycerides (TG), and to increase high-density lipoprotein cholesterol (HDL-C)
- Has not been studied in Fredrickson Type I, III, and V dyslipidemias
- Originally approved in 2009 and only recently brought to market
- Contraindicated in: patients with a known hypersensitivity; active liver disease; co-administration with cyclosporine; pregnancy and lactation
- Cases of myopathy and rhabdomyolysis have been reported with HMG-CoA reductase inhibitors, including pitavastatin. These risks can occur at any dose level, but increase in a dose-dependent manner

Zypitamag (pitavastatin magnesium)

- Risk can occur at any dose level, but increase in a dose-dependent manner and Zypitamag should be used with caution in patient with predisposing factours for myopathy
- Increases in serum transaminases (including AST/ALT) have been reported with statin products, including pitavastatin. In most cases, elevations were transient and resolved/improved on continued therapy or after a brief interruption
- Liver enzyme tests are recommended before the initiation of Zypitamag and if signs or symptoms of liver injury occur
- Increases in HbA1c and fasting serum glucose levels have been reported with HMG-CoA reductase inhibitors, including pitavastatin

Zypitamag (pitavastatin magnesium)

- Zypitamag has several significant drug interactions:

  cyclosporine - increases Zypitamag exposure; contraindicated

  erythromycin - increases Zypitamag exposure; max dose of 1mg daily

  rifampin - increases Zypitamag exposure; max dose of 2mg daily

  gemfibrozil - increases risk of myopathy/rhabdomyolysis; avoid use together

  fibrates - increases risk of myopathy/rhabdomyolysis; use caution

  niacin - increases risk of skeletal muscle problems; dosage reduction

  colchicine - increases risk of myopathy/rhabdomyolysis; use caution

  warfarin - monitor PT and INR if Zypitamag is added

- Rhabdomyolysis, myopathy and liver enzyme abnormalities were the most significant adverse reactions

Zypitamag (pitavastatin magnesium)

- Other adverse reactions reported in more then 2% of patients in clinical trials included: back pain; constipation; diarrhea; myalgia and pain in extremities
- Safety and effectiveness in pediatric patients have not been established
- Patients with moderate and severe renal impairment as well as end-stage renal disease on hemodialysis should receive a starting dose of 1 mg once daily and a maximum dose of 2 mg once daily
- As noted earlier, Zypitamag is contraindicated in patients with active liver disease, including unexplained persistent elevations of hepatic transaminase levels

Zypitamag (pitavastatin magnesium)

- Approved as 1mg, 2mg and 4mg tablets, dosed as 2mg-4mg once daily
- Doses greater than 4mg/day were associated with an increased risk for severe myopathy in premarketing clinical studies
- Efficacy of Zypitamag was evaluated in a multicenter, randomized, double-blind, placebo-controlled, dose-ranging study was performed to evaluate the efficacy of pitavastatin compared with placebo in 251 patients with primary hyperlipidemia
- Non-inferority of efficacy compared to other statins was also demonstrated in active-controlled studies against select strengths of simvastatin (studies NK-104-102 and NK-104-304), atorvastatin (studies NK-104-301 and NK-104-305), pravastatin (study NK-104-306)

P&T Public Therapeutic Class Votes

Questions?

Agenda Items For The Next Meeting Monday 22 October 2018

Please send agenda items to:

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- Suzi Berman – Suzanne.Berman@azahcccs.gov
- AHCCCS Pharmacy Department Mailbox- AHCCCSPharmacyDept@azahcccs.gov

P&T Meeting Dates

- **2018 Next Meeting Date:**
  - Monday October 22, 2018
- **2019 Meeting Dates:**
  - January 16, 2019
  - April 10, 2019
  - July 10, 2019
  - October 16, 2019

Thank You