AHCCCS
Arizona Health Care Cost Containment System

AHCCCS Pharmacy and Therapeutics Committee

April 13, 2017

Introductions & Minutes Approval

- January 25, 2017 Meeting Minutes
- Review & Vote

Magellan Class Reviews

Therapeutic Classes

- Opioid Dependent Treatment
- Hypoglycemics – Incretin Mimetics/ Enhancers
- Hypoglycemics – Insulin & Related Agents
- COPD Agents

Opioid Dependent Treatment

Sarah Martinez, PharmD

Opioid Dependence Treatment

Class Overview

- Single agent products:
  - Buprenorphine sublingual tablets
  - Naltrexone
    - Tablets (ReVia)
    - Extended-release injectable suspension (Vivitrol)
  - Naloxone (Evzio, Narcan) – Emergency

Opioid Dependence Treatment

Class Overview

- Buprenorphine/naloxone:
  - Buccal film (Bunavail)
  - Sublingual film (Suboxone)
  - Sublingual tablets (generic, Zubsolv)

Opioid Dependence Treatments

Product/Class Updates:

- Zubsolv is now available at a lower dose, 0.7 mg/0.18 mg

Opioid Dependence Treatments

Product/Class Updates:

- American College of Physicians - Paper on prevention and treatment of substance use disorders involving illicit and prescription drugs. Key recommendations include expansion of access to naloxone and medication-assisted treatment for opioid use disorders, establishment of a national prescription drug monitoring program and use of evidence-based guidelines for pain management

Hypoglycemics, Incretin Mimetics/Enhancers

Sarah Martinez, PharmD

Hypoglycemics, Incretin Mimetics/Enhancers

Class Overview

- Class consists of three types of agents:
  - Amylin Analogue (Symlin)
    - Slows gastric emptying, suppresses glucagon secretion, and centrally modulates appetite
    - May also be used for type 1 diabetes

Hypoglycemics, Incretin Mimetics/Enhancers

Class Overview

- Class consists of three types of agents:
  - DPP-4 Enzyme Inhibitors
    - Single entity and combination oral products (e.g. sitagliptin (Januvia), sitagliptin/metformin (Janumet)
    - Increases insulin secretion and reduces glucagon secretion by preventing inactivation of GLP-1

Hypoglycemics, Incretin Mimetics/Enhancers

Class Overview

- Class consists of three types of agents:
  - GLP-1 Receptor Agonists
    - Single entity (e.g. Byetta) and new combination products (e.g. Xultophy)
    - Enhance glucose-dependent insulin secretion by beta cell, suppress inappropriately elevated glucagon secretion, and slow gastric emptying

Hypoglycemics, Incretin Mimetics/Enhancers

Class Overview

- Type 2 Diabetes Guidelines:
  - Metformin is recommended as first line
    - DPP-4 or GLP-1 receptor be added or used instead
  - Symlin should only be considered in patients who have failed to achieve adequate glycemic control with insulin

Hypoglycemics, Incretin Mimetics/Enhancers

New Product : Xultophy (insulin degludec/liraglutide)

- Indicated as adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes inadequately controlled with basal insulin or Victoza (liraglutide).
- Black box warning, contraindications, warnings, adverse effects, and drug interactions are similar to those for Victoza and insulin degludec.

Hypoglycemics, Incretin Mimetics/Enhancers

New Product : Xultophy (insulin degludec/liraglutide)

- Given subcutaneously once daily and comes in a 3 mL prefilled pen (100 U, 3.6 mg/mL)

Hypoglycemics, Incretin Mimetics/Enhancers

New Product: Xultophy (insulin degludec/liraglutide)

- Three 26-week trials -1,393 patients with T2DM Study 1, 2, and 3 switched patients from liraglutide, insulin degludec, or insulin glargine U-100 to the fixed-dose combination insulin degludec/liraglutide. Dosages for the combination product and the basal-insulin comparators were titrated based on fasting plasma glucose (FPG) of 72 to 90 mg/dL

Hypoglycemics, Incretin Mimetics/Enhancers

New Product: Xultophy (insulin degludec/liraglutide)

- Studies (study 1):
  - At 26-weeks, change in HbA1c was -1.31% in the combination group compared to -0.36% in the liraglutide group. Percent of patients that achieved HbA1c < 7% was 74.6% and 30.2%, respectively. At study end, mean FPG was lower with the combination than with liraglutide (112 versus 153 mg/dL)

Hypoglycemics, Incretin Mimetics/Enhancers

New Product: Xultophy (insulin degludec/liraglutide)

- Studies (study 2):
  - Percentage of patients that achieved HbA1c < 7% was 57.3% in the combination group and 22.6% in the insulin degludec group. In addition, mean FPG at study end was lower with the combination product than insulin degludec (110 versus 118 mg/dL).

Hypoglycemics, Incretin Mimetics/Enhancers

New Product: Xultophy (insulin degludec/liraglutide)

- Studies (study 3):
  - HbA1c changed by -1.67% for the combination and -1.16% for insulin glargine. Percentage of patients that achieved HbA1c < 7% was 68.3% in the combination group compared to 46.2% in the insulin glargine group. Mean change in FPG was similar between groups.

Hypoglycemics, Incretin Mimetics/Enhancers

New Product in Class: Adlyxin (lixisenatide)

- Indicated as adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes.
- There are no contraindications. Warnings include serious hypersensitivity reactions, pancreatitis, hypoglycemia with concomitant administration of sulfonylurea or basal insulin, acute kidney injury, and immunogenicity.

Hypoglycemics, Incretin Mimetics/Enhancers

New Product in Class: Adlyxin (lixisenatide)

- Delays gastric emptying, which may impact the absorption of orally administered drugs. Oral contraceptives should be taken at least one hour before or 11 hours after Adlyxin.
- Nausea, vomiting, headache, diarrhea, and dizziness are the most common adverse effects
- No human data are available to indicate a drug-associated risk in pregnancy

Hypoglycemics, Incretin Mimetics/Enhancers

New Product in Class: Adlyxin (lixisenatide)

- Given subcutaneously once daily within one hour before the first meal of the day
- Available in a 50 or 100 mcg/mL prefilled pen (3 mL—14 doses)

Hypoglycemics, Incretin Mimetics/Enhancers

New Product in Class: Adlyxin (lixisenatide)

- GetGoal-X: Randomized, open-label, parallel-group, multicenter, non-inferiority study assessing the HbA1c change of lixisenatide once daily versus exenatide twice daily in a total of 634 adult patients with T2DM inadequately controlled with metformin. Lixisenatide once daily achieved the primary efficacy objective of noninferiority to exenatide twice daily in terms of HbA1c reduction from baseline to week 24.

Hypoglycemics, Incretin Mimetics/Enhancers

New Product in Class: Adlyxin (lixisenatide)

- GetGoal-X: Agents had comparable reductions in fasting plasma glucose
- Body weight was decreased from baseline for patients receiving each agent
- Gastrointestinal adverse events occurred less frequently in the lixisenatide group
- Symptomatic hypoglycemia also occurred less frequently in the lixisenatide group

Hypoglycemics, Incretin Mimetics/Enhancers

New Product in Class: Adlyxin (lixisenatide)

- ELIXA: randomized, multicenter, double-blind, placebo-controlled trial designed to assess the effects of lixisenatide on cardiovascular morbidity and mortality.
- The trial included 6,068 patients with T2DM who experienced an acute coronary event within the last 180 days before screening.

Hypoglycemics, Incretin Mimetics/Enhancers

New Product in Class: Adlyxin (lixisenatide)

- ELIXA: The primary end point was first occurrence of any of the following: death from cardiovascular causes, nonfatal myocardial infarction, non-fatal stroke, or hospitalization for unstable angina. End point occurred in 406 patients (13.4%) in the lixisenatide group and in 399 (13.2%) in the placebo group, which showed the noninferiority of lixisenatide to placebo ($p<0.001$) but not superiority ($p=0.81$).

Hypoglycemics, Incretin Mimetics/Enhancers

New Product in Class: Soliqua (insulin glargine/lixisenatide)

- Indicated as adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes inadequately controlled with basal insulin or Adlyxin (lixisenatide).
- Contraindications, warnings, adverse effects, and drug interactions are similar to those for Adlyxin and insulin glargine.

Hypoglycemics, Incretin Mimetics/Enhancers

New Product in Class: Soliqua (insulin glargine/lixisenatide)

- Soliqua is given subcutaneously once daily within an hour before the first meal of the day and comes in a 3 mL prefilled pen (100 U, 33 mcg/mL).

Hypoglycemics, Incretin Mimetics/Enhancers

New Product in Class: Soliqua (insulin glargine/lixisenatide)

- Randomized, 30-week, active-controlled, open-label, 2-treatment arm, parallel-group study - 736 patients with T2DM treated with stable doses of basal insulin for at least 6 months with or without oral antidiabetic drugs
- Randomized to either combination insulin glargine/lixisenatide or insulin glargine U-100

Hypoglycemics, Incretin Mimetics/Enhancers

New Product in Class: Soliqua (insulin glargine/lixisenatide)

- Target FPG was achieved in 33% of patients in both groups at 30 weeks
- At 30 weeks, there was a statistically greater change in HbA1c from baseline for the combination product compared to insulin glargine

Hypoglycemics, Incretin Mimetics/Enhancers

New Product in Class: Soliqua (insulin glargine/lixisenatide)

- More patients on the combination product achieved HbA1c <7.0% (55%) compared with 30% on insulin glargine.
- Mean body weight decreased by 0.7 kg with the combination and increased by 0.7 kg with insulin glargine ($p<0.0001$).

Hypoglycemics, Incretin Mimetics/Enhancers

New Product in Class: Soliqua (insulin glargine/lixisenatide)

- Study compared to the individual components in 1,170 patients with T2DM inadequately controlled on metformin, with or without a second oral antidiabetic agent
- Patients were randomized to open-label once-daily insulin glargine/lixisenatide, insulin glargine, or lixisenatide

Hypoglycemics, Incretin Mimetics/Enhancers

New Product in Class: Soliqua (insulin glargine/lixisenatide)

- At 30 weeks, greater reductions in HbA1c from baseline were reported with the combination compared with either component alone (-1.6%, -1.3%, -0.9%, respectively).
- More patients achieved HbA1c <7% with the combination (74%) versus insulin glargine (59%) or lixisenatide (33%) ($p<0.0001$ for all).

Hypoglycemics, Incretin Mimetics/Enhancers

New Product in Class: Soliqua (insulin glargine/lixisenatide)

- Mean change in body weight with the combination was -0.3 kg, lixisenatide -2.3 kg, and insulin glargine +1.1 kg, differences were significant.

Hypoglycemics, Incretin Mimetics/Enhancers

Product Updates

- Nesina, Kazano, and Oseni are now available as generics.
- The FDA added new information to the Warnings & Precautions sections of saxagliptin- and alogliptin-containing products regarding the increased risk of heart failure, which may be higher in the presence of existing heart or kidney disease.

Hypoglycemics, Incretin Mimetics/Enhancers

Guideline Updates

- The 2017 American Diabetes Association recommendations regarding this class of drugs for glycemic treatment approaches places greater emphasis on the use of Victoza due to its outcomes trial results.

Hypoglycemics, Incretin Mimetics/Enhancers

Guideline Updates

- The 2017 American College of Physicians recommendations for type 2 diabetes oral treatment list metformin as first line. DPP-4 inhibitors are listed among the many oral second line options.

Hypoglycemics, Insulin and Related Agents

Sarah Martinez, PharmD

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

New Product in Class: Basaglar (insulin glargine)

- First insulin product approved through an abbreviated approval pathway under a 505(b)(2) application that relies mostly on Lantus data for safety and efficacy.
- It is regarded by the FDA as a '*follow-on*' agent to Lantus.

Hypoglycemics, Insulin and Related Agents

New Product in Class: Basaglar (insulin glargine)

- Indicated to improve glycemic control in adults with diabetes.
- Contraindicated during episodes of hypoglycemia.
- There may be drug interactions when given with drugs that affect glucose metabolism.

Hypoglycemics, Insulin and Related Agents

New Product in Class: Basaglar (insulin glargine)

- Warnings include hypoglycemia or hyperglycemia with changes in insulin regimens, hypoglycemia, hypersensitivity reactions, medication errors or sharing pens, and hypokalemia.
- Signs and symptoms of hypoglycemia may be reduced or absent when used with adrenergic blockers.

Hypoglycemics, Insulin and Related Agents

New Product in Class: Basaglar (insulin glargine)

- Hypoglycemia, allergic reactions, and injection site reactions are the most common adverse effects.
- Basaglar is pregnancy category C.

Hypoglycemics, Insulin and Related Agents

New Product in Class: Basaglar (insulin glargine)

- Basaglar is given subcutaneously once daily at an individualized dose. It is available in a 100 U/mL prefilled KwikPen (3 mL).

Hypoglycemics, Insulin and Related Agents

Product Updates

- The 2017 American Diabetes Association recommendations regarding this class of drugs for glycemic treatment approaches is largely unchanged from the 2016 edition.
- Tresiba is now indicated for treatment of patients one year and older (previously indicated only in adults).

COPD Agents

Sarah Martinez, PharmD

COPD Agents

Class Overview

- Single agent products:
  - Roflumilast (oral PDE4 inhibitor)
  - Ipratropium (short-acting anticholinergic)
    - Inhalation solution (Atrovent)
    - Inhalation aerosol MDI (Atrovent HFA)

COPD Agents

Class Overview

- Long-acting anticholinergics:
  - Umeclidinium (Incruse Ellipta)
  - Tiotropium (DPI (Spiriva HandiHaler), inhalation spray (Spiriva Respimat)
  - Aclidinium bromide (inhalation powder (Tudorza Pressair)
  - Glycopyrrolate (Seebri Neohaler)

COPD Agents

Class Overview

- Combination products:
  - Albuterol/ipratropium (short acting)
    - Inhalation solution
    - Combivent Respimat (MDI)

COPD Agents

Class Overview

- Combination products -LAMA/LABA agents:
  - Tiotropium/olodaterol (Stiolto Respimat)
  - Indacaterol/glycopyrrolate (Utibron Neohaler)
  - Umeclidinium/vilanterol inhalation powder DPI (Anoro Ellipta)
  - Formoterol/glycopyrrolate (Bevespi Aerosphere)

COPD Agents

Class Overview

- GOLD Guidelines Group A:
  - Short-acting inhaled bronchodilator used on an as-needed basis is recommended as first choice while a long-acting beta2-agonist or anticholinergic and the combination of short-acting inhaled beta2-agonist and short-acting anticholinergic are considered as alternatives

COPD Agents

Class Overview

- GOLD Guidelines Group B:
  - Regular use of a long-acting bronchodilator (beta2-agonist or anticholinergic) is recommended while the combination of a long-acting beta2-agonist and a long-acting anticholinergic is an alternative treatment.

COPD Agents

Class Overview

- GOLD Guideline Group C:
  - Fixed combinations of inhaled corticosteroid/long-acting bronchodilators (beta2-agonist or anticholinergic)
  - Alternatively, a phosphodiesterase-4 (PDE4) inhibitor plus a long-acting bronchodilator or a long-acting anticholinergic plus a long-acting beta2-agonist.

COPD Agents

Guideline Updates

- The 2017 update to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines observe that combination bronchodilator use may be more appropriate in patients with less advanced disease, but data does not definitively show LAMA/LABA treatment to be more effective than ICS/LABA.

COPD Agents

Product Updates

- Spiriva Respimat is now indicated for use in patients 6 years of age and older for long-term treatment of asthma. (Previously approved for asthma in patients 12 years of age and older. Also indicated for COPD in adults). The Spiriva Handihaler is only approved for adults with COPD.

Executive Session

P&T Public Class Vote Opioid Dependent Treatment

P&T Public Class Vote Hypoglycemics Incretin Mimetics & Enhancers

P&T Public Class Vote Hypoglycemics Insulin & Related Agents

P&T Public Class Vote
COPD Agents

Long Acting Opioid Prior Authorization Exclusions Discussion

Sara Salek MD, CMO, AHCCCS

Recommended Exclusions

- Active oncology diagnosis
- Hospice care
- End-of-life care (other than hospice)

Opioid 7-Day Quantity Limitation Update

Sara Salek MD, CMO, AHCCCS

Governor's Executive Order 2016-06
Prescription Opioid—Initial Fill Limitation

- On October 24, 2016, Governor Doug Ducey issued Executive Order 2016-06 which limits the *initial* opioid prescription for adults as well as the *initial and refill* opioid prescriptions for children through the Arizona Health Care Cost Containment System (AHCCCS) and the Arizona Department of Administration (ADOA).
- AHCCCS issued a draft policy for a two-week public comment period in December 2016 and subsequently held a stakeholder session on January 11, 2017.

Policy Links

- 310-V Prescription Medications/Pharmacy Services, G. 7-Day Supply Limit Of Prescription Opioid Medications-Contractor Requirements (pages 10-11)
- Policy 310-V, Exhibit 310-V-2, 7-Day Supply Limit Of Prescription Opioid Medications Exclusions Specifications
- Policy 310-V, Exhibit 310-V-3, ICD-10-CM Diagnosis Code Description

BIOSIMILAR UPDATE

- Basaglar by Lilly is a clinically equivalent biosimilar for Lantus Insulin. Both are glargine insulin.
- Per Policy 310V Section B. 4. 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.
- Lantus is the most cost effective glargine insulin product because it approximately 100% federally rebated.
- Due to the cost differential, AHCCCS will continue to require the brand name, Lantus, to be the the only and preferred glargine insulin product available on the AHCCCS Drug List.

New Drug Reviews

Suzi Berman, RPh

New Products

- Eucrisa – Crisaborole
- Vemlidy – Tenofovir Alafenamide

Eucrisa – Crisaborole

- Is a phosphodiesterase 4 inhibitor indicated to treat mild to moderate eczema (atopic dermatitis in patient 2 years of age and older.
- Supplied as 2% - 60 & 100GM topical ointments
- Black Box Warning – None
- Adverse Reactions – Site pain and contact urticaria.

Eucrisa – Crisaborole

- Clinical Trials
- Two multicenter, double blinded vehicle-controlled trials. Patients randomized 2:1 for Eucrisa
- Ages 2-79 with 86.3% from ages 2-17
- Rating scale used: Investigator's Static Global Assessment (ISGA) severity scale 0-4
- Baseline Scores
  - 38.5% had a score of 2(mild) and
  - 61.5% had a score of 3 (moderate)

Eucrisa – Crisaborole

- Clinical Trial Results
- Endpoints: Those with a clear score (0) or almost clear (1) with a 2-grade or > improvement.
- Trial 1: 32.85% vs. 25.4% achieved the endpoint
- Trial 2: 48.5% vs. 29.7% achieved the endpoint
- Problem- Trial was not a heat to head trial
- While the results are statistically significant- using the vehicle as a comparator does not indicate how this drug would fit in our current armamentarium of drugs

Eucrisa – Crisaborole

- Recommendation is to not add Eucrisa to the AHCCCS Drug Lists because we have many other products that are efficacious and less costly.
- Eucrisa is available through prior authorization based on medical necessity.

P&T Public Vote on Eucrisa- Crisaborole Recommendation

Vemlidy – Tenofovir Alafenamide

- Antiretroviral indicated for the treatment of chronic Hepatitis B in adults with compensated disease
- Dosage: 25mg tablet once daily
- Not to be used as monotherapy for HIV+ patients
- Black Box Warning- None
- Adverse events > 5% are headache, abdominal pain, fatigue, cough, nausea and back pain.
- No contraindications
- Co-administration with anticonvulsants, anti-mycobacterials and herbal medications is not recommended

Vemlidy – Tenofovir Alafenamide (TAF)

- Clinical Trials –
- 2 48 week, randomized double blinded
- Study 108 – Hb antigen negative treatment naïve and experienced
  - Randomized 2:1 with TAF vs. Tenofovir disoproxil fumarate (TDF)
  - Primary endpoint was HBV DNA levels < 29 iu/ml at week 48
  - For Naïve patients, 94% of TAF and 93% of TDF met the endpoint
  - For experienced patients, 93% of both groups met the endpoint
  - ALT normalization occurred in 50% of the TAF group and 32% of the TDF group.

Vemlidy – Tenofovir Alafenamide (TAF)

- Study 110 - Hb+ antigen treatment naïve and experienced
  - Randomized 2:1 with TAF vs. tenofovir disoproxil fumarate (TDF)
  - Primary endpoint was HBV DNA levels < 29 iu/ml at week 48
  - Overall 64% of TAF and 67% of TDF met the endpoint
  - For treatment naive patients, 68% of TAF and 70% of TDF met the primary endpoint
  - For treatment experienced patients, 50% of TAF and 57% of TDF met the primary endpoint
  - ALT normalization occurred in 45% of the TAF group and 36% of the TDF group.

Vemlidy – Tenofovir Alafenamide (TAF)

- Vemlidy (TAF) and Viread (TDF) are equally efficacious in meeting the primary endpoint of reducing the Hep B viral load.
- Vemlidy has a slightly better statistically significant profile when normalizing the liver function tests.
- The recommendation is not to add Vemlidy to the AHCCCS Drug List because there are first line agents available that are more cost effective.
- Vemlidy is available through the prior authorization process.

Vemlidy – Tenofovir Alafenamide (TAF)

- Recommendation is to not add this drug to the AHCCCS Drug List, there are other first line agents available that are more cost-effective.
- AASLD has not issued the new guidelines for the Hep B virus
- Vemlidy is available through prior authorization based on medical necessity.

P&T Public Vote on Vemlidy – Tenofovir Alefenamide Recommendation

Fluoride Oral Tablets

- Currently not listed on the AHCCCS Drug List
- The AHCCCS Dental Director is requesting we add Fluoride oral tablets to the AHCCCS Drug List to ensure that when it is provided when medically necessary.
- AHCCCS recommendation is to add Fluoride oral agents to the AHCCCS Drug List with prior authorization.

P&T Public Vote on Fluoride Recommendation

Agenda Items For The Next Meeting Monday, July 10, 2017

Please send agenda items to:

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Thank You.