AHCCCS
Arizona Health Care Cost Containment System

AHCCCS Pharmacy and Therapeutics Committee

May 17, 2016

P&T Operational Policy: Pharma Testimony

- Register to present at least 30 days prior to P&T
- Information presented is restricted to randomized double blinded active control studies and published *or* accepted for publication in peer reviewed journal(s)
- Limited to 3 min per drug per class

- Not accepted:
  - Online publications
  - Poster presentations
  - Placebo-controlled, observational, open-label and non-randomized studies
  - Anecdotal reports

P&T Operational Policy: In-Person Public Comment Protocol

- Register to present at least 14 days prior to P&T
- First-come, first serve and limited to 15 total
- Limited to 3 minutes per drug

Magellan Class Reviews

- Opioid Dependence Treatment
- Hepatitis C
- Hypoglycemics, Incretin Mimetics/Enhancers
- Hypoglycemics, Insulin and Related Agents
- COPD Agents

Opioid Dependence Treatment

Opioid Dependence Treatment

Class Overview

- The opioid dependence treatment class includes:
  - Single agent products:
    - Buprenorphine
    - Naltrexone
    - Naloxone
  - Combination products:
    - Buprenorphine/naloxone

Opioid Dependence Treatment

Indications

Drug	Manufacturer	Indication
buprenorphine sublingual tablets	generic	Treatment of opiate dependence and is preferred for induction only
buprenorphine/naloxone buccal film (Bunavail®)	BioDelivery Sciences International	Maintenance treatment of opiate dependence
buprenorphine/naloxone sublingual film (Suboxone®)	Reckitt Benckiser	Treatment of opiate dependence (induction and maintenance)
buprenorphine/naloxone sublingual tablets (Zubsolv®)	Orexo	Treatment of opiate dependence (induction and maintenance)
buprenorphine/naloxone sublingual tablets	generic	Maintenance treatment of opiate dependence

Opioid Dependence Treatment

Indications conti.

Drug	Manufacturer	Indication
naltrexone tablets (ReVia®)	Duramed, generic	Treatment of opiate dependence
		Treatment of alcohol dependence in conjunction with a behavior modification program
naltrexone extended-release injectable suspension (Vivitrol®)	Alkermes	Prevention of relapse to opioid dependence, following opioid detoxification
		Treatment of alcohol dependence in patients who are able to abstain from alcohol in an outpatient setting
naloxone hydrochloride injection (Evzio®)	Kaleo, generic	Emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression
naloxone hydrochloride nasal spray (Narcan®)	Adapt	Emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression

Opioid Dependence Treatments

New Product in Class: Bunavail (buprenorphine/naloxone buccal film)

- Indicated for maintenance treatment of opiate dependence
- Contraindications, warnings, adverse effects, and drug interactions are similar to other buprenorphine/naloxone products
- Pregnancy category: C
- Dosing:
  - In patients who have been initially inducted using buprenorphine sublingual tablets
    - If switching from Suboxone sublingual tablets, equivalency chart in drug package insert should be followed
    - Adults: dose adjustments should be made in increments/decrements of 2.1/ 0.3 mg to a level that suppresses withdrawal symptoms; recommended target single daily dose is 8.4/1.4 mg daily
    - Maintenance dose range: 2.1/0.3 mg to 12.6/2.1 mg daily; higher doses show no clinical advantage; no more than 2 films should be applied to 1 cheek at a time

Opioid Dependence Treatments

New Product in Class: Bunavail (buprenorphine/naloxone buccal film) conti.

- It is available as 2.1/0.3 mg, 4.2/0.7 mg, and 6.3/1 mg buccal films
- The exposure of buprenorphine from 1 Bunavail 4.2/0.7 mg buccal film is equivalent to 1 Suboxone 8/2 mg sublingual tablet
- The naloxone exposure from Bunavail buccal film is 33% less than with Suboxone sublingual tablets
- First use of the medication should be supervised by a medical professional to assess proper technique; self-administered is appropriate thereafter

Opioid Dependence Treatments

New Product in Class: Evzio (naloxone injection)

- Indicated for emergency treatment of known/suspected opioid overdose, as manifested by respiratory and/or CNS depression
- Contraindications, warnings, adverse effects, and drug interactions are the same as other naloxone products including severe withdrawal symptoms
- Pregnancy category: B
- Dosing: 0.4 mg by IM or SC injection into the anterolateral aspect of thigh in adult/pediatric patient; additional doses may be used every 2 to 3 minutes until emergency medical assistance arrives
- It is available as 0.4 mg/0.4 mL solution in a pre-filled auto-injector with an electronic voice instructor; supplied as 2 Evzio 0.4 mg auto-injectors and a single Trainer

Opioid Dependence Treatments

New Product in Class: Narcan (naloxone nasal spray)

- Indicated for emergency treatment of known/suspected opioid overdose, as manifested by respiratory and/or CNS depression
- Contraindications, warnings, adverse effects, and drug interactions are similar to other naloxone products including severe withdrawal symptoms
  - Additional adverse reactions include: musculoskeletal pain, nasal dryness, edema, congestion, and inflammation
  - Monitoring for the need for continued surveillance and repeated doses or possible resuscitative measures needed
- Pregnancy category: n/a; may precipitate withdrawal in the fetus

Opioid Dependence Treatments

New Product in Class: Narcan (naloxone nasal spray) conti.

- Dosing: Administer 1 spray into a single nostril; may administer additional doses using a new nasal spray with each dose if no response/relapse occurs; additional doses may be administered every 2 to 3 minutes as needed until emergency assistance arrives
- It is available as a 4 mg/0.1 mL nasal spray (supplied as 2 blister packages, each containing a single nasal spray, per carton)

Opioid Dependence Treatments

Product Updates

- Zubsolv gained the indication of induction treatment of opiate dependence; former indication was for maintenance treatment only

Opioid Dependence Treatments

Clinical Trials

- There are no published comparative clinical studies available comparing products

Testimony

- Pharma
  - Deborah Profant: Alkermes: Vivitrol
  - Patricia Trifunov: Velocity Biogroup: Bunavail
  - William Mullen: Indivior: Suboxone
  - Thomas Begres: Adapt Pharma: Narcan Nasal Spray
  - J Carvel Jackson: Orexo: Zubsolv
- Public
  - Michael Sucher
  - Lloyd Vacovsky
  - Doray Elkins
  - Kathleen Adams

Hepatitis C Agents

Hepatitis C Agents

Class Overview

- The Hepatitis C Agent class includes:
  - Single entity products:
    - Interferons
    - Ribavirin
    - Oral Protease Inhibitors
    - Oral NS5A Inhibitor
    - Oral NS5B Polymerase Inhibitors
  - Combination products:
    - NS5A inhibitor and NS3/4A protease inhibitor
    - NS5A inhibitor and NS5B Inhibitor
    - NS5A inhibitor; protease inhibitor; CYP3A inhibitor; and NS5B polymerase inhibitor
    - NS5A inhibitor; protease inhibitor; and CYP3A inhibitor

Hepatitis C Agents

Indications

Drug	Manufacturer	Indication
Interferons		
peginterferon alfa-2a (Pegasys®)	Genentech	Chronic hepatitis C Treatment of adults with chronic hepatitis C as part of a combination regimen with other hepatitis C virus antiviral drugs in patients ≥ 5 years old with compensated liver disease; monotherapy is not recommended unless a patient has a contraindication to, or significant intolerance, to other HCV antiviral drugs Chronic hepatitis B Treatment of HBeAg-positive and HBeAg-negative chronic hepatitis B in adults with compensated liver disease and evidence of viral replication and liver inflammation

Hepatitis C Agents

Indications conti.

Drug	Manufacturer	Indication
peginterferon alfa-2b (PEGIntron®)	Merck Sharp & Dohme	Chronic hepatitis C For patients with compensated liver disease in combination with ribavirin (Rebetol) and an approved Hepatitis C Virus (HCV) NS3/4A protease inhibitor in adult patients (≥18 years old) with HCV genotype 1 infection; For patients with compensated liver disease in combination with ribavirin (Rebetol) in patients with genotypes other than genotype 1, pediatric patients (3-17 years of age), or in patients with genotype 1 infection where the use of an HCV NS3/4A protease inhibitor is not warranted based on tolerability, contraindications, or other clinical factors; Monotherapy should only be used in the treatment of chronic hepatitis C in patients with compensated liver disease if there are contraindications to, or significant intolerance of, ribavirin and is indicated for use only in previously untreated adult patients; combination therapy provides substantially better response rates than monotherapy

Hepatitis C Agents

Indications conti.

Drug	Manufacturer	Indication
Ribavirin		
ribavirin (Copegus®)	generic	Chronic hepatitis C In combination with peginterferon alfa-2a (Pegasys) in patients ≥ 5 years of age with compensated liver disease and have not been previously treated with interferon alfa; Includes patients with histological evidence of cirrhosis (Child-Pugh class A) Includes adult patients with clinically stable HIV disease and CD4 count > 100 cells/mm^2; Copegus must not be used as monotherapy; safety and efficacy have not been demonstrated with treatment >48 weeks; safety and efficacy have not been established in liver or other organ transplant recipients, patients with decompensated liver disease, or previous non-responders to interferon therapy

Hepatitis C Agents

Indications conti.

Drug	Manufacturer	Indication
ribavirin (Rebetol®)	generic, Merck Sharp & Dohme	<u>Chronic hepatitis C</u> In combination with interferon alfa-2b (pegylated [PEG-Intron] or non pegylated [Intron-A®]) in patients (≥ 3 years of age) with compensated liver disease; Rebetol must not be used as monotherapy; Combination therapy with ribavirin/peginterferon alfa-2b is preferred over ribavirin/interferon alfa-2b as this combination provides substantially better response rates; Patients with the following characteristics are less likely to benefit from retreatment after failing a course of therapy: previous nonresponse, previous peginterferon treatment, significant bridging fibrosis or cirrhosis, and genotype 1 infection; no safety and efficacy data are available for treatment of >1 year

Hepatitis C Agents

Indications conti.

Drug	Manufacturer	Indication
ribavirin (Ribasphere®, Ribasphere RibaPak®, RibaTab)'	generic	Chronic hepatitis C *Capsules* In combination with interferon alfa 2b (pegylated and non pegylated) in patients ≥3 years of age with compensated liver disease; Ribasphere must not be used as monotherapy; combination therapy with ribavirin/peginterferon alfa-2b is preferred over ribavirin/interferon alfa-2b as this combination provides substantially better response rates; Patients with the following characteristics are less likely to benefit from retreatment after failing a course of therapy: previous nonresponse, previous peginterferon treatment, significant bridging fibrosis or cirrhosis, and genotype 1 infection; No safety and efficacy data are available for treatment of longer than 1 year

Hepatitis C Agents

Indications conti.

Drug	Manufacturer	Indication
ribavirin (Ribasphere®, Ribasphere RibaPak®, RibaTab)' conti.	generic	*Tablets* In combination with peginterferon alfa-2a (Pegasys) in adults with compensated liver disease and adults who have not been previously treated with interferon alpha; Patients in whom efficacy was demonstrated included patients with compensated liver disease and histological evidence of cirrhosis (Child-Pugh class A) and patients with HIV disease that is clinically stable and CD4 Count > 100 cells/mm^2; Safety and efficacy data are not available for treatment longer than 48 weeks; The safety and efficacy of ribavirin and peginterferon alfa-2a therapy have not been established in liver or other organ transplant recipients, patients with decompensated liver disease, or previous non-responders to interferon

Hepatitis C Agents

Indications conti.

Drug	Manufacturer	Indication
ribavirin (Moderiba™)	Abbvie	Chronic hepatitis C In combination with peginterferon alfa-2a for the treatment of adults with chronic hepatitis C virus infection who have compensated liver disease and have not been previously treated with interferon alfa; Patients in whom efficacy was demonstrated included patients with compensated liver disease and histological evidence of cirrhosis (Child-Pugh class A) and patients with HIV disease that is clinically stable and CD4 count > 100 cells/mm^3; Moderiba should not be used as monotherapy; Safety and efficacy data are not available for treatment longer than 48 weeks; The safety and efficacy of ribavirin and peginterferon alfa-2a therapy have not been established in liver or other organ transplant recipients, patients with decompensated liver disease, or previous non-responders to interferon

Hepatitis C Agents

Indications conti.

Drug	Manufacturer	Indication
Oral Protease Inhibitors		
simeprevir (Olysio®)	Janssen	<u>Chronic hepatitis C genotype 1 or 4 infection</u> As a component of a combination antiviral treatment regimen; simeprevir monotherapy is not recommended; When used in combination with peginterferon and ribavirin, screening patients with HCV genotype 1a infection for the presence of the NS3 Q80K polymorphism at baseline is strongly recommended as efficacy is substantially reduced in these patients and alternative therapy should be considered; Not recommended in patients who have previously failed therapy with a treatment that included simeprevir (Olysio) or other HCV protease inhibitors;
Oral NS5A Inhibitor		
daclatasvir (Daklinza™)	BMS	<u>Chronic hepatitis C genotype 1 or 3</u> In combination with sofosbuvir with or without ribavirin; Sustained virologic response (SVR) rates are reduced in HCV genotype 3 infected patients with cirrhosis receiving daclatasvir in combination with sofosbuvir for 12 weeks

Hepatitis C Agents

Indications conti.

Drug	Manufacturer	Indication
Oral NS5B Polymerase Inhibitors		
sofosbuvir (Sovaldi®)	Gilead	Chronic hepatitis C genotype 1, 2, 3, or 4 As a component of a combination antiviral treatment regimen
Oral Combination Products		
elbasvir/grazoprevir (Zepatier™)	Merck	Chronic hepatitis C genotype 1 or 4 Co-formulated fixed dose tablet of elbasvir (an NS5A inhibitor) and grazoprevir (an NS3/4A protease inhibitor); Indicated for use with or without ribavirin; Testing for NS5A resistance-associated polymorphisms needed for genotype 1a
ledipasvir/sofosbuvir (Harvoni®)	Gilead	Chronic hepatitis C genotype 1, 4, 5, or 6 Co-formulated fixed dose tablet of ledipasvir (an NS5A inhibitor) and sofosbuvir (an NS5B Inhibitor); Indicated for use with or without ribavirin

Hepatitis C Agents

Indications conti.

Drug	Manufacturer	Indication
ombitasvir/ paritaprevir/ritonavir + dasabuvir (Viekira Pak®)	Abbvie	Chronic hepatitis C genotype 1 Viekira Pak includes the combination of ombitasvir (a NS5A inhibitor), paritaprevir (a protease inhibitor), ritonavir (a potent CYP3A inhibitor to pharmacologically boost paritaprevir), and dasabuvir (a NS5B polymerase inhibitor); Indicated for use with or without ribavirin, including in those with compensated cirrhosis
ombitasvir/ paritaprevir/ritonavir (Technivie®)	Abbvie	Chronic hepatitis C genotype 4 (without cirrhosis) Technivie includes the combination of ombitasvir (a NS5A inhibitor), paritaprevir (a protease inhibitor), and ritonavir (a potent CYP3A inhibitor to pharmacologically boost paritaprevir); Indicated for use in combination with ribavirin

Hepatitis C Agents

New Product in Class: Daklinza (daclatasvir)

- Indicated for chronic hepatitis C genotype 1 or 3 in combination with sofosbuvir with/without ribavirin
- Contraindicated with the use of strong inducers of CYP3A (e.g. phenytoin); co-administration of amiodarone and Daklinza in combination with sofosbuvir is not recommended; CYP3A inducers/inhibitors may impact Daklinza plasma levels; daclatasvir may increase the effect of buprenorphine, dabigatran, statins, and digoxin
- Most common side effects are: fatigue, headache, nausea, and diarrhea
- Pregnancy category: N/A; other agents available have category B (e.g. Harvoni, Sovaldi, Viekira, and Technivie)
- Safety and effectiveness has not been established in pediatrics as with other new therapies

Hepatitis C Agents

New Product in Class: Daklinza (daclatasvir) conti.

- Dosing:
  - 60 mg orally once daily in combination with sofosbuvir 400 mg orally once daily with/without ribavirin for 12 weeks
  - Ribavirin should be added to the regimen for genotype 1 patients with decompensated cirrhosis (Child-Pugh B or C) and post-transplant patients
  - Ribavirin should be added to the regimen for genotype 3 patients with compensated (Child-Pugh A) or decompensated (Child-Pugh B or C) cirrhosis and post-transplant patients
  - Ribavirin dosing:
    - Genotype 1 or 3 with Child-Pugh A: 1,000 mg/day for patients < 75 kg and 1,200 mg/day for patients ≥ 75 kg
    - Genotype 1 or 3 with Child-Pugh B or C or post-transplantation: 600 mg/day and increasing to 1,000 mg/day as tolerated

Hepatitis C Agents

New Product in Class: Daklinza (daclatasvir) conti.

- Dosing is the same regardless of HIV coinfection
- It is available as 30 mg and 60 mg tablets
- SVR rates are reduced in genotype 3 patients with cirrhosis
- Optimal duration of daclatasvir and sofosbuvir with/without ribavirin has not been established in genotype 3 patients with cirrhosis or genotype 1 patients with Child-Pugh C cirrhosis
- No dosage adjustment is recommended for patients with any degree of renal impairment

Hepatitis C Agents

Daklinza clinical trials

- A phase 3, open-label trial conducted in patients with HCV genotype 3 infection evaluated the 12-week regimen of daclatasvir 60 mg plus sofosbuvir 400 mg in treatment-naïve (n=101) or treatment-experienced (n=51) patients. Co-primary endpoints were the proportions of treatment-naïve and treatment-experienced patients achieving a SVR12. SVR12 rates were 90% in treatment-naïve patients (98% non-cirrhosis and 58% with cirrhosis) and 86% in treatment-experienced patients (92% non-cirrhosis and 69% with cirrhosis), respectively.
- An open-label trial evaluated the efficacy of daclatasvir and sofosbuvir, with/without ribavirin, in genotype 1 through 3 HCV patients (n=211). Patients were randomized 1:1:1 to sofosbuvir for 1 week, then daclatasvir plus sofosbuvir for 23 weeks, daclatasvir plus sofosbuvir for 24 weeks, or daclatasvir plus sofosbuvir with ribavirin for 24 weeks. All patients with genotype 2 and 3 were treatment-naïve (n=44), while genotype 1 patients were both treatment-naïve (n=126) and treatment-experienced (n=41). After 12 weeks of treatment, 98% of treatment-experienced genotype 1 patients, 98% of treatment-naïve genotype 1 patients, 92% of genotype 2, and 89% of genotype 3 met SVR12.

Hepatitis C Agents

Daklinza clinical trials conti.

- An open-label trial in patients with HCV (genotypes 1 through 4)/HIV coinfection evaluated the efficacy of daclatasvir (60 mg daily) and sofosbuvir (400 mg daily). SVR12 in treatment-naïve genotype 1 patients was 96.4% in the 12-week group and 75.6% in the 8-week group (95% CI). In treatment-experienced patients, the SVR12 was 97.7% (95% CI). Across all genotypes, SVR12 was 97% and 76% in the 12- and 8-week groups, respectively, and SVR12 was 98.1% in treatment-experienced patients (95% CI).
- The safety and efficacy of daily daclatasvir (60 mg/day) and sofosbuvir (400 mg/day) with ribavirin (600 mg/day) were evaluated in a multicenter, 12-week, open-label trial with a 24-week follow up in 2 cohorts of patients with HCV (no patients with genotype 5 enrolled): (1) compensated or decompensated cirrhosis (n=60) and (2) post-transplantation recurrence (within 3 months of screening; n=53). In genotype 1 patients with cirrhosis, 82% (95% CI) achieved SVR12. SVR12 rates in genotypes 2, 3, and 4 were 80%, 83%, and 100%, respectively. SVR12 was higher in patients with Child-Pugh A and B (93%) than Child-Pugh C (56%). SVR12 was achieved by 95% (95% CI) and 91% of post-transplant patients with genotypes 1 and 3, respectively. SVR12 was also achieved by the single patient with genotype 6 included in this cohort; no patients with genotypes 2 or 4 were included in this cohort.

Hepatitis C Agents

New Product in Class: Zepatier (elbasvir/grazoprevir)

- A NS5A inhibitor and NS3/4A protease inhibitor combination product indicated for chronic hepatitis C genotype 1 or 4 with/without ribavirin
- Contraindicated in: patients with moderate /severe hepatic impairment (Child-Pugh B/C); concomitant OATP1B1/3 inhibitor or strong CYP3A inducer use; and in patients taking concurrent medications with known interactions (e.g. anticonvulsants, antimycobacterials , herbals, HIV drugs, immunosuppressants)
- Warning: 1% of patients had increased ALT from normal to >5 times the upper limit of normal (ULN); monitoring warranted
- No dosage adjustment is recommended for patients with renal impairment
- Most common side effects are: fatigue, diarrhea, bilirubin elevation, and headache
- Pregnancy category: N/A; other agents available have category B (e.g. Harvoni, Sovaldi, Viekira, and Technivie)

Hepatitis C Agents

New Product in Class: Zepatier (elbasvir/grazoprevir)

- Safety and effectiveness has not been established in pediatrics as with other new therapies
- Dosing: fixed dose combination: elbasvir 50 mg/grazoprevir 100 mg orally one daily with/without food and with/without ribavirin for 12 to 16 weeks
- Ribavirin should be added to the regimen for genotype 1a treatment-naïve or PegIFN/RBV-experienced patients with baseline NS5A polymorphisms, genotype 1a or 1b who are PegIFN/RBV/NS3/4A PI-experienced, and genotype 4 patients who are PegIFN/RBV-experienced
  - Ribavirin dosing: weight based (range: 800 to 1,200 mg/day) administered in 2 divided doses with food; dosing adjusted for renal impairment
- Available 50 mg/100 mg fixed-dose tablet

Hepatitis C Agents

Zepatier clinical trials

- The efficacy of grazoprevir/elbasvir in treatment-naïve patients with genotype 1 chronic HCV with or without cirrhosis was demonstrated in the C-EDGE TN (n=382) and C-EDGE COINFECTION (n=189) trials. C-EDGE TN was a phase 3, randomized, double-blind, placebo-controlled trial in treatment-naïve patients with genotype 1 or 4 infection with/without cirrhosis. Overall, SVR12 was achieved in 95% of patients following 12 weeks of treatment, 92% in genotype 1a, 98% in genotype 1b, 94% in the non-cirrhotic patients, and 97% in cirrhotic patients. C-EDGE COINFECTION was an open-label, single-arm trial in treatment-naïve HCV/HIV-1 coinfected patients with genotype 1 or 4 infection with/without cirrhosis. Overall, SVR12 was achieved in 95% of patients following 12 weeks of treatment, 94% in genotype 1a, 96% in genotype 1b, 94% in the non-cirrhotic patients, and 100% in cirrhotic patients.

Hepatitis C Agents

Zepatier clinical trials conti.

- C-EDGE TE (n=377) was a randomized, open-label comparative trial in subjects with genotype 1 or 4 infection, with/without cirrhosis, with/without HCV/HIV-1 co-infection, who had failed prior therapy with PegIFN + RBV therapy. SVR12 was achieved in 94% of patients following 12 weeks of therapy and 97% following 16 weeks of therapy. A SVR12 rate of 90% was achieved in patients with genotype 1a and 100% in patients with genotype 1b treated for 12 weeks. An SVR12 rate of 95% was achieved in patients with genotype 1a and 100% in patients with genotype 1b treated for 16 weeks.
- C-SCAPE (n=20) was a randomized, open-label trial of genotype 4 patients without cirrhosis in which patients were randomized in a 1:1 ratio to elbasvir/grazoprevir once daily for 12 weeks with or without ribavirin. In C-EDGE TE, a total of 37 genotype 4 treatment-experienced subjects received a 12- or 16-week grazoprevir/elbasvir with or without RBV regimen. The SVR12 rate among randomized patients treated with grazoprevir/elbasvir + RBV for 16 weeks was 100%.

Hepatitis C Agents

Zepatier clinical trials conti.

- C-SALVAGE (n=79) was an open-label single-arm trial in subjects with genotype 1 infection, with or without cirrhosis, who had failed prior treatment with boceprevir, simeprevir, or telaprevir in combination with PegIFN + RBV. Overall, SVR12 was achieved in 96% of subjects. Treatment outcomes were consistent in genotype 1a and genotype 1b subjects, in subjects with different response to previous HCV therapy, and in subjects with or without cirrhosis. Treatment outcomes were generally consistent in subjects with or without NS3 resistance-associated substitutions at baseline, although limited data are available for subjects with specific NS3 resistance-associated substitutions.
- C-SURFER (n=235) was a randomized, double-blind, placebo-controlled trial in subjects with genotype 1 infection, with or without cirrhosis, with chronic kidney disease (CKD) Stage 4 (eGFR 15 to 29 mL/min/1.73 m^2) or CKD Stage 5 (eGFR < 15 mL/min/1.73 m^2), including subjects on hemodialysis, who were treatment-naïve or who had failed prior therapy with IFN or PegIFN ± RBV therapy. Overall, an SVR12 was achieved in 94% of patients, 97% in genotype 1a, 92% in genotype 1b, 93% in dialysis patients, and 100% and 93% in patients with CKD stages 4 and 5, respectively.

Hepatitis C Agents

New Product in Class: Technivie (ombitasvir/paritaprevir/ritonavir)

- A NS5A, protease, and CYP3A inhibitor combination product indicated for chronic hepatitis C genotype 4 (without cirrhosis); taken with ribavirin
- Contraindicated: in patients with moderate and severe hepatic impairment (Child-Pugh Class B/C); with drugs that are highly dependent on CYP3A for clearance; with drugs that are moderate or strong inducers of CYP3A
- Warning: ALT elevations; discontinue ethinyl estradiol-containing medications; HCV/HIV-1 co-infected patients should be on a suppressive antiretroviral drug; not indicated in patients with cirrhosis (monitoring required)
- No dosage adjustments are required for mild, moderate, or severe renal impairment; has not been studied in patients on dialysis
- Most common side effects are: fatigue, nausea, insomnia, pruritus, asthenia, bilirubin increase, skin reactions

Hepatitis C Agents

New Product in Class: Technivie (ombitasvir/paritaprevir/ritonavir)

- Pregnancy category: B; other agents available also have category B (e.g. Harvoni, Sovaldi, and Viekira)
- Safety and effectiveness has not been established in pediatrics as with other new therapies
- Dosing: 2 ombitasvir, paritaprevir, ritonavir 12.5/75/50 mg tablets once daily (in the morning) with a meal plus weight-based ribavirin (<75 kg = 1,000 mg and ≥ 75 kg = 1,200 mg) for 12 weeks. Treatment without ribavirin for 12 weeks may be considered in patients unable to take or tolerate ribavirin
- Available: ombitasvir, paritaprevir, ritonavir 12.5/75/50 mg fixed-dose tablet

Hepatitis C Agents

Technivie clinical trials

- PEARL-I was a randomized, global, multicenter, open-label trial that enrolled 135 adults with HCV genotype 4 infection without cirrhosis who were either treatment-naïve or did not achieve a virologic response with prior treatment with pegylated interferon + ribavirin (PEG/RBV). All 42 of the treatment-naïve patients taking ombitasvir + paritaprevir + ritonavir with ribavirin for 12 weeks achieved a SVR12 (100%). All 49 of the treatment-experienced patients taking ombitasvir + paritaprevir + ritonavir with ribavirin for 12 weeks achieved an SVR12 (100%). Out of the 44 treatment-naïve patients taking ombitasvir + paritaprevir + ritonavir without ribavirin, 40 patients achieved an SVR12 (91%). Of the 129 patients that achieved a SVR12, all 129 maintained their response 24 weeks after the end of treatment (SVR24).

Hepatitis C Agents

Product Updates

- Olysio
  - Now also indicated for chronic hepatitis C genotype 4 infection
  - Combo with peginterferon + ribavirin is contraindicated with decompensated cirrhosis (moderate to severe hepatic impairment); hepatic failure and decompensation reported in combination with peginterferon alfa and ribavirin
  - Co-administration of simeprevir and sofosbuvir + amiodarone not recommended
  - Peginterferon and ribavirin therapy should be continued beyond 12 weeks for a total of 48 weeks therapy in patients with cirrhosis and HIV co-infection
  - An open-label, single-center, randomized study evaluated efficacy of simeprevir + sofosbuvir vs. peginterferon alfa-2b + ribavirin + sofosbuvir for 12 weeks in adult genotype 1a patients with mild cirrhosis (Child-Pugh Class A) (n=82). A greater number of patients taking simeprevir/sofosbuvir regimen achieved SVR12 vs. those in interferon regimen (93% vs. 75%, respectively; p=0.02)

Hepatitis C Agents

Product Updates

- Viekira
  - Indicated for use with or without ribavirin, including in those with compensated cirrhosis
  - Contraindicated in patients with moderate and severe hepatic impairment (Child-Pugh Class B and C)
  - Hepatic decompensation and failure, including cases requiring liver transplantation or resulting in a fatal outcome, have been reported; monitoring required

Hepatitis C Agents

Product Updates

- Harvoni
  - Newly added indications of chronic hepatitis C genotype 4, 5, and 6
  - Co-administration of amiodarone is not recommended
  - Dosing: ledipasvir 90 mg/sofosbuvir 400 mg orally once daily *with or without* ribavirin for 12 or 24 weeks
    - Ribavirin should be added to the regimen for genotype 1 treatment-naïve and treatment-experienced patients with decompensated cirrhosis (Child-Pugh B or C)
    - Ribavirin should be added to the regimen for genotype 1 or 4 patients treatment-naïve and treatment-experienced liver transplant recipients with compensated (Child-Pugh A) cirrhosis or without cirrhosis
      - Ribavirin dosing:
        - Noncirrhotic or Child-Pugh A cirrhosis post-transplantation: 1,000 mg/day for patients < 75 kg and 1,200 mg for patients ≥ 75 kg
        - Child-Pugh B or C: 600 mg once daily and increasing to 1,000 mg/day or 1,200 mg/day weight-based dosing as tolerated

Hepatitis C Agents

Product Updates

- Interferon alfacon -1 (Infergen®), an interferon product, and 2 oral protease inhibitors, boceprevir (Victrelis®) and telaprevir (Incivek®), have been discontinued

Hepatitis C Agents

AASLD/IDSA HCV Guidelines Recommendation Updates

Treatment Experience	Treatment	Duration (weeks)	Rating
Genotype 1a – Recommended Treatments			
Treatment-Naïve	Patients **without** cirrhosis: •elbasvir/grazoprevir (no baseline high-fold NS5A RAVs) •daclatasvir + sofosbuvir Patients **with compensated** cirrhosis: •elbasvir/grazoprevir (no baseline high-fold NS5A RAVs) •ledipasvir/sofosbuvir	 12 12 12 12	 Class I, Level A Class I, Level B Class I, Level A Class I, Level A
Treatment-Experienced (previous failure of PEG-IFN /RBV)	Patients **without** cirrhosis: •elbasvir/grazoprevir (no baseline high-fold NS5A RAVs) •sofosbuvir + simeprevir •daclatasvir + sofosbuvir Patients **with compensated** cirrhosis: •elbasvir/grazoprevir (no baseline high-fold NS5A RAVs)	 12 12 12 12	 Class I, Level A Class I, Level A Class IIa, Level B Class I, Level A

Hepatitis C Agents

AASLD/IDSA HCV Guidelines Recommendation Updates

Treatment Experience	Treatment	Duration (weeks)	Rating
Genotype 1a – Alternative Treatments			
Treatment-Naïve	Patients **without** cirrhosis: •elbasvir/grazoprevir + weight-based RBV (high baseline high-fold NS5A RAVs)	16	Class IIa, Level B
	Patients **with compensated** cirrhosis: •paritaprevir/ritonavir/ombitasvir + dasabuvir + weight-based RBV	24	Class I, Level A
	•sofosbuvir + simeprevir ± weight-based RBV (no Q80K polymorphism)	24	Class I, Level A
	•daclatasvir + sofosbuvir ± weight-based RBV	24	Class IIa, Level B
	•elbasvir/grazoprevir + weight-based RBV (high baseline high-fold NS5A RAVs)	16	Class IIa, Level B

Hepatitis C Agents

AASLD/IDSA HCV Guidelines Recommendation Updates

Treatment Experience	Treatment	Duration (weeks)	Rating
Genotype 1a – Alternative Treatments			
Treatment-Experienced (previous failure of PEG-IFN /RBV)	Patients **without** cirrhosis: •elbasvir/grazoprevir + weight-based RBV (high baseline high fold NS5A RAVs)	16	Class I, Level B
	Patients **with compensated** cirrhosis: •paritaprevir/ritonavir/ombitasvir + dasabuvir + weight-based RBV	24	Class I, Level A
	•elbasvir/grazoprevir + weight-based RBV (high baseline high-fold NS5A RAVs)	16	Class I, Level B
	•daclatasvir + sofosbuvir ± weight-based RBV	24	Class IIa, Level B
	•sofosbuvir + simeprevir ± weight-based RBV (Q80K variant negative)	24	Class IIa, Level B

Hepatitis C Agents

AASLD/IDSA HCV Guidelines Recommendation Updates

Treatment Experience	Treatment	Duration (weeks)	Rating
Genotype 1b – Recommended Treatments			
Treatment-Naïve	Patients **without** cirrhosis:		
	•elbasvir/grazoprevir	12	Class I, Level A
	•daclatasvir + sofosbuvir	12	Class I, Level B
	Patients **with compensated** cirrhosis:		
	•elbasvir/grazoprevir	12	Class I, Level A
	•ledipasvir/sofosbuvir	12	Class I, Level A
	•paritaprevir/ritonavir/ombitasvir + dasabuvir	12	Class I, Level A
Treatment-Experienced (previous failure of PEG-IFN /RBV)	Patients **without** cirrhosis:		
	•elbasvir/grazoprevir	12	Class I, Level A
	•paritaprevir/ritonavir/ombitasvir + dasabuvir	12	Class I, Level A
	•sofosbuvir + simeprevir	12	Class I, Level A
	•daclatasvir + sofosbuvir	12	Class IIa, Level B
	Patients **with compensated** cirrhosis:		
	•elbasvir/grazoprevir	12	Class I, Level A

Hepatitis C Agents

AASLD/IDSA HCV Guidelines Recommendation Updates

Treatment Experience	Treatment	Duration (weeks)	Rating
Genotype 1b – Alternative Treatments			
Treatment-Naïve	Patients **with compensated** cirrhosis: •sofosbuvir + simeprevir ± weight-based RBV •daclatasvir + sofosbuvir ± weight-based RBV	 24 24	 Class I, Level A Class IIa, Level B
Treatment-Experienced (previous failure of PEG-IFN /RBV)	Patients **with compensated** cirrhosis: •daclatasvir + sofosbuvir ± weight-based RBV •sofosbuvir + simeprevir ± weight-based RBV	 24 24	 Class IIa, Level B Class IIa, Level B

Hepatitis C Agents

AASLD/IDSA HCV Guidelines Recommendation Updates

Treatment Experience	Treatment	Duration (weeks)	Rating
Genotype 1 (regardless of subtype) – Recommended Treatments			
Treatment-Experienced (previous failure of PEG-IFN / RBV + an HCV protease inhibitor [NS3], including telaprevir, boceprevir, or simeprevir)	Patients **without** cirrhosis:		
	•daclatasvir + sofosbuvir	12	Class IIa, Level B
	•elbasvir/grazoprevir + weight-based RBV (genotype 1b or 1a with no baseline high-fold NS5A RAVs)	12	Class IIa, Level B
	•elbasvir/grazoprevir + weight-based RBV (genotype 1a with high baseline high-fold NS5A RAVs)	16	Class IIa, Level B
	Patients **with compensated** cirrhosis:		
	•daclatasvir + sofosbuvir ± weight-based RBV	24	Class IIa, Level B
	•elbasvir/grazoprevir + weight-based RBV (genotype 1b or 1a with no baseline high-fold NS5A RAVs)	12	Class IIa, Level B
	•elbasvir/grazoprevir + weight-based RBV (genotype 1a with high baseline high-fold NS5A RAVs)	16	Class IIa, Level B

Hepatitis C Agents

AASLD/IDSA HCV Guidelines Recommendation Updates

Treatment Experience	Treatment	Duration (weeks)	Rating
Genotype 1 (regardless of subtype) – Recommended Treatments			
Treatment-Experienced (previous failure of simeprevir + sofosbuvir)	Patients **without** cirrhosis: •Defer treatment, pending availability of data, in those who do not have reasons for urgent treatment	--	Class IIb, Level C
	Patients **with compensated** cirrhosis or other patients who require urgent treatment: •Testing for resistance-associated variants that confer decreased susceptibility recommended in patients with compensated cirrhosis or without urgent treatment needed; treatment should be tailored as follows:		Class II, Level C
	•Dual direct acting antiviral therapy is recommended + weight-based RBV (unless contraindicated)	24	
	•If available, nucleotide-based (e.g., sofosbuvir) triple or quadruple direct acting antiviral therapy may be considered with duration + weight-based RBV (unless contraindicated)	12-24	

Hepatitis C Agents

AASLD/IDSA HCV Guidelines Recommendation Updates

Treatment Experience	Treatment	Duration (weeks)	Rating
Genotype 1 (regardless of subtype) – Recommended Treatments			
Treatment-Experienced (previous failure of sofosbuvir + RBV ± PEG-IFN)	Patients **without** cirrhosis: •ledipasvir/sofosbuvir + weight-based RBV	12	Class IIb, Level B
	Patients **with compensated** cirrhosis: •ledipasvir/sofosbuvir + weight-based RBV	24	Class IIa, Level B

Hepatitis C Agents

AASLD/IDSA HCV Guidelines Recommendation Updates

Treatment Experience	Treatment	Duration (weeks)	Rating
Genotype 1 (regardless of subtype) – Recommended Treatments			
Treatment-Experienced (previous failure of any nonstructural protein 5A [NS5A] inhibitor)	Patients **without** cirrhosis: •Defer treatment, pending availability of data, in those who do not have reasons for urgent treatment	--	Class IIb, Level C
	Patients **with compensated** cirrhosis or other patients who require urgent treatment: •Testing for resistance-associated variants that confer decreased susceptibility recommended in patients with compensated cirrhosis or without urgent treatment needed; treatment should be tailored as follows:		Class IIb, Level C
	•Dual direct acting antiviral therapy is recommended + weight-based RBV (unless contraindicated)	24	
	•If available, nucleotide-based (e.g., sofosbuvir) triple or quadruple direct acting antiviral therapy may be considered with duration + weight-based RBV (unless contraindicated)	12-24	

Hepatitis C Agents

AASLD/IDSA HCV Guidelines Recommendation Updates

Treatment Experience	Treatment	Duration (weeks)	Rating
Genotype 2 – Recommended Treatments			
Treatment-Naïve	Patients **without** cirrhosis: •daclatasvir + sofosbuvir (RBV ineligible)	12	Class IIa, Level B
	Patients **with compensated** cirrhosis: •daclatasvir + sofosbuvir (RBV ineligible) •sofosbuvir + weight-based RBV	16-24 16-24	Class IIa, Level B Class IIa, Level C
Treatment-Experienced (previous failure of PEG-IFN/ RBV)	Patients **without** cirrhosis: •daclatasvir + sofosbuvir (RBV ineligible)	12	Class IIa, Level B
	Patients w**ith compensated** cirrhosis: •daclatasvir + sofosbuvir (RBV ineligible) •sofosbuvir + weight-based RBV	16-24 16-24	Class IIa, Level B Class IIa, Level B
Treatment-Experienced (previous failure of sofosbuvir + RBV)	Patients **with compensated or without** cirrhosis: •daclatasvir + sofosbuvir ± weight-based RBV (patients ineligible for interferon)	24	Class IIa, Level C
	•sofosbuvir + weight-based RBV + PEG-IFN	12	Class IIa, Level C

Hepatitis C Agents

AASLD/IDSA HCV Guidelines Recommendation Updates

Treatment Experience	Treatment	Duration (weeks)	Rating
Genotype 3 – Recommended Treatments			
Treatment-Naïve	Patients **without** cirrhosis: •daclatasvir + sofosbuvir •sofosbuvir + weight-based RBV + weekly PEG-IFN (interferon eligible) Patients **with compensated** cirrhosis: •sofosbuvir + weight-based RBV + weekly PEG-IFN (interferon eligible) •daclatasvir + sofosbuvir ± weight-based RBV	 12 12 12 24	 Class I, Level A Class I, Level A Class I, Level A Class IIa, Level B
Treatment-Experienced (previous failure of PEG-IFN/ RBV)	Patients **without** cirrhosis: •daclatasvir + sofosbuvir •sofosbuvir + weight-based RBV + PEG-IFN Patients **with compensated** cirrhosis: •sofosbuvir + weight-based RBV + PEG-IFN •daclatasvir + sofosbuvir + weight-based RBV	 12 12 12 24	 Class I, Level A Class I, Level A Class I, Level A Class IIa, Level B

Hepatitis C Agents

AASLD/IDSA HCV Guidelines Recommendation Updates

Treatment Experience	Treatment	Duration (weeks)	Rating
Genotype 3 – Recommended Treatments			
Treatment-Experienced (previous failure of sofosbuvir + RBV)	Patients **with** compensated or **without** cirrhosis: •daclatasvir + sofosbuvir + weight-based RBV •sofosbuvir + weight-based RBV + PEG-IFN	 24 12	 Class IIa, Level C Class IIa, Level C
Genotype 3 – Alternative Treatments			
Treatment-Naïve	Patients **with** or **without** cirrhosis: •sofosbuvir + weight-based RBV (interferon and daclatasvir ineligible)	24	Class I, Level A

Hepatitis C Agents

AASLD/IDSA HCV Guidelines Recommendation Updates

Treatment Experience	Treatment	Duration (weeks)	Rating
Genotype 4 – Recommended Treatments			
Treatment-Naïve	Patients **without** cirrhosis:		
	•paritaprevir/ritonavir/ombitasvir + weight-based RBV	12	Class I, Level A
	•elbasvir/grazoprevir	12	Class IIa, Level B
	•ledipasvir/sofosbuvir	12	Class IIa, Level B
	Patients **with compensated** cirrhosis:		
	•paritaprevir/ritonavir/ombitasvir + weight-based RBV	12	Class I, Level B
	•elbasvir/grazoprevir	12	Class IIa, Level B
	•ledipasvir/sofosbuvir	12	Class IIa, Level B

Hepatitis C Agents

AASLD/IDSA HCV Guidelines Recommendation Updates

Treatment Experience	Treatment	Duration (weeks)	Rating
Genotype 4 – Recommended Treatments			
Treatment-Experienced (previous failure of PEG-IFN/ RBV)	Patients **without** cirrhosis:		
	•paritaprevir/ritonavir/ombitasvir + weight-based RBV	12	Class I, Level A
	•elbasvir/grazoprevir	12	Class IIa, Level B
	•elbasvir/grazoprevir + weight-based RBV (those with on-treatment failure)	16	Class IIa, Level B
	•ledipasvir/sofosbuvir	12	Class IIa, Level B
	Patients **with compensated** cirrhosis:		
	•paritaprevir/ritonavir/ombitasvir + weight-based RBV	12	Class I, Level A
	•elbasvir/grazoprevir	12	Class IIa, Level B
	•elbasvir/grazoprevir + weight-based RBV (those with on-treatment failure)	16	Class IIa, Level B
	•ledipasvir/sofosbuvir + weight-based RBV	12	Class IIa, Level B
	•ledipasvir/sofosbuvir	24	Class IIa, Level B

Hepatitis C Agents

AASLD/IDSA HCV Guidelines Recommendation Updates

Treatment Experience	Treatment	Duration (weeks)	Rating
Genotype 4 – Alternative Treatments			
Treatment-Experienced	Patients **without** cirrhosis: •sofosbuvir + weight-based RBV + PEG-IFN •sofosbuvir + weight-based RBV Patients **with compensated** cirrhosis •sofosbuvir + weight-based RBV	 12 24 24	 Class IIa, Level B Class IIa, Level B Class IIa, Level B
Genotype 6 – Recommended Treatments			
Treatment-Naïve	Patients **with or without** cirrhosis: •ledipasvir/sofosbuvir	 12	 Class IIa, Level B
Treatment-Experienced	Patients **with or without** cirrhosis: •ledipasvir/sofosbuvir	 12	 Class IIa, Level C
Genotype 5 or 6 – <u>NOT</u> Recommended Treatments			
Treatment-Naïve	•PEG-IFN + RBV ± simeprevir	24-48	Class IIb, Level A

Hepatitis C Agents

AASLD/IDSA HCV Guidelines Recommendation Updates

- The updated AASLD/IDSA hepatitis C guidelines do not address HCV in pediatric patients
  - The 2009 guidelines recommend the following as standard treatment for children ages 2 to 17 years: peginterferon alfa-2b (PEGIntron) 60 mcg/m^2 SC weekly with ribavirin 15 mg/kg daily for 48 weeks
  - The 2011 AASLD guidelines did not cover the treatment of pediatric patients with the exception of the statement that telaprevir (Incivek) and boceprevir (Victrelis), which are no longer available, are not recommended for use in children and adolescents younger than 18 years of age
  - Safety and effectiveness of Harvoni, Viekira Pak, Technivie, Olysio, Daklinza, Zepatier, and Sovaldi have not been established in pediatric patients

Hepatitis C Agents

AASLD/IDSA HCV Guidelines Recommendation Updates

- The updated AASLD/IDSA hepatitis C guidelines for post-liver transplant:
  - Genotype 1 or 4:
    - Treatment-naïve or –experienced (including compensated cirrhosis): are Harvoni + weight-based ribavirin (Class I, Level A) or Daklinza + Sovaldi + low initial dose (titrated) ribavirin (Class I, Level B) for 12 weeks
    - Treatment-naïve with compensated liver disease but are ribavirin ineligible: Harvoni (Class I, Level B) or Daklinza + Sovaldi (Class II, Level C) for 24 weeks
    - Treatment-naïve or –experienced with decompensated cirrhosis: Harvoni + with low initial dose (titrated) ribavirin for 12 weeks (Class I, Level B)

Hepatitis C Agents

AASLD/IDSA HCV Guidelines Recommendation Updates

- The updated AASLD/IDSA hepatitis C guidelines for post-liver transplant:
  - Genotype 2:
    - Treatment-naïve or treatment-experienced (including compensated cirrhosis): Daklinza + Sovaldi + low initial dose ribavirin (titrated) for 12 weeks (Class II, Level A) or Sovaldi + weight-based ribavirin for 24 weeks (Class II, Level C)
      - Ribavirin ineligible patients is Daklinza + Sovaldi for 24 weeks (Class II, Level C)
    - Treatment-naïve with decompensated cirrhosis: Sovaldi + ribavirin (titrated to weight-based dosing) for 24 weeks (Class II, Level C)

Hepatitis C Agents

AASLD/IDSA HCV Guidelines Recommendation Updates

- The updated AASLD/IDSA hepatitis C guidelines for post-liver transplant:
  - Genotype 3:
    - Treatment-naïve or treatment-experienced (including those with compensated cirrhosis): Daklinza + Sovaldi + low initial dose ribavirin (titrated) for 12 weeks (Class II, Level A); Daklinza + Sovaldi for 24 weeks is recommended when the patient is ineligible for ribavirin (Class II, Level C

Testimony

- Pharma
  - Coleen Fong: Gilead: Harvoni
  - Laura Hill: Abbvie: Viekira Pak
  - John Michael Thomas: Bristol Myers Squibb: Daklinza
  - Ryan Racino: Merck: Zepatier
- Public
  - Mark Wong
  - Kim K.

Hypoglycemics, Incretin Mimetics/Enhancers

Hypoglycemics, Incretin Mimetics/Enhancers

Class Overview

- Class consists of three types of agents
  - Amylin Analogue
    - Single entity SC product
    - Slows gastric emptying, suppresses glucagon secretion, and centrally modulates appetite
  - DPP-4 Enzyme Inhibitors
    - Single entity and combination oral products
    - Increases insulin secretion and reduces glucagon secretion by preventing inactivation of GLP-1
  - GLP-1 Receptor Agonists
    - Single entity SC products, once weekly options
    - Enhance glucose-dependent insulin secretion by beta cell, suppress inappropriately elevated glucagon secretion, and slow gastric emptying
- Products should not be used for Type 1 diabetes (except Symlin)

Hypoglycemics, Incretin Mimetics/Enhancers

Indications

Drug	Manufacturer	Indication
Amylin Analogue		
pramlintide (Symlin®)	AstraZeneca	Adjunct therapy in type 1 and type 2 diabetes patients who use mealtime insulin therapy and have failed to achieve desired glucose control despite optimal insulin therapy (with or without concurrent sulfonylurea and/or metformin in type 2 patients)
DPP-4 Enzyme Inhibitors		
alogliptin (Nesina®)	Takeda	Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (T2DM)
alogliptin/metformin (Kazano®)	Takeda	Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (T2DM)
alogliptin/ pioglitazone (Oseni®)	Takeda	Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (T2DM)

Hypoglycemics, Incretin Mimetics/Enhancers

Indications conti.

Drug	Manufacturer	Indication
DPP-4 Enzyme Inhibitors		
linagliptin (Tradjenta®)	Boehringer Ingelheim	Adjunct to diet and exercise to improve glycemic control in adults with T2DM
linagliptin/empagliflozin (Glyxambi®)	Boehringer Ingelheim	Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both empagliflozin and linagliptin is appropriate
linagliptin/metformin (Jentadueto®)	Boehringer Ingelheim	Adjunct to diet and exercise to improve glycemic control in adults with T2DM when treatment with both linagliptin and metformin is appropriate
saxagliptin (Onglyza®)	AstraZeneca	Adjunct to diet and exercise to improve glycemic control in adults with T2DM

Hypoglycemics, Incretin Mimetics/Enhancers

Indications conti.

Drug	Manufacturer	Indication
DPP-4 Enzyme Inhibitors		
saxagliptin/metformin ER (Kombiglyze XR™)	AstraZeneca	Adjunct to diet and exercise to improve glycemic control in adults with T2DM when treatment with both saxagliptin and metformin is appropriate
sitagliptin (Januvia®)	Merck Sharp & Dohme	Adjunct to diet and exercise to improve glycemic control in adults with T2DM; sitagliptin has been studied in combination with metformin, pioglitazone, glimepiride, and metformin with glimepiride
sitagliptin/metformin (Janumet®)	Merck Sharp & Dohme	Adjunct to diet and exercise to improve glycemic control in adults with T2DM when treatment with both agents is appropriate
sitagliptin/metformin ER (Janumet XR®)	Merck Sharp & Dohme	Adjunct to diet and exercise to improve glycemic control in adults with T2DM when treatment with both sitagliptin and metformin ER is appropriate

Hypoglycemics, Incretin Mimetics/Enhancers

Indications conti.

Drug	Manufacturer	Indication
GLP-1 Receptor Agonists		
albiglutide (Tanzeum®)	GlaxoSmithKline	Adjunct to diet and exercise to improve glycemic control in adults with T2DM
dulaglutide (Trulicity®)	Eli Lilly	Adjunct to diet and exercise to improve glycemic control in adults with T2DM
exenatide (Byetta®)	AstraZeneca	Adjunct to diet and exercise to improve glycemic control in adults with T2DM who are taking metformin, a sulfonylurea, thiazolidinedione (TZD), or a combination of metformin and a sulfonylurea or TZD but have not achieved adequate glycemic control Add-on therapy to insulin glargine, with or without metformin and/or a TZD, in conjunction with diet and exercise for adults with type 2 diabetes who are not achieving adequate glycemic control on insulin glargine alone

Hypoglycemics, Incretin Mimetics/Enhancers

Indications conti.

Drug	Manufacturer	Indication
GLP-1 Receptor Agonists		
exenatide ER (Bydureon®)	AstraZeneca	Adjunct to diet and exercise to improve glycemic control in adults with T2DM
liraglutide (Victoza®)	Novo Nordisk	Adjunct to diet and exercise to improve glycemic control in adults with T2DM

Hypoglycemics, Incretin Mimetics/Enhancers

New Product in Class: Glyxambi (linagliptin/empagliflozin)

- Indicated for adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes when treatment with both empagliflozin and linagliptin is appropriate
- Contraindications, warnings, adverse effects, and drug interactions are similar to other hypoglycemic medications such as Jardiance and Tradjenta.
  - SGLT2 component is associated with: a contraindication in patients with severe renal impairment, ESRD, or dialysis; symptomatic hypotension, nasopharyngitis, urinary track infections, ketoacidosis can occur
  - DDP-4 enzyme inhibitors are associated with: severe adverse reactions within the first 3 months of use; pancreatitis; severe/disabling joint pain
- Pregnancy category: C

Hypoglycemics, Incretin Mimetics/Enhancers

New Product in Class: Glyxambi (linagliptin/empagliflozin) conti.

- Dosing: 5 mg/10 mg once daily in the morning; may increase to 5 mg/25 mg once daily without regard to food
- It is available as a 5 mg/10 mg and 5 mg/25 mg fixed-dose combination tablet
- Glyxambi increases urinary glucose excretion by inhibiting SGLT2, the major transporter responsible for the reabsorption of filtered glucose from the kidney
- Associated with a reduction in body weight compared to linagliptin alone

Hypoglycemics, Incretin Mimetics/Enhancers

Glyxambi Clinical Trials

- A double-blind, randomized, active-controlled study compared the safety/efficacy of linagliptin 5 mg with empagliflozin 10 mg or 25 mg to the individual components in 686 patients with type 2 diabetes
- At week 24, the fixed dose linagliptin/empagliflozin combinations provided statistically significant improvements in HbA1c ($p<0.0001$) and FPG ($p<0.001$) compared to individual components
- The combination treatment also resulted in a statistically significant reduction in body weight compared to linagliptin ($p<0.0001$); however, no statistically significant differences in body weight were seen when compared to empagliflozin alone

Hypoglycemics, Incretin Mimetics/Enhancers

Product Updates

- The FDA has issued a warning for DPP-4 inhibitors regarding severe and disabling joint pain

Hypoglycemics, Incretin Mimetics/Enhancers

Guideline Updates

- American Diabetes Association (ADA) updated their Standards of Medical Care in Diabetes in 2016
  - Continue to recommend:
    - Therapy should be based on patient- and drug-related variables
    - Metformin is the preferred first line agent for Type 2 diabetes; if metformin cannot be used, another oral agent could be chosen, such as a sulfonylurea, thiazolidinedione (TZD), or a DPP-4 inhibitor
    - If oral monotherapy at maximal tolerated dose does not achieve or maintain the HbA1c target over 3 months, a second oral agent, a GLP-1 receptor agonist, or insulin should be added
    - HbA1c goals have remained the same (except as listed below)
  - Update:
    - For pediatric patients, the ADA now recommends a target HbA1c of <7.5% for all age-groups, although individualization is still supported

Hypoglycemics, Incretin Mimetics/Enhancers

Guideline Updates

- The American Academy of Clinical Endocrinologists (AACE) and the American College of Endocrinology (ACE) updated their algorithm and practice guidelines for the management of type 2 diabetes in 2016
  - Continue to recommend:
    - HbA1c goals: ≤ 6.5% for healthy patients with low hypoglycemic risk; > 6.5% for patients with concurrent illness and at risk of hypoglycemia
    - Choice of therapy should be based on cost, ease of use, other medications, risk factors, and initial HbA1c
    - HbA1c level drives product selection; metformin is the preferred treatment of choice for monotherapy and first-line agent for dual and triple therapy
  - Update:
    - The guidelines have added SGLT2 inhibitors as a safe choice for monotherapy for patients with a HbA1c < 7.5% at entry along with metformin, a GLP-1 receptor agonist, DPP-4 inhibitor, or alpha-glucosidase inhibitor; TZDs and sulfonylureas should be used with caution

Testimony

- Pharma
  - Michele Jones: Novo Nordisk: Victoza
  - Ralph Gualtieri: Merck: Januvia
  - William O'Neill: Boehringer Ingelheim: Jardiance
- Public
  - None

Hypoglycemics, Insulin and Related Agents

Hypoglycemics, Insulin and Related Agents

Class Overview

- Class consists of six groups
  - Rapid acting insulins
  - Regular (R) insulins
  - Intermediate (N) insulins
  - Long-acting insulins
  - Rapid/Intermediate-acting combination insulins
  - Regular/Intermediate-acting combination insulins

Hypoglycemics, Insulin and Related Agents

Indications

Drug	Manufacturer	Indication
Rapid-Acting Insulins		
human insulin inhalation powder (Afrezza®)	Mankind	To improve glycemic control in adults with type 1 or type 2 diabetes mellitus
insulin aspart (Novolog®)	Novo Nordisk	To improve glycemic control in adults and children with diabetes mellitus
insulin glulisine (Apidra™)	Sanofi-Aventis	To improve glycemic control in adults and children with diabetes mellitus
insulin lispro (Humalog®)	Lilly	For the treatment of patients with diabetes mellitus for the control of hyperglycemia

Hypoglycemics, Insulin and Related Agents

Indications conti.

Drug	Manufacturer	Indication
Regular (R) Insulins		
human insulin (Humulin®)	Lilly	For the treatment of patients with diabetes mellitus for the control of hyperglycemia
human insulin (Novolin®)	Novo Nordisk	For the treatment of patients with diabetes mellitus for the control of hyperglycemia
Intermediate (N) Insulins		
human insulin (Humulin)	Lilly	For the treatment of patients with diabetes mellitus for the control of hyperglycemia
human insulin (Novolin)	Novo Nordisk	For the treatment of patients with diabetes mellitus for the control of hyperglycemia

Hypoglycemics, Insulin and Related Agents

Indications conti.

Drug	Manufacturer	Indication
Long-Acting Insulins		
insulin degludec (Tresiba®)	Novo Nordisk	To improve glycemic control in adults with diabetes mellitus.
insulin detemir (Levemir®)	Novo Nordisk	For once or twice daily subcutaneous administration for the treatment of adult and pediatric patients with type 1 diabetes mellitus or adult patients with type 2 diabetes mellitus who require basal insulin for the control of hyperglycemia
insulin glargine (Lantus®)	Sanofi-Aventis	To improve glycemic control in adults and children with type 1 diabetes mellitus and adults with 2 diabetes mellitus
insulin glargine (Toujeo®)	Sanofi-Aventis	To improve glycemic control in adults with diabetes mellitus

Hypoglycemics, Insulin and Related Agents

Indications conti.

Drug	Manufacturer	Indication
Rapid/Intermediate-Acting Combination Insulins		
insulin aspart (Novolog® Mix)	Novo Nordisk	To improve glycemic control in patients with diabetes mellitus
insulin lispro (Humalog® Mix)	Lilly	For the treatment of patients with diabetes mellitus for the control of hyperglycemia
Regular/Intermediate-Acting Combination Insulins		
human insulin (Humulin)	Lilly	For the treatment of patients with diabetes mellitus for the control of hyperglycemia
human insulin (Novolin)	Novo Nordisk	For the treatment of patients with diabetes mellitus for the control of hyperglycemia

Hypoglycemics, Insulin and Related Agents

New Product in Class: Afrezza (human insulin inhalation powder)

- Indicated to improve glycemic control in adults with type 1 or type 2 diabetes mellitus
- Contraindications, warnings, adverse effects, and drug interactions:
  - Should not be used in patients with chronic lung disease
  - In long-term studies, patients without chronic lung disease experienced a small decline in lung function as measured by FEV_1; long-term pulmonary safety is unknown
  - Lung cancer reported in patients treated with Technosphere® insulin inhalation powder; caution needed in patients with current/previous lung cancer or who are at increased risk for lung cancer
  - In studies with type 1 diabetes patients, more patients using insulin inhalation powder experienced DKA than those receiving comparators (0.43% vs. 0.14%, respectively)
  - Patients may experience cough (26.9%) and throat pain or irritation (4.8%)
  - Must be used with a long-acting insulin in patients with T1DM and should not be used in patients who smoke/have recently stopped smoking (< 6 months ago)

Hypoglycemics, Insulin and Related Agents

New Product in Class: Afrezza (human insulin inhalation powder) conti.

- Pregnancy category: C
- Safety and efficacy has not been established for pediatrics
- Dosing: used at beginning of meals; dosing should be titrated to glycemic control in combination with a long acting insulin; the recommended initial mealtime dose is 4 units; dosing conversions from SC insulins are available in drug package insert
- It is available in cartridges of 4, 8, and 12 units

Hypoglycemics, Insulin and Related Agents

New Product in Class: Afrezza (human insulin inhalation powder) conti.

- Option for patients that have barriers to injectable administration (e.g. visual impairment or neuropathy)
- Insulin inhalation powder is not included in practice guidelines at this time
- Subject to REMS program
- Previous inhaled insulin, Exubera®, was withdrawn from the market due to poor sales; poor sales of Afrezza have caused Sanofi to stop partnership with Mankind in early April 2016

Hypoglycemics, Insulin and Related Agents

Afreeza Clinical Trials

- A 24-week open-label, active-controlled study enrolled patients with inadequately controlled T1DM to evaluate glucose lowering of mealtime insulin inhalation powder used with a basal insulin. Patients (n=344) were randomized 1:1 to insulin inhalation powder or insulin aspart used at each meal of the day. At week 24, treatment with basal insulin plus inhaled insulin provided less HbA1c reduction than insulin aspart (-0.21 vs. -0.4%, respectively), and the difference (-0.19%) was statistically significant (95% CI, 0.02 to 0.36). Mean reduction provided by basal insulin plus inhaled insulin narrowly met the pre-specified non-inferiority margin of 0.4%. A greater proportion of patients in the insulin aspart group achieved a HbA1c target of ≤7% (30.7% vs. 18.3%; p=0.0158).
- A 52-week, open-label trial randomized 618 patients with T2DM who had been receiving SC insulin therapy to a basal/bolus regimen with insulin glargine 100 U/mL plus insulin inhalation powder or to a twice daily regimen with 70/30 biphasic insulin. At Week 52, mean change in HbA1c were -0.59% and -0.71% for insulin glargine/inhaled insulin and biphasic insulin, respectively. Non-inferiority (margin 0.4%) of inhaled insulin plus basal insulin was demonstrated compared to biphasic insulin (difference 0.12%; 95% CI, -0.05 to 0.29). A greater proportion of patients in the biphasic insulin group achieved the HbA1c target ≤7% (26.8% vs. 22.1%, respectively; p=0.28).

Hypoglycemics, Insulin and Related Agents

Afreeza Clinical Trials conti.

- In a 52-week, open-label trial, 539 patients with T1DM were randomized to insulin glargine 100 U/mL (basal) plus either insulin inhalation powder or insulin aspart. This trial did not meet its primary efficacy endpoint of noninferiority margin of 0.4% for insulin inhalation powder compared with insulin aspart. At Week 52, mean change in HbA1c was -0.13% and -0.37% for insulin inhalation powder and insulin aspart, respectively (difference 0.24; 95% CI, 0.08 to 0.404). A similar proportion of patients achieved HbA1c ≤7% in both groups (16.3% vs. 16%, respectively).

Hypoglycemics, Insulin and Related Agents

New Product in Class: Tresiba (insulin degludec)

- Indicated to improve glycemic control in adults with diabetes mellitus
- Contraindications, warnings, adverse effects, and drug interactions are similar to other SC insulin agents; contraindicated during episodes of hypoglycemia
- Safety and efficacy has not been established for pediatrics
- Pregnancy category: C
- Dosing: once daily dosing (separated by at least 8 hours); dosing should be individualized based on diabetes type and whether the patient is insulin-naïve
- It is available as a U-100 (100 U/mL) and U-200 (200 U/mL): 3 mL FlexTouch pen

Hypoglycemics, Insulin and Related Agents

Tresiba Clinical Trials

- The efficacy and safety of insulin degludec used in combination with mealtime insulin aspart for the treatment T1DM were evaluated in an open-label, active-controlled trial. A total of 455 patients with inadequately controlled diabetes were randomized to insulin degludec U-100 or insulin detemir once-daily in the evening (32% of patients ended up having to use insulin detemir dosed twice daily). At week 26, the difference in HbA1c reduction from baseline between insulin degludec and insulin detemir was -0.09% (95% CI, -0.23 to 0.05); non-inferiority was met. At week 26, 41.1% of patients on insulin degludec and 37.3% of those on insulin detemir achieved HbA1c <7%.
- In a 52-week, open-label study, 629 patients with inadequately controlled T1DM were randomized to insulin degludec U-100 once-daily with the evening meal or insulin glargine U-100 once-daily. At week 52, the difference in HbA1c reduction from baseline between insulin degludec and insulin glargine was -0.01% (95% CI, -0.14 to 0.11); non-inferiority was met. At week 52, 39.8% of patients on insulin degludec and 42.7% of those on insulin glargine achieved HbA1c <7%.

Hypoglycemics, Insulin and Related Agents

Tresiba Clinical Trials conti.

- In a 26-week open-label study, 493 patients with inadequately controlled T1DM were randomized to insulin degludec U-100 injected once daily with the main evening meal, insulin degludec injected once daily at any time of day, or insulin glargine dosed once daily in the evening. At week 26, the difference in HbA1c reduction from baseline between insulin degludec administered at the same time and at alternating times, each compared to insulin glargine was 0.16% and 0.17%, respectively; non-inferiority was met.
- An open-label study randomized 1,030 insulin-naïve patients with inadequately controlled T2DM to insulin degludec U-100 once-daily with the evening meal or insulin glargine U-100 once-daily. At week 52, the difference in HbA1c reduction from baseline between insulin degludec and insulin glargine was 0.09% (95% CI, -0.04 to 0.22); non-inferiority was met. At week 52, 51.7% of patients on insulin degludec and 54.1% of those on insulin glargine achieved HbA1c <7%.

Hypoglycemics, Insulin and Related Agents

Tresiba Clinical Trials conti.

- A total of 457 insulin-naïve patients with T2DM were randomized to insulin degludec U-200 once-daily with the evening meal or insulin glargine U-100 once-daily in an open-label study. At week 26, the difference in HbA1c reduction from baseline between insulin degludec and insulin glargine was 0.04% (95% CI, -0.11 to 0.19); non-inferiority was met. At week 26, 52.2% of patients on insulin degludec and 55.9% of those on insulin glargine achieved HbA1c <7%.
- In an open-label study, 435 insulin-naïve patients with T2DM were randomized to insulin degludec U-100 once-daily with the evening meal or insulin glargine U-100 once-daily. At week 26, the difference in HbA1c reduction from baseline between insulin degludec and insulin glargine was 0.11% (95% CI, -0.03 to 0.24). At week 26, 40.8% of patients on insulin degludec and 48.6% of those on insulin glargine achieved HbA1c < 7%; non-inferiority was met.

Hypoglycemics, Insulin and Related Agents

Tresiba Clinical Trials conti.

- In an open-label study, 687 patients with T2DM were randomized to insulin degludec U-100 injected once-daily with the main evening meal, insulin degludec injected once daily at any time each day, or insulin glargine U-100 injected once-daily. At week 26, the difference in HbA1c reduction from baseline between insulin degludec administered at the same time and at alternating times, each compared to insulin glargine was 0.18% and 0.04%, respectively; non-inferiority was met. The proportion of patients who achieved HbA1c <7% were 40.8% for those given insulin degludec dosed at the same time each day, 38.9% for insulin degludec dosed at varying times, and 43.9% for insulin glargine.
- A total of 992 patients with T2DM were randomized to insulin degludec U-100 injected once-daily with the main evening meal, or insulin glargine U-100 injected once-daily. At week 52, the difference in HbA1c reduction from baseline between insulin degludec and insulin glargine was 0.08% (95% CI, -0.05 to 0.21); non-inferiority was met. A similar proportion of patients achieved HbA1c <7% in each group.

Hypoglycemics, Insulin and Related Agents

New Product in Class: Toujeo (insulin glargine)

- Indicated to improve glycemic control in adults with diabetes mellitus
- Contraindications, warnings, adverse effects, and drug interactions are similar to other SC insulin agents
  - The full glucose lowering effect of Toujeo may not be seen for at least 5 days
  - Contraindicated during episodes of hypoglycemia
- Safety and efficacy has not been established for pediatrics (Lantus is approved for use in T1DM children from 6 to 15 years old)
- Pregnancy category: n/a

Hypoglycemics, Insulin and Related Agents

New Product in Class: Toujeo (insulin glargine)

- Dosing: SC once daily anytime during the day, at the same time every day; dosing should be individualized based on the diabetes type and whether the patient is insulin-naïve
  - In clinical studies, the steady state for the 24 hour glucose lowering effect of insulin glargine 300 U/mL was approximately 27% lower than an equivalent dose of insulin glargine 100 U/mL (Lantus). The glucose lowering effect of insulin glargine 300 U/mL increases with subsequent daily use.
- It is available as a 300 U/mL 1.5 mL prefilled SoloStar pen
  - Lantus (also insulin glargine) is available as a 100 U/mL product in a 10 mL vial or 3 mL prefilled SoloStar pen

Hypoglycemics, Insulin and Related Agents

Toujeo Clinical Trials

- In a 26-week open-label study, 546 adults with T1DM were randomized to basal-bolus treatment with insulin glargine 300 U/mL or 100 U/mL administered once daily in the morning or in the evening. At week 26, treatment with insulin glargine 300 U/mL provided a similar reduction in HbA1c as insulin glargine 100 U/mL (-0.4% vs. -0.44%, respectively); pre-specified non-inferiority margin of 0.4% was met. Patients treated with insulin glargine 300 U/mL used 17.5% more basal insulin than patients treated with insulin glargine 100 U/mL.
- In a 26-week open-label study, 804 adults with type 2 diabetes were randomized to a once daily treatment in the evening with insulin glargine 300 U/mL or 100 U/mL. At week 26, insulin glargine 300 U/mL provided a mean reduction in HbA1c that met the pre-specified non-inferiority margin of 0.4% compared to insulin glargine 100 U/mL. Patients treated with insulin glargine 300 U/mL used 11% more basal insulin compared to those treated with insulin glargine 100 U/mL.

Hypoglycemics, Insulin and Related Agents

Toujeo Clinical Trials

- In two 26-week, open-label studies, 1,670 adults with T2DM were randomized to either insulin glargine 300 U/mL or 100 U/mL once daily in combination with non-insulin anti-diabetic drugs. At week 26, treatment with insulin glargine 300 U/mL provided a mean reduction in HbA1c that met the pre-specified non-inferiority margin of 0.4% compared to insulin glargine 100 U/mL. Patients treated with insulin glargine 300 U/mL used 12% to 15% more basal insulin than patients treated with insulin glargine 100 U/mL.

Hypoglycemics, Insulin and Related Agents

Product Updates

- Humalog is now available in a U-200 (200 units/mL): 3 mL prefilled KwikPen; should not be used intravenously
- The NovoPen Echo®, has replaced the NovoPen® Junior; NovoPen Echo provides half-unit dosing and a memory function; NovoPen Echo should only be used with Novo Nordisk insulin cartridges

Hypoglycemics, Insulin and Related Agents

Guideline Updates

- American Diabetes Association (ADA) updated their Standards of Medical Care in Diabetes in 2016
  - Continue to recommend:
    - Therapy should be based on patient- and drug-related variables
    - Metformin is the preferred first line agent for Type 2 diabetes; if metformin cannot be used, another oral agent could be chosen, such as a sulfonylurea, thiazolidinedione (TZD), or a DPP-4 inhibitor
    - If oral monotherapy at maximal tolerated dose does not achieve or maintain the HbA1c target over 3 months, a second oral agent, a GLP-1 receptor agonist, or insulin should be added
    - HbA1c goals have remained the same (except as listed below)
  - Update:
    - For pediatric patients, the ADA now recommends a target HbA1c of <7.5% for all age-groups, although individualization is still supported

Hypoglycemics, Insulin and Related Agents

Guideline Updates

- The American Academy of Clinical Endocrinologists (AACE) and the American College of Endocrinology (ACE) updated their algorithm and practice guidelines for the management of type 2 diabetes in 2016
  - Continue to recommend:
    - HbA1c goals: ≤ 6.5% for healthy patients with low hypoglycemic risk; > 6.5% for patients with concurrent illness and at risk of hypoglycemia
    - Choice of therapy should be based on cost, ease of use, other medications, risk factors, and initial HbA1c
    - HbA1c level drives product selection; metformin is the preferred treatment of choice for monotherapy and first-line agent for dual and triple therapy
  - Update:
    - The guidelines have added SGLT2 inhibitors as a safe choice for monotherapy for patients with a HbA1c < 7.5% at entry

Testimony

- Pharma
  - Michele Jones: Novo Nordisk: Tresiba, Levemir, Novolog (up to 9 minutes)
  - Nana Numapau: Sanofi: Toujeo
- Public
  - None

COPD Agents

COPD Agents

Class Overview

- The COPD Agent drug class includes:
  - Single agent products:
    - Aclidinium bromide
    - Glycopyrrolate
    - Ipratropium
    - Roflumilast
    - Tiotropium
    - Umeclidinium
  - Combination products:
    - Albuterol/ipratropium
    - Indacaterol/glycopyrrolate
    - Tiotropium/olodaterol
    - Umeclidinium/vilanterol

COPD Agents

Indications

Drug	Manufacturer	Indication
aclidinium bromide inhalation powder (Tudorza® Pressair®)	AstraZeneca	For the long-term, maintenance treatment of bronchospasm associated with COPD, including chronic bronchitis and emphysema
albuterol/ipratropium inhalation solution	generic	For the treatment of bronchospasm associated with COPD in patients requiring more than 1 bronchodilator
albuterol/ipratropium MDI CFC-free (Combivent® Respimat®)	Boehringer-Ingelheim	For use in patients with COPD on a regular aerosol bronchodilator who continue to have evidence of bronchospasm and require a second bronchodilator
glycopyrrolate (Seebri™ Neohaler®)	Novartis	For the long-term, maintenance treatment of airflow obstruction in patients with COPD
indacaterol/glycopyrrolate (Utibron™ Neohaler®)	Novartis	For the long-term, maintenance treatment of airflow obstruction in patients with COPD
ipratropium inhalation solution	generic	For maintenance treatment of bronchospasm associated with COPD, including chronic bronchitis and emphysema
ipratropium inhalation aerosol MDI (Atrovent® HFA)	Boehringer-Ingelheim	As a bronchodilator for maintenance treatment of bronchospasm associated with COPD, including chronic bronchitis and emphysema

COPD Agents

Indications conti.

Drug	Manufacturer	Indication
roflumilast (Daliresp®)	AstraZeneca	As a treatment to reduce the risk of COPD exacerbations in patients with severe COPD associated with chronic bronchitis and a history of exacerbations
tiotropium inhalation powder DPI (Spiriva HandiHaler®)	Boehringer-Ingelheim	For the long-term, once-daily maintenance treatment of bronchospasm associated with COPD, including chronic bronchitis and emphysema; to reduce COPD exacerbations
tiotropium bromide inhalation spray (Spiriva® Respimat®)	Boehringer-Ingelheim	For the long-term, once-daily, maintenance treatment of bronchospasm associated with COPD and for reducing COPD exacerbations; for the long-term, once-daily, maintenance treatment of asthma in patients ≥ 12 years old
tiotropium/olodaterol (Stiolto™ Respimat®)	Boehringer-Ingelheim	For treatment of airflow obstruction in patients with COPD
umeclidinium inhalation powder (Incruse® Ellipta®)	GlaxoSmithKline	For the long-term, once-daily, maintenance treatment of airflow obstruction in COPD patients
umeclidinium/vilanterol inhalation powder DPI (Anoro® Ellipta®)	GlaxoSmithKline	For the long-term, once-daily maintenance treatment of airflow obstruction in patients with COPD, including chronic bronchitis and/or emphysema

COPD Agents

New Product in Class: Seebri Neohaler (glycopyrrolate)

- Indicated for the long-term, maintenance treatment of airflow obstruction in patients with COPD; not indicated for acute treatment
- Contraindications, warnings, adverse effects, and drug interactions are similar to other inhaled anticholinergics
- Safety and efficacy has not been established for pediatrics like other agents indicated for COPD
- Pregnancy category: C
  - Ipratropium is the only Category B agent in the class
- Dosing: 1 inhalation twice daily
- It is available as a breath activated device delivering 15.6 mcg per actuation

COPD Agents

New Product in Class: Utibron™ Neohaler® (indacaterol/glycopyrrolate)

- Indicated for long-term, maintenance treatment of airflow obstruction in patients with COPD; not indicated for acute therapy
- Contraindications, warnings, adverse effects, and drug interactions are similar to other inhaled LABA/anticholinergics; Other noteworthy items for medication include:
  - Boxed warning in patients with asthma without use of a long-term asthma control medication due to the risk of asthma related death
  - Use cautiously with dual inhibitors of CYP and P-glycoprotein
  - Hypertension reported as adverse reaction
- Safety and efficacy has not been established for pediatrics as with other medications in class to treat COPD
- Pregnancy category: C
  - Ipratropium only medication in with Category B
- Dosing: 1 inhalation twice daily
- It is available as a breath activated device delivering 27.5/15.6 mcg per actuation

COPD Agents

Utibron Neohaler Clinical Trials

- The safety and efficacy of indacaterol/glycopyrrolate were evaluated in 2 placebo-controlled confirmatory trials and a 12-month long-term safety trial in COPD patients (n=615). The primary endpoint of the 12-week, randomized, double-blind, placebo- and active-controlled, parallel group confirmatory trials was the least squares mean change from baseline in FEV_1 $AUC_{(0\text{-}12h)}$. The combination therapy of indacaterol/glycopyrrolate demonstrated a larger increase in mean change from baseline in FEV_1 $AUC_{(0\text{-}12h)}$ versus placebo. The combination therapy of indacaterol/glycopyrrolate demonstrated a larger increase in mean change from baseline in FEV_1 $AUC_{(0\text{-}12h)}$ versus indacaterol and glycopyrrolate. In Trial 1, improvement in SGRQ (St. George Respiratory Questionnaire) score was higher with indacaterol/glycopyrrolate than with comparators: glycopyrrolate, indacaterol, and placebo. In Trial 2, the SGRQ responder rate was 57%, 46%, 48%, and 39%, for indacaterol/glycopyrrolate, glycopyrrolate, indacaterol, and placebo, respectively.

COPD Agents

New Product in Class: Stiolto™ Respimat® (tiotropium/olodaterol)

- Indicated for treatment of airflow obstruction in patients with COPD; not indicated for acute therapy
- Contraindications, warnings, adverse effects, and drug interactions are similar to other inhaled LABA/anticholinergics; other notable items for medication include:
  - Boxed warning in patients with asthma without use of a long-term asthma control medication due to the risk of asthma related death
  - Use cautiously with dual inhibitors of CYP and P-glycoprotein
  - Patients with renal impairment should be monitored
- Safety/efficacy has not been established for pediatrics as with other drugs in class for COPD
- Pregnancy category: C
  - Ipratropium Category B
- Dosing: 2 inhalations once daily
- It is available as 2.5/2.5 mcg per actuation

COPD Agents

Stiolto Respimat Clinical Trials

- The efficacy of Stiolto Respimat is based on two 4-week dose-ranging trials (n=592) and 2 multicenter, phase 3, replicate, randomized, 52-week, double-blind active-controlled trials (n=5,162) in patients with COPD. The primary endpoint, FEV_1 $AUC_{(0\text{-}3h)}$ at 24 weeks, was 241, 256, 139, and 133 mL in the tiotropium/olodaterol 2.5/5 mcg, tiotropium/olodaterol 5/5 mcg, tiotropium 2.5 mcg, tiotropium 5 mcg, and olodaterol 5 mcg groups, respectively ($p<0.0001$ for tiotropium/olodaterol 5/5 mcg compared single components). Significant differences between the 5/5 mcg fixed combination and the individual components were also seen in the SGRQ score at 24 weeks ($p<0.05$).

COPD Agents

Product Updates

- Spiriva® Respimat® now is indicated for the long-term, once-daily, maintenance treatment of asthma patients ≥ 12 years old
  - Dose: 2 inhalations of 1.25 mcg/actuation once daily
    - Maximum benefits may take up to 4 to 8 weeks
  - Availability:1.25 and 2.5 mcg tiotropium per actuation
- Tudorza Pressair has included a warning about hypersensitivity to atropine or milk proteins.

COPD Agents

Spiriva Respimat Clinical Trials for Asthma

Efficacy of tiotropium bromide inhalation spray is based on 5 randomized, double-blind, placebo-controlled confirmatory trials in non-smoking adults (n=3,476) and 2 trials in adolescents aged 12 to 17 years. All trials included inhaled corticosteroid background therapy (additional asthma treatments were also allowed) and rescue therapy.

- Trial 1: compared once daily tiotropium 2.5 mcg, tiotropium 5 mcg, and placebo (n=309). After 12 weeks, the mean difference in peak and trough FEV_1 of 2.5 mcg compared to placebo were 0.16 L and 0.11 L, respectively, 95% CI. The FEV_1 improvement in the 5 mcg group was generally lower than improvement in the 2.5 mcg.
- Trials 2 (n=524) and 3 (n=509) compared tiotropium 2.5 mcg once daily, tiotropium 5 mcg once daily, salmeterol 50 mcg twice daily, and placebo. The primary outcomes were peak FEV_1 and trough FEV_1 at Week 24. Peak FEV_1 and trough FEV_1 responses were greater with both tiotropium doses and salmeterol compared to placebo in the pooled analysis, $p<0.0001$. Seven-question Asthma Control Questionnaire (ACQ-7) response was higher with all 3 active treatments compared to placebo, $p<0.0039$.

COPD Agents

Clinical Trial Updates

Anoro Ellipta versus Advair trial

- Two 12-week, multicenter, double-blind, parallel-group, double-dummy, randomized trials compared the efficacy of Anoro Ellipta to Advair in patients (n=1,403) with moderate to severe COPD. Patients with infrequent exacerbations were randomized 1:1 to once-daily Anoro Ellipta 62.5/25 mcg or twice-daily Advair 250/50 mcg. Anoro Ellipta demonstrated significant improvement in lung function compared to Advair, $p<0.001$. Trough FEV_1 values were also superior with Anoro Ellipta in both trials; however, no difference was seen between groups in dyspnea ratings or SGRQ improvement.

COPD Agents

Meta Analysis Updates

- A meta-analysis of 27 randomized controlled trials assessed efficacy of long-acting anticholinergics (e.g., tiotropium, aclidinium, or glycopyrronium [comparable to glycopyrrolate]) in 48,140 patients with COPD. All products were superior to placebo in number of moderate-to-severe asthma exacerbations but no differences were found between agents. A similar meta-analysis of 24 trials (n=21,311) included the above agents in addition to umeclidinium. Compared to placebo, aclidinium, glycopyrronium, tiotropium, and umeclidinium demonstrated a change in 24-week trough $FEV_{1,}$ SGRQ improvement, and rescue medication use. No significant differences were found between agents.
- A meta-analysis of 27 trials (n=30,361) comparing efficacy of fixed-dose combinations of LABAs and long-acting anticholinergic agents (e.g., aclidinium/formoterol, glycopyrronium/indacaterol, tiotropium/olodaterol, and umeclidinium/vilanterol) found that all agents have similar efficacy (aclidinium and glycopyrronium products are not available in the U.S.).

COPD Agents

Guideline Updates

- Updated 2015 Global Initiative for Asthma (GINA) guidelines state that the assessment of asthma control should include control of the manifestations and expected future risk to the patient. GINA classifies asthma in 3 levels of control and provides a 5-step treatment approach. Tiotropium inhalation spray was added in this edition of the guidelines as an add-on option for Steps 4 and 5 in patients ≥ 18 years with exacerbation history.
- In 2016 GOLD guidelines were also updated; treatment is based on patient risk/symptoms group categories; guidelines do not recommend one product over another within drug class; 2016 GOLD update did not contain any significant changes to recommendations for drug therapy.

Testimony

- Pharma
  - William O'Neill (Boehringer Ingelheim) Spiriva, Stiolto (up to 6 minutes)
- Public
  - None

Executive Session

Drug Class Recommendations

Recommendations: Opioid Dependence Treatment

BH Drug List Recommendations (preferred products):

- Naloxone vial and syringe (solution for injection)
- Naloxone nasal spray (Narcan)
- Naltrexone oral (ReVia)
- Naltrexone ER injectable suspension (Vivitrol)
  - Recommend remove PA
- Buprenorphine/naloxone sublingual film (Suboxone)
  - Remove PA
  - No grandfathering

AHCCCS Drug List (preferred products):

- Naloxone vial and syringe (solution for injection)
- Naloxone nasal spray (Narcan)

Recommendations: Hepatitis C Agents

PDL Recommendations (preferred products):

- Peg-Intron
- Pegasys Vial, ProClick, Syringe
- Ribavirin tablet and capsule
- Zepatier
- Technivie
- Viekira
- Daklinza
- Harvoni (currently preferred)
- Sovaldi (currently preferred)

Recommendations: Hypoglycemics, Incretin Mimetics/Enhancers

PDL Recommendations (preferred products):

- Janumet
- Janumet XR
- Januvia
- Jentadueto
- Tradjenta
- Byetta Pens
- Symlin Pens
- Victoza

Grandfathering: Yes for all except Bydureon Pen

Recommendations: Hypoglycemics, Insulin and Related Agents

PDL Recommendations (preferred products):

- Humalog vial and pen
- Humalog mix vial and pen
- Humulin 70/30 vial
- Humulin vial
- Humulin 500 U/M vial and pen
- Levemir vial and pen
- Lantus Solostar Pen
- Lantus vial

Grandfathering: No

Recommendations: COPD Agents

PDL Recommendations (preferred products):

- Ipratropium inhalation solution
- Ipratropium/albuterol inhalation solution
- Spiriva
- Atrovent HFA
- Combivent Respimat

No Grandfathering

Oral oncology agents: Follow-up from 2-17-16 P&T

Suzi Berman RPh

Oral Oncology Agents

- Follow-up from 2-17-16 P&T
  - Recommendation to form P&T Subcommittee to review oral oncology agents
- AHCCCS review
  - Currently, a total of 68 oral oncology agents commercially available managed through pharmacy benefit
    - 34 listed on AHCCCS Drug List
    - 34 not listed

Oral Oncology Agents

- AHCCCS recommendation:
  - As oral oncology agents highly specialized for oncologic condition, recommend taking the approach with this specific class of adding all new oral agents with PA after formal new drug review
- Committee Discussion
- Committee Vote

New Drug Reviews

Suzi Berman RPh
AHCCCS

New Product Reviews

- Alecensa - Alectinib
- Cotellic - Cobimetinib Fumarate
- Ninlaro - Ixazomib Citrate
- Tagrisso - Osimertinib Mesylate
- Aristada - Aripiprazole Lauroxil
- Belbuca - Buprenorphine

New Product Reviews cont'd

- Dyanavel XR - Amphetamine
- Genvoya - Cobicistat, Elvitegravir, Emtricitabine & Tenofovir
- Invega Trinza - Paliperidone Palmitate
- Keveyis - Dichlorphenamide
- Quillichew ER - Methylphenidate ER
- Uptravi – Selexipag
- Rexulti - Brexpiprazole

Alecensa (Alectinib)

- A tyrosine kinase receptor inhibitor that blocks the activity of anaplastic lymphoma kinase (ALK) and is used to treat non-small cell lung cancer (NSCLC)
- Indicated for treatment of metastatic NSCLC in patients who test positive for the abnormal ALK gene.
- Dosage: 4-150mg capsules orally twice daily
- Black Box Warnings – None
- Placebo controlled studies were not completed
- Pre-clinical studies have shown superiority of Alecensa over Xalkori (crizotinib) in animals.

Alecensa (Alectinib)

- Head-to-head studies in Japan were stopped for meeting its head to head comparison with Alecensa. Outcome data was not available prior to this meeting but preliminary results indicate progression free survival was greater with Alecensa.
- Adverse reactions reported in ≥ 10% of the participants:
  - Liver toxicity, Interstitial Lung Disease, Bradycardia,
  - Myalgia, Creatinine Elevation, Fetal Toxicity
- Recommendation is to add Alecensa to the AHCCCS Drug List with prior authorization.
- Committee Discussion

Cotellic (Cobimetinib)

- A selective inhibitor of mitogen activated protein kinase (MEK inhibitor) indicated for unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, in combination with Zelboraf (vemurafenib).
- Approximately 50% of all melanomas contain BRAF mutations.
- Dosage: 60mg orally daily for 21 days of each 28 day cycle.
- Black Box Warnings – None
- Studies were completed with Cotellic or placebo both in combination with Zelboraf.

Cotellic (Cobimetinib) cont'd

- Primary study endpoint was the measurement of progression free survival:
  - 9.9 months with Cotellic vs. 6.2 months of placebo
- Adverse reactions reported in $\geq$ 20% of the participants:
  - Diarrhea, Photosensitivity reaction
  - Fever, Nausea & Vomiting
- Recommendation is to add Cotellic to the AHCCCS Drug List with prior authorization.
- Committee Discussion

Ninlaro (Ixazomib)

- A protease inhibitor indicated in combination with Revlimid (lenalidomide) and dexamethasone for the treatment of multiple myeloma in patients who have received atleast one prior chemotherapy.
- Dosage: 4mg orally day 1, 8 & 15 of a 28-day cycle. 2.3 & 3mg available for dose reductions.
- Black Box Warning – None
- Phase III randomized placebo controlled, double blinded study with the primary end point of progression free survival (PFS).

Ninlaro (Ixazomib) cont'd

- Study results: Progression Free Survival rate of Ninlaro 20.9 months vs. 14.7 months for placebo. Improved PFS across all subgroups.
- Adverse reactions reported by 20% of the participants:
  - Peripheral edema and neuropathy
  - Skin rash
  - Nausea & vomiting
  - Constipation & diarrhea
  - Eye diseases
  - Blood dyscrasias (low red and white blood counts)

Ninlaro (Ixazomib) cont'd

- Recommendation is to add Ninlaro to the AHCCCS Drug List with prior authorization.
- Committee Discussion

Tagrisso (Osimertinib Mesylate)

- A tyrosine kinase inhibitor used to treat metastatic epidermal growth factor receptor (EGFR) T790M mutation positive, non-small cell lung cancer (NSCLC) patients, detected by an FDA approved test
- Prevalence: 10-15% of all NSCLC patients
- Dosage: 1-80mg tablet daily
- Black Box Warnings – None
- Placebo controlled and head to head studies were not completed.

Tagrisso (Osimertinib Mesylate)

- Clinical trials were completed with patients that were positive for the EGFR mutation who had developed resistance to prior treatment.
- Objective Response Rate: 59%
- Adverse reactions reported in ≥ 10% of the participants:
  - Diarrhea 42%, Rash 41%, dry skin 31%,
  - Nail toxicity 25%, eye disorders 18%, nausea 17%
  - Decreased appetite 16%, constipation 15%,
  - Pruritus 14%, cough 14%, fatigue 14%
  - Back pain 13%, stomatitis 12%

Tagrisso (Osimertinib Mesylate)

- Recommendation is to add Tagrisso to the AHCCCS Drug List with prior authorization.
- Committee Discussion

Aristada (Aripiprazole Lauroxil)

- A prodrug, precursor of aripiprazole, indicated to treat schizophrenia.
- Black Box Warning: Increased mortality in elderly patients with dementia-related psychosis
- Dosage Form- 441-882mg IM injection given after tolerability of the oral aripiprazole for 2 weeks. Oral dose of aripiprazole must be given daily for 21 days post injection for the first month.
- Half-life: Aristada 441,662 & 882 mg: 29.2 to 34.9 days
  Abilify Maintena 300mg: 29.9 days
  Abilify Maintena 400mg: 46.5 days

Aristada (Aripiprazole Lauroxil)

- Placebo controlled study efficacy was measured by a reduction in the PANSS score:
  - 441mg - Mean Baseline 92.9 mean change -20.9
  - 882mg - Mean Baseline 92.0 mean change -21.8
  - Placebo - Mean Baseline 93.9 mean change -9.8
- Head to head studies were not done.
- Adverse reactions reported in $\geq$ 10% of the participants:
  - Akathesia, Decreased HDL cholesterol, weight gain
  - Increased serum cholesterol & triglycerides

Aristada (Aripiprazole Lauroxil)

- Recommendation is to not add Aristada to the AHCCCS Drug List or the Behavioral Health Drug List and review the long-acting injectable atypical antipsychotics as a supplemental rebate therapeutic class after July 1st.

- Aristada is available through the prior authorization process.

- Committee Discussion

Belbuca (Buprenorphine)

- A partial mu-opioid agonist and kappa-opioid antagonist indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.
- Black Box Warning: Potential for addiction, abuse, and misuse: life-threatening respiratory depression; accidental exposure to children and neonatal opioid withdrawal syndrome.
- Dosage Form:. Buccal Film: 75 mcg, 150 mcg, 300 mcg, 450 mcg, 600 mcg, 750 mcg, and 900 mcg given inside the lining of the cheek every 12-24 hours.

Belbuca (Buprenorphine)

- Dosage titrated to the morphine sulfate equivalent dose of the prior long acting medication.
- The efficacy of Belbuca was evaluated in three 12-week double-blind, placebo-controlled trials for moderate-to-severe chronic low back pain using pain scores as the primary efficacy endpoints.
- Two of the studies demonstrated efficacy in patients with low back pain.
- The third study did not show a statistically significant pain reduction for study participants using Belbuca as compared to placebo.

Belbuca (Buprenorphine)

- Adverse reactions reported in ≥ 10% of the participants:
  - Constipation
  - Nausea
- Recommendation is to not add Belbuca to the AHCCCS Drug List because there are many other long-acting agents available that are more cost-effective.
- Belbuca is available through the prior authorization process.
- Committee Discussion

Dyanavel XR (Amphetamine)

- A long-acting stimulant indicated for the treatment of ADHD in children 6 years of age and older.
- Black Box Warning for potential abuse and dependence
- Dosage: Suspension (2.5mg/ml) given orally once daily
- Clinical trials- very limited number of participants (108)
  - The clinical trial began as 5-week open label study transitioned to a double-blinded 1-week classroom study comparing Dyanavel XR to placebo. Efficacy was evaluated by teachers and others and results were considered statistically significant to placebo.

Dyanavel XR (Amphetamine)

- Adverse reactions reported ≥ 10%, per the company, are similar to other long-acting amphetamines:
  - Increased blood pressure, Headache, Insomnia
  - Abdominal pain, Decreased appetite, Dry mouth
- Recommendation is to not add Dyanavel XR to the AHCCCS Drug List or the Behavioral Health Drug List because there are other more cost effective stimulants available on these drug lists.
- Dyanavel XR is available through the prior authorization process.
- Committee Discussion

Genvoya - (Cobicistat, Elvitegravir, Emtricitabine & Tenofovir)

- A combination 4 drugs indicated as a complete regimen for HIV-1 infection in persons 12 years of age and older who have no antiretroviral treatment history or to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA <50 copies/ml) on a stable antiretroviral for at least 6 months with no history of treatment failure and no known substitutions associated with resistance to the individual agents of the drugs below:
  - Cobicistat – CCR5 Antagonist
  - Elvitegravir – Integrase Inhibitor
  - Emtricitabine - Nucleoside Reverse Transcriptase Inhibitor
  - Tenofovir - Nucleotide Reverse Transcriptase Inhibitor

Genvoya - (Cobicistat, Elvitegravir, Emtricitabine & Tenofovir)

- Genvoya was developed to maintain the high virologic suppression rate seen with Stribild while minimizing the renal and bone effects.
- Black Box Warnings:
  - Lactic acidosis/severe hepatomegaly with steatosis
  - Post treatment acute exacerbation of Hepatitis B – Test patients for Hep B infection prior to treatment
- Dosage: 1 tablet orally daily with food.
- Not recommended for patients with renal or severe hepatic impairment.

Genvoya - (Cobicistat, Elvitegravir, Emtricitabine, Tenofovir)

- Clinical trials: Highest rates of disease suppression reported in treatment-naïve patients for 48-week studies: 92-93% of participants.
- Recommendation is to add Genvoya to the AHCCCS Drug List with prior authorization.
- Committee Discussion

Invega Trinza (Paliperidone Palmitate)

- An atypical antipsychotic, long-acting injectable indicated for the treatment of schizophrenia after a patient has tolerated treatment with Invega Sustenna® for at least four months.
- Dosage: IM injection lasting 3-months.
- Black Box Class Warnings: Increased mortality in elderly patients with dementia-related psychosis.
- The efficacy for treatment was evaluated in a head-to-head study comparing Trinza to monthly injections of Invega Sustenna (paliperidone palmitate). The results were evaluated on the time to relapse.

Invega Trinza (Paliperidone Palmitate)

- The results of the trial: Invega Trinza was non-inferior to Invega Sustenna.
- Adverse reactions reported in ≥ 10% of study participants
  - Injection site reaction
  - Weight increase
  - Headache
  - Upper respiratory tract infection
  - Agitation/Restlessness, and
  - Parkinsonism
- Minimal adverse reactions; patients in the trial previously tolerated the 4-month trial use of Sustenna.

Invega Trinza (Paliperidone Palmitate)

- Recommendation is to not add Invega Trinza to the AHCCCS Drug List or the Behavioral Health Drug List and review the long-acting injectable atypical antipsychotics as a supplemental rebate therapeutic class after July 1st.
- Invega Trinza is available through the prior authorization process.
- Committee Discussion

Keveyis (Dichlorphenamide)

- A carbonic anhydrase inhibitor diuretic indicated for the treatment of primary hyperkalemic periodic paralysis (HYP), primary hypokalemic periodic paralysis (HOP), and related variants. These are disorders, usually inherited, that cause episodes of muscle weakness and paralysis.
- Dosage Form: 50mg tablet orally twice daily.
- Black Box Warnings: None
- Two double blinded trials were completed over 9 weeks. Patients had less attacks with Keveyis vs. Placebo
  0.3 for Keveyis vs. 2.4 for placebo for HOP
  0.9 for Keveyis vs. 4.8 for placebo for HYP

Keveyis (Dichlorphenamide)

- Adverse reactions reported in ≥ 10% of study participants.
  - Parathesias
  - Cognitive Disorders, Confused State, Rash
  - Foul, salty, rancid, or metallic taste/mouth sensations
- Recommendation is to add this drug to the AHCCCS Drug List with prior authorization because it is the only FDA approved product to treat this potassium related periodic paralysis disorder. No other proven treatments are available.
- Committee Discussion

Quillichew ER (Methylphenidate)

- A stimulant indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD).
- Dosage Form: Extended-release chewable tablet given once daily.
- Black Box Warning for high potential for abuse and dependence.
- Clinical trials- very limited number of participants (90). The clinical trial began as 6-week open label study and transitioned to a double-blinded 1-week classroom study comparing Quillichew ER to placebo. Efficacy was evaluated by teachers and others and results were considered statistically significant and superior to placebo.

Quillichew ER (Methylphenidate)

- Adverse reactions reported in ≥ 10% of study participants- same as for methylphenidate:
  - Headache, Insomnia, Irritability,
  - Decreased Appetite, Nausea, Dry Mouth
- Recommendation is to not add Quillichew ER to the AHCCCS Drug List or the Behavioral Health Drug List because there are other methylphenidate products on both drug lists that are more cost effective.
- Committee Discussion

Uptravi (Selexipag)

- Indicated and is the only approved oral selective IP receptor agonist targeting the prostacyclin pathway in Pulmonary Arterial Hypertension (PAH)
- Maximum Dose: 1600mcg twice daily. 200mcg, 400mcg, 600mcg, 800mcg, 1000mcg, 1200mcg, 1400mcg & 1600mg are also available if 1600mcg twice daily is not tolerated.
- Black Box Warnings: None
- Clinical Trials

Uptravi (Selexipag)

- Approximately 1200 patients were randomized to Uptravi or placebo 80% of the patients were on other PH medications and 20% were not on other therapies.
- The trial endpoints were based on hospitalization for worsening of PAH, disease progression, death from any cause, and the need for lung transplantation or atrial ballooning.
- These primary endpoints showed a 40% reduction in the primary endpoints mainly for hospitalizations and disease progression. The trial concluded at 36 months after 331 events.

Uptravi (Selexipag)

- Adverse reactions reported in ≥ 10% of study participants
  - Headache 65%
  - Nausea 33%
  - Vomiting 18%
  - Myalgia 16%
  - Skin Rash 11%
  - Diarrhea 42%
  - Jaw Pain 26%
  - Limb Pain 17%
  - Flushing 12%
- Recommendation is to not add this drug to the AHCCCS Drug List, there are several options to treat PAH that are more cost effective.
- Uptravi is available through the prior authorization process
- Committee Discussion

Rexulti (Brexpiprazole)

- An atypical antipsychotic indicated for schizophrenia and adjunctive therapy to major depressive disorder.
- Dosage Form: 1 tablet daily available in multiple doses, 0.25mg – 4mg
  - Adjustments made for hepatic & renal impairment
- Black Box Warnings:
  - Increased mortality in elderly patients with dementia-related psychosis, and
  - Antidepressants increase the risk of suicidal thoughts in patients 24 years and younger

Rexulti (Brexpiprazole)

- Mechanism of action is unknown.
- Clinical Trials – Placebo Double Blinded Studies
  - Results based on the PANSS score reduction
  - Average PANSS Baseline: 95+
  - 6.5 Average PANSS point reduction when comparing Rexulti to Placebo
  - Incremental Improvement
- Adverse reactions reported in ≥ 10% of study participants
  - Akathisia
  - Increased Triglycerides
  - Weight gain

Rexulti (Brexpiprazole)

- Comparing the studies of Abilify to the studies of Rexulti, the reduction in the PANSS scores for Abilify was greater, indicating Abilify as a more efficacious drug.
- Recommendation is to not add Rexulti to the AHCCCS Drug List or the Behavioral Health Drug List.
- Rexulti is available through the prior authorization process.
- Committee Discussion

Biologic Update

- Glatopa
  - Biosimilar for Copaxone (Glatiramer Acetate)
  - AHCCCS Medical Policy Manual: 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.
  - AHCCCS and its Contractors shall continue to cover only the brand name Copaxone because it is more cost effective than Glatopa.

P&T Operational Policy

- Suggested Revisions

August P&T Agenda Items

Next Meeting Scheduled for August 16, 2016