

**Magellan Rx**  
MANAGEMENT<sup>SM</sup>

Magellan Medicaid  
Administration

# Washington Drug Utilization Review (DUR) Board Meeting

February 16<sup>th</sup>, 2022

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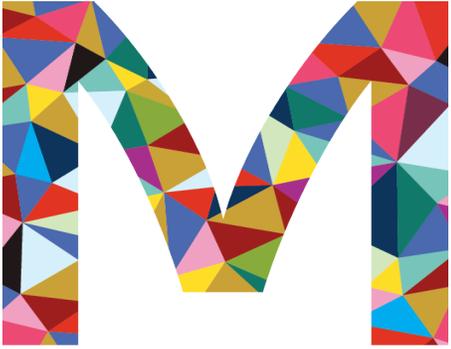
# Agenda Topics

Overview of Disease  
State

Indications

Dosage & Formulations

Guideline Updates



## Antibiotics:

- Aminoglycosides- Inhaled
- Monobactams- Inhaled

## Respiratory Agents:

- Cystic Fibrosis Agents



# Disease State Description - Cystic Fibrosis

- Cystic Fibrosis (CF) is a serious autosomal recessive multiorgan disorder
- Affects ~31,199 children and adults in the U.S. and is the most common fatal genetic disease in Caucasians
  - The median survival in patients with CF is 48.4 years with 80% of patients reaching adulthood
  - Children are anticipated to live to approximately 40 years of age with current treatments
  - In 2019, adults comprised approximately 56% of the CF population, while in 1989, they comprised approximately 31.1%
- Mutations lead to the disease of the exocrine gland function, resulting in the formation of thick mucus that builds up in the lungs, digestive tract, and other parts of the body
  - CF transmembrane conductance regulator (CFTR) functions as a chloride channel
  - Mutations in CFTR results in abnormalities of chloride transport across epithelial cells on mucosal surfaces
- Goals of CF treatment include:
  - Maintaining lung function by controlling infection and clearing mucus in the airway
  - Maintaining appropriate growth by providing nutritional support (e.g., enzyme, mineral, and multivitamin supplements)
  - Managing disease complications (e.g., insulin therapy in patients who develop diabetes)

*Cystic Fibrosis Foundation, 2019*

# Guidelines - Cystic Fibrosis

- Goals of CF treatment include maintaining lung function by controlling infection and clearing mucus in the airway, maintaining appropriate growth by providing nutritional support (e.g., enzyme, mineral, and multivitamin supplements) and managing disease complications (e.g., insulin therapy in patients who develop diabetes)
- *CFTR* modulators (potentiators or correctors) are the newest class of medications available for this disease and improve chloride ion transport abnormalities
- Cystic Fibrosis Foundation, 2013
  - Inhaled treatments (e.g., tobramycin, dornase alfa, hypertonic saline, corticosteroids) and oral treatments (e.g., antibiotics, corticosteroids) for treatment of symptoms, exacerbations, and/or infections
  - Chronic treatment of ivacaftor for individuals 6 years of age and older with at least one *G551d CFTR* mutation to improve lung function and quality of life and to reduce exacerbations
- Clinical Pharmacogenetics Implementation Consortium (CPIC), 2014
  - Recommend ivacaftor therapy based on *CFTR* genotype in CF patients  $\geq 6$  years old who are homozygous or heterozygous for the *G551D CFTR* variant
  - CPIC further states that there are no data regarding whether or not ivacaftor can replace other established therapy
- Please note: Orkambi, Symdeko, and Trikafta were not approved in 2013/2014 and were not addressed in either guideline

# Updated Information - Cystic Fibrosis

- **ivacaftor (Kalydeco)**

- In December 2020, FDA approved Kalydeco for the treatment of cystic fibrosis (CF) in patients aged 4 to < 6 months of age and weighing  $\geq 5$  kg who have  $\geq 1$  mutation in the CFTR gene that is responsive to ivacaftor based on clinical and/or in vitro assay data; previously, it was only approved in patients  $\geq 6$  months of age

- **Indication**

- Treatment of cystic fibrosis (CF) in patients age 4 months and older who have one mutation in the CFTR gene that is responsive to ivacaftor based on clinical and/or in vitro assay data
- If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of a CFTR mutation followed by verification with bi-directional sequencing when recommended by the mutation test instructions for use

- **Dosage**

- Adults and children  $\geq 6$  years of age: one 150 mg tablet orally every 12 hours (300 mg/day)
- **Pediatric patients 4 months to < 6 months of age and < 5 kg: one 25 mg packet mixed with 1 teaspoon (5 mL) of soft food or liquid and administered orally every 12 hours with fat-containing food**
- Pediatric patients 6 months to < 6 yo and weighing 5 kg to < 7 kg: one 25 mg packet mixed with 1 teaspoon (5 mL) of soft food or liquid and administered orally every 12 hours with fat-containing food
- Pediatric patients 6 months to < 6 yo and weighing 7 kg to < 14 kg: one 50 mg packet mixed with 1 teaspoon (5 mL) of soft food or liquid and administered orally every 12 hours with fat-containing food
- Pediatric patients 6 months to < 6 yo and > 14 kg: one 75 mg packet mixed with 1 teaspoon (5 mL) of soft food or liquid and administered orally every 12 hours with fat-containing food

- **Availability**

- 150 mg tablets
- 25 mg, 50 mg, 75 mg oral granules in unit-dose packets

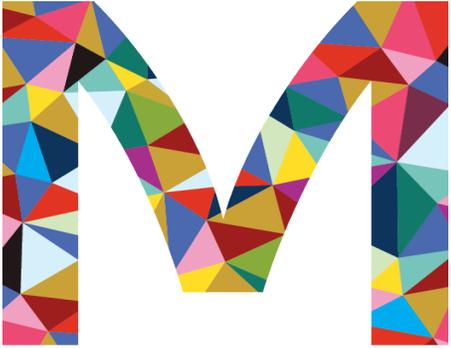
# Updated Information - Cystic Fibrosis

- **elexacaftor/tezacaftor/ivacaftor (Trikafta)**

- December 2020, PI updated to expand the indication to include patients with cystic fibrosis (CF) who have a mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene that is responsive based on in vitro data; updated indication: treatment of CF in patients aged  $\geq 12$  years old who have  $\geq 1$  F508del mutation in the CFTR gene or a mutation in the CFTR gene that is responsive based on in vitro data
- June 2021: FDA approved Trikafta for the treatment of cystic fibrosis (CF) in patients aged 6 through 11 years old with at least one F508del mutation in the CFTR gene or a mutation in the CFTR gene that is responsive based on in vitro data.
- June 2021: FDA also approved a new dosage containing elexacaftor 50 mg/tezacaftor 25 mg/ivacaftor 37.5 mg copackaged with ivacaftor 75 mg tablet to accommodate dosing in the new age group.
- **Indications**
  - Treatment of cystic fibrosis (CF) in patients aged 6 years and older who have at least one F508del mutation in the CFTR gene or a mutation in the CFTR gene that is responsive based on in vitro data
  - If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to confirm the presence of at least one F508del mutation or a mutation that is responsive based on in vitro data
- **Dosage**
  - Stratified by age and weight
- **Availability**
  - Fixed-dose combination containing elexacaftor 50 mg, tezacaftor 25 mg and ivacaftor 37.5 mg co-packaged with ivacaftor 75 mg
  - Fixed-dose combination containing elexacaftor 100 mg, tezacaftor 50 mg, and ivacaftor 75 mg co-packaged with ivacaftor 150 mg

# Updated Information - Cystic Fibrosis

- **tezacaftor/ivacaftor + ivacaftor (Symdeko)**
  - **December 2020, PI updated to expand the indicated Cystic Fibrosis (CF) patient population to include additional mutations in the CFTR gene that have been identified as responsive based upon in vitro data**



## Anticoagulants:

- Factor Xa and Thrombin Inhibitors - Oral



# Disease State Description - Anticoagulants

## Venous Thromboembolism (VTE)

- It manifests as deep vein thrombosis (DVT) and pulmonary embolism (PE) and is a major consequence of various surgical procedures and medical conditions
- DVT occurs when a thrombus composed of cellular material bound together with fibrin strands forms in the deep venous portion of the extremities, most commonly the legs
  - The exact number of patients impacted by DVT and PE is unknown; however, it is estimated these conditions affect between 300,000 and 600,000 people in the U.S. every year
  - If left untreated, approximately 30% of patients who develop PE will die within the first few hours of the event
- Generally, the risk of VTE increases with the number of risk factors present, major traumas, and age
- Due to the risk of morbidity and fatal PE associated with DVT, prophylaxis has become the standard of care for patients at high risk for thrombosis

*National Heart, Lung, and Blood Institute, 2017*

## CAD (Coronary Artery Disease) and Peripheral Artery Disease (PAD)

- Approximately 14 million Americans have CAD, and 8.5 million over the age of 40 years have PAD
- Prevention and treatment of atherosclerosis focus on modifiable risk factors
- Therapy includes lifestyle changes and the medical treatment of hypertension, hyperlipidemia, and diabetes mellitus
- Antiplatelet medications (e.g., aspirin, clopidogrel, prasugrel, ticagrelor, vorapaxar) are indicated for reduction of thrombotic CV events in patients with established CAD or PAD

*American College of Cardiology, 2016*

# Disease State Description - Anticoagulants

## Atrial Fibrillation (AF)

- A common arrhythmia ranging in prevalence from 2% in patients under 65 years of age to 9% for those 65 or older
  - The prevalence is higher in men than in women and increases with age
  - More than a third of patients with AF are 80 years of age or older
- Patients with AF can have a reduction in cardiac output resulting in pooling of blood in the heart, atrial thrombus formation, and potential systemic embolization
  - Ischemic stroke is the most frequent clinical manifestation of AF associated embolization
  - AF increases the risk of stroke 5-fold
- In patients with AF, ACCP recommends measuring thromboembolism risk using the CHA<sub>2</sub>DS<sub>2</sub>-VASc score, which considered risk factors such as gender, age, history of stroke, TIA, or thromboembolism, as well as history of congestive heart failure (CHF), hypertension, diabetes mellitus, or vascular disease (prior myocardial infarction [MI], peripheral artery disease, or aortic plaque)
  - The score ranges from 0 to 9, with higher numbers indicating more risk

*American College of Cardiology, 2017*

# Treatment Guidelines - Anticoagulants

## American Heart Association/American College of Cardiology (AHA/ACC), 2020

- Published guidelines on the diagnosis and treatment of hypertrophic cardiomyopathy (HCM)
- Notable pharmacologic recommendations include the following:
  - For symptomatic patients with left ventricular outflow tract (LVOT) obstruction, nonvasodilating beta-blockers are recommended, but alternatives for select patients include verapamil, diltiazem, or disopyramide
  - For non-obstructive hypertrophic cardiomyopathy with preserved left ventricular ejection fraction (LVEF), beta-blockers, verapamil, or diltiazem are recommended and consideration of anticoagulants as the default treatment option for patients who also have atrial fibrillation independent of the CHA2DS2VASc score
  - Additional guidance on the use of antiarrhythmic therapy and heart failure agents is included as well

## American College of Cardiology (ACC), 2020

- Published an expert consensus decision pathway on managing bleeding episodes in patients taking oral anticoagulants
- It updates parts of the 2017 ACC Expert Consensus Decision Pathway for Periprocedural Management of Anticoagulation in Patients With Nonvalvular Atrial Fibrillation
- Provides guidance for temporary or permanent interruption of therapy, general approaches to bleeding management, decision support for treatment with a reversal agent, and indications and timing for reinstating anticoagulant treatment
- The panel does not recommend routine administration of platelets for patients on antiplatelet agents for major bleeding
- They do not recommend routine oral anticoagulant reversal for nonmajor bleeding, but clinicians may interrupt therapy until patient is clinically stable and hemostasis is achieved

# Updated Information - Anticoagulants

- **dabigatran etexilate (Pradaxa)**
  - **June 2021: FDA approved Pradaxa for the treatment of VTE and to reduce the risk of VTE in pediatric patients  $\geq 3$  months old. Previously, it was only approved for these indications in adults**
  - **June 2021: FDA also approved 20 mg, 30 mg, 40 mg, 50 mg, 110 mg, and 150 mg oral pellet packets for administration with select soft foods (baby rice cereal + water, mashed carrots or banana, apple sauce) or apple juice. The oral pellets are indicated for the treatment of VTE and to reduce the risk of VTE in pediatric patients 3 months to  $< 12$  years old**
  - **Indication**
    - **For the treatment of venous thromboembolic events (VTE) in pediatric patients aged 3 months to less than 12 years of age who have been treated with a parenteral anticoagulant for at least 5 days**
    - **To reduce the risk of recurrence of VTE in pediatric patients aged 3 months to less than 12 years of age who have been previously treated**
  - **Precautions**
    - **BBW: Premature discontinuation increases the risk of thrombotic events**
    - **BBW: Epidural or spinal hematomas have occurred in patients treated with Pradaxa who are receiving neuraxial anesthesia or undergoing spinal puncture. These hematomas may result in long-term or permanent paralysis**
  - **Dosage**
    - **Treatment of Pediatric Venous Thromboembolic Events (VTE):**
      - **For pediatric patients aged 3 months to less than 2 years: age- and weight-based dosage, twice daily after at least 5 days of parenteral anticoagulant**
      - **For pediatric patients 2 years to less than 12 years: weight-based dosage, twice daily after at least 5 days of parenteral anticoagulant**
  - **Availability**
    - **Oral pellets: 20 mg, 30 mg, 40 mg, 50 mg, 110 mg, 150 mg per packet**

# Updated Information - Anticoagulants

- **rivaroxaban (Xarelto)**
  - **December 2021: The FDA approved a new oral suspension formulation (1 mg/mL once reconstituted)**
  - **December 2021: The FDA approved 2 new indications (1) the treatment of VTE and reduction in the risk of recurrent VTE in pediatric patients from birth to < 18 years; and (2) for thromboprophylaxis in pediatric patients ≥ 2 years old with congenital heart disease after the Fontan procedure**
  - **Indication**
    - To reduce risk of stroke and systemic embolism in nonvalvular atrial fibrillation
    - For treatment of deep vein thrombosis (DVT)
    - For treatment of pulmonary embolism (PE)
    - For reduction in the risk of recurrence of DVT or PE
    - For the prophylaxis of DVT, which may lead to PE in patients undergoing knee or hip replacement surgery
    - For prophylaxis of venous thromboembolism (VTE) in acutely ill medical patients
    - To reduce the risk of major cardiovascular events in patients with coronary artery disease (CAD)
    - To reduce the risk of major thrombotic vascular events in patients with peripheral artery disease (PAD), including patients after recent lower extremity revascularization due to symptomatic PAD
    - **For treatment of VTE and reduction in the risk of recurrent VTE in pediatric patients from birth to less than 18 years**
    - **For thromboprophylaxis in pediatric patients 2 years and older with congenital heart disease after the Fontan procedure**
  - **Dosage**
    - Stratified by indication and age (found in PI or TCR)
  - **Availability**
    - Tablets: 2.5 mg, 10 mg, 15 mg, and 20 mg
    - **For oral suspension: 1 mg/mL once reconstituted**



## Antidiabetics:

- Amylin Analogs
- SGLT2 Inhibitors
- DPP4 Inhibitor
- DPP4 Inhibitor/ SGLT2 Inhibitor Combinations
- DPP4 Inhibitor/ TZD Combinations
- GLP1 Agonists
- GLP1 Agonist/ Insulin Combinations



# Disease State Description - Diabetes Mellitus

- It is estimated that over 34 million Americans have diabetes mellitus (DM)
  - Of which, 90-95% have Type 2 Diabetes
  - Diabetes is responsible for increased morbidity and mortality
- Adequate glycemic control is crucial to minimize chronic microvascular (e.g., blindness, renal dysfunction) and macrovascular (e.g., cardiovascular disease [CVD]) complications
- Exogenous insulin supplements deficient levels of endogenous insulin, and temporarily restores the ability of the body to properly utilize carbohydrates, fats, and proteins
- Multiple insulin products are available and are used as replacement therapy in the management of both T1DM and T2DM when glycemic goals are not met with oral antidiabetic agents
- In addition to exogenous insulin, there are several pathways by which blood glucose may be regulated in diabetic patients
- The sodium-glucose cotransporter 2 (SGLT2) inhibitors reduce renal glucose reabsorption in the proximal convoluted tubule, leading to increased urinary glucose excretion

American Diabetes Association, 2020

# Guidelines- Diabetes Mellitus

- Kidney Disease Improving Global Outcomes (KDIGO), 2020

- Guidelines on managing diabetes in CKD
- Recommend an individualized HbA1c target from < 6.5% to < 8% in diabetic patients with CKD, based on CKD severity, macrovascular complications, comorbidities, life expectancy, hypoglycemia awareness and management resources, and hypoglycemic risk of medication
- In addition to lifestyle therapy, KDIGO recommends first-line treatment with metformin and an SGLT2 inhibitor in most patients with an estimated glomerular filtration rate (eGFR)  $\geq 30$  mL/min/1.73 m<sup>2</sup>
- A GLP-1RA (generally preferred), DPP-4 inhibitor, insulin, SU, TZD, and/or AGI may be added as needed for glycemic control
- These additions are guided by patient preference, comorbidities, eGFR, and cost. They advise against use of a GLP-1RA with a DPP-4 inhibitor

- The American College of Cardiology (ACC), 2020

- Published an expert consensus decision pathway for CV risk reduction in patients with T2DM
- They identify opportunities to initiate an SGLT2 inhibitor or GLP-1RA with demonstrated CV or renal benefit in patients with T2DM
- A medication from either class may be initiated in any patient with T2DM and ASCVD at the time of diagnosis of T2DM or ASCVD or any time after diagnosis, including at hospital discharge for ASCVD
- An agent from either class can also be started in patients with T2DM without established ASCVD but who are at high risk of ASCVD
- In addition, initiation of an SGLT2 inhibitor with demonstrated CV or renal benefit is recommended in patients with HF and/or diabetic kidney disease; a GLP-1RA is an alternative in patients with eGFR < 30 ml/min/1.73 m<sup>2</sup>

# Guidelines- Diabetes Mellitus

- American Gastroenterological Association (AGA), 2021

- Estimates that up to 70% of individuals with T2DM have nonalcoholic fatty liver disease (NAFLD)
- The AGA inform that GLP-1RAs, SGLT2 inhibitors, and pioglitazone can improve the cardiometabolic profile and reverse steatosis in patients with diabetes and NAFLD
- They recommend an GLP-1RA or pioglitazone in patients with indeterminate or high risk clinically significant liver fibrosis
- SGLT2 inhibitors appear to provide benefit in patients with nonalcoholic steatohepatitis (NASH) and associated comorbidities (e.g. congestive heart failure, CKD)
- AGA advises to prescribe GLP-1RAs and SGLT2 inhibitors according to the ADA guidelines

# Guidelines- Diabetes Mellitus

- American Diabetes Association (ADA), 2021

- In 2021, the American Diabetes Association (ADA) Standards of Medical Care in Diabetes continued to include the sodium-glucose cotransporter 2 (SGLT2) inhibitors in the management algorithm for T2DM
- The position statement recommends HbA1c < 7% as a reasonable target for most nonpregnant adult patients
- **In patients using ambulatory glucose profile/glucose management indicator to assess glycemia, a parallel goal is a time in range of > 70% with time below range < 4%**
- A more stringent HbA1c goal of < 6.5% may be considered for select patients (e.g., those with short duration of diabetes, long life expectancy, and no significant cardiovascular disease [CVD]) if this can be achieved without significant hypoglycemia
- Less-stringent HbA1c goals (< 8%) may be appropriate for patients with a history of severe hypoglycemia, limited life expectancy, advanced microvascular or macrovascular complications, extensive comorbid conditions, and those with longstanding diabetes in whom the general goal is difficult to attain
- **During pregnancy, the ADA recommends a target HbA1c of 6% to 6.5% is reasonable, but can be adjusted based on hypoglycemia risk; more frequent (e.g., monthly) HbA1c monitoring may be required**
- **For diabetes technology, an automated insulin delivery system should be considered in adults with T1DM who have the skills to use the device in order to improve time in range and reduce A1C and hypoglycemia (A-rated recommendation)**
  - These systems may also be useful to improve glycemia in children (B-rated recommendation)
- Regarding obesity management, ADA states that lorcaserin should no longer be used, as the FDA requested its market withdrawal
- For pharmacologic T2DM therapy, ADA advises to interrupt SGLT2 inhibitor therapy before scheduled surgery to avoid diabetic ketoacidosis, this aligns with label revisions for SGLT2 inhibitors
- For management of CVD in patients with T2DM, ADA advises to consider an SGLT2 inhibitor in patients with HF with reduced ejection fraction to reduce risk of worsening HF and CV death

# Updated Information - SGLT2 Inhibitors

- **dapagliflozin (Farxiga)**
  - **May 2021: FDA approved new indication to reduce the risk of sustained eGFR decline, end stage kidney disease (ESKD), CV death, and hospitalization for heart failure (hHF) in adults with chronic kidney disease (CKD) at risk of progression**
  - **Indications**
    - As an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus
    - To reduce the risk of hospitalization for heart failure in adults with type 2 diabetes mellitus and either established cardiovascular disease or multiple cardiovascular risk factors
    - To reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure with reduced ejection fraction (NYHA class II-IV)
    - **To reduce the risk of sustained eGFR decline, end stage kidney disease cardiovascular death and hospitalization for heart failure in adults with chronic kidney disease at risk of progression**
  - **Precautions**
    - Pregnancy: Advise females of the potential risk to a fetus especially during the second and third trimesters
    - Necrotizing Fasciitis of the Perineum (Fournier's Gangrene): Serious, life-threatening cases have occurred in patients with diabetes, both females and males. Assess patients presenting with pain or tenderness, erythema, or swelling in the genital or perineal area, along with fever or malaise
    - Volume depletion: Before initiating, assess volume status and renal function in the elderly, patients with renal impairment or low systolic blood pressure, and in patients on diuretics
  - **Dosing**
    - Type 2 Diabetes Mellitus: Recommended starting dose is 5 mg once daily (Max: 10 mg daily)
    - Heart Failure: 10 mg once daily
    - Assess volume status and correct volume depletion before initiating
  - **Formulations**
    - Tablets: 5 and 10 mg

# Updated Information - Glucagon-like-Peptide 1 (GLP-1)

- **exenatide (Bydureon Pen, Bydureon Bcise)**
  - **July 2021: FDA approved use as adjunct to diet and exercise to improve glycemic control in pts with T2DM to include pediatric patients ≥ 10 years old; previously, only approved in adults**
  - **Indications**
    - **As an adjunct to diet and exercise to improve glycemic control in adults and pediatric patients aged 10 years and older with type 2 diabetes mellitus**
  - **Precautions**
    - BBW: Thyroid C-cell tumors
    - BBW: Contraindicated in patients with personal or family history of Multiple Endocrine Neoplasia
    - Pregnancy: Use during pregnancy only if the potential benefit justifies the risk to the fetus
    - Acute Gallbladder Disease: If cholelithiasis or cholecystitis are suspected, gallbladder studies are indicated
  - **Dosing**
    - Administer 2 mg by subcutaneous injection once every seven days (weekly), at any time of day and with or without meals
  - **Formulations**
    - Injection: 6 mg/mL solution in a 3 mL pre-filled, single-patient-use pen that delivers doses of 0.6 mg, 1.2 mg, 1.8 mg, 2.4 mg or 3 mg
    - Extended-release injectable suspension: 2 mg of exenatide in a 0.85 mL single-dose autoinjector



## Antidiabetics: Insulin

- Intermediate Acting
- Long Acting
- Pre-Mixed
- Rapid-Acting
- Short-Acting



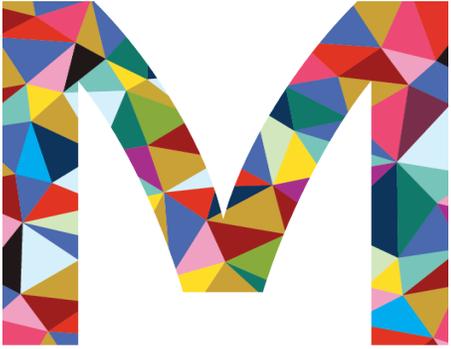
# Updated Information - Long-Acting Insulin

- **insulin glargine-yfgn (Semglee)**

- **July 2021: FDA has approved insulin glargine-yfgn (Semglee) as an interchangeable biosimilar to insulin glargine (Lantus). Semglee is a long-acting human insulin analog indicated to improve glycemic control in adults and peds patients with T1DM and in adults with T2DM; it is not recommended for treating diabetic ketoacidosis**
- **Indications**
  - **To improve glycemic control in adults and pediatric patients with type 1 diabetes mellitus and in adults with type 2 diabetes mellitus**
- **Precautions**
  - **Hyperglycemia or hypoglycemia with changes in insulin regimen: Make changes to a patient’s insulin regimen (e.g., insulin strength, manufacturer, type, injection site or method of administration) under close medical supervision with increased frequency of blood glucose monitoring**
  - **Hypokalemia: May be life-threatening. Monitor potassium levels in patients at risk of hypokalemia and treat if indicated**
  - **Fluid retention and heart failure with concomitant use of thiazolidinediones (TZDs): Observe for signs and symptoms of heart failure; consider dosage reduction or discontinuation of TZD if heart failure occurs**
- **Dosing**
  - **Individualize dosage based on metabolic needs, blood glucose monitoring, glycemic control, type of diabetes, prior insulin use**
- **Formulations**
  - **Injection: 100 units/mL (U-100) available as:**
    - **10 mL multiple-dose vial**
    - **3 mL single-patient-use prefilled pen**

# Updated Information - Long-Acting Insulin

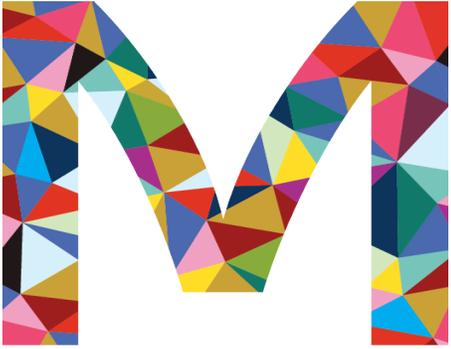
- **insulin glargine-aglr (Rezvoglar)**
  - **December 2021:** The FDA has approved the 2nd biosimilar insulin product to Lantus (insulin glargine), insulin glargine-aglr (Rezvoglar). It is a long-acting human insulin analog indicated to improve glycemic control in adults and pediatric patients with type 1 DM and in adults with type 2 DM
  - **Indications**
    - To improve glycemic control in adults and pediatric patients with type 1 diabetes mellitus and in adults with type 2 diabetes mellitus
    - Limitations of use: Not recommended for treating diabetic ketoacidosis
  - **Precautions**
    - Hyperglycemia or hypoglycemia with changes in insulin regimen: Make changes to a patient's insulin regimen (e.g., insulin strength, manufacturer, type, injection site or method of administration) under close medical supervision with increased frequency of blood glucose monitoring
    - Hypokalemia: May be life-threatening. Monitor potassium levels in patients at risk of hypokalemia and treat if indicated
    - Fluid retention and heart failure with concomitant use of thiazolidinediones (TZDs): Observe for signs and symptoms of heart failure; consider dosage reduction or discontinuation of TZD if heart failure occurs
  - **Dosing**
    - Individualize dosage based on metabolic needs, blood glucose monitoring, glycemic control, type of diabetes, prior insulin use
  - **Formulations**
    - Injection: 100 units/mL (U-100) available as:
      - 3 mL single-patient-use prefilled pen



## Growth Factors

- Endocrine and Metabolic Agents: Growth Hormone Releasing Hormones (GHRH)





# Growth Hormones

## - Endocrine and Metabolic Agents: Growth Hormone



# Overview of Disease State & Guidelines – Growth Hormones

- Growth hormone deficiency (GHD)

- Results from inadequate production of growth hormone (GH) and can produce various medical conditions dependent on age
- Adults with GHD may have diminished lean body mass, poor bone density, and a number of physical and psychological manifestations
- GHD can be congenital or acquired in childhood or adult life, in addition to being partial or complete
- The condition is usually permanent and may be an isolated deficiency or occur in association with deficiencies of other pituitary hormones. In most cases, the diagnosis of GHD should be based on results from 2 provocative tests as recommended by the Pediatric Endocrine Society (PES)
- The 2009 American Association of Clinical Endocrinologists Guidelines for Clinical Practice indicates no evidence exists to support any specific growth hormone product over another

# Updated Information – Growth Hormone

- **lonapegsomatropin-tcgd (Skytrofa)**
  - **August 2021: FDA has approved Skytrofa for the treatment of pediatric patients  $\geq 1$  year old who weigh  $\geq 11.5$  kg and have growth failure due to inadequate secretion of endogenous growth hormone (GH)**
  - **Indications**
    - The treatment of pediatric patients 1 year and older who weigh at least 11.5 kg and have growth failure due to inadequate secretion of endogenous growth hormone (GH)
  - **Precautions/Contraindications**
    - **Increased Risk of Neoplasm**: There are risks of malignancy progression in patients with active malignancy. Monitor patients with preexisting tumors for progression or recurrence
    - **Glucose Intolerance and Diabetes Mellitus**: Periodically monitor glucose levels in all patients. Doses of concurrent antihyperglycemic drugs in diabetics may require adjustment
    - **Hypothyroidism**: May first become evident or worsen
    - **Pancreatitis**: Consider pancreatitis in patients with persistent severe abdominal pain
  - **Dosing**
    - Should be administered subcutaneously into the abdomen, buttock, or thigh with regular rotation of the injection sites
    - The recommended dose is 0.24 mg/kg body weight once-weekly
  - **Formulations**
    - For injection: 3 mg, 3.6 mg, 4.3 mg, 5.2 mg, 6.3 mg, 7.6 mg, 9.1 mg, 11 mg and 13.3 mg

# Updated Information – Growth Hormone

- **Drug Shortage**

- **Somatropin (Zomacton)- 5/21/2021**

- Ferring has notified Health Care Practitioners of a supply shortage for Zomacton 10 mg due to COVID-19 travel restrictions causing delays in qualifying new filling lines
    - Ferring recommended that Health Care Practitioners stop prescribing Zomacton 10 mg to new patients and transition current patients and future patients to Zomacton 5 mg or to other treatment options
    - They also requested that HCPs and patients to contact Ferring's ZoGo support services

# Appendices



# Treatment Guidelines - Anticoagulants

## American College of Chest Physicians (ACCP), 2018

- Guidelines suggest no antithrombotic therapy
  - In patients with AF without valvular heart disease, including those with paroxysmal AF, who are at low risk for stroke (CHA<sub>2</sub>DS<sub>2</sub>VASc  $\geq 0$  in males or  $\geq 1$  in females)
- Guidelines recommend oral anticoagulation therapy
  - Patients with AF, including those with paroxysmal AF, without valvular heart disease who have 1 non-sex CHA<sub>2</sub>DS<sub>2</sub>VASc stroke risk factor are suggested to receive oral anticoagulation while patients considered at high risk of stroke (e.g., CHA<sub>2</sub>DS<sub>2</sub>VASc  $\geq 2$  in males or  $\geq 3$  in females)
- Where oral anticoagulation is recommended or suggested, ACCP suggests using a novel oral anticoagulant (NOAC) rather than adjusted-dose vitamin K antagonist therapy

## AHA/ACC/HRS Guidelines, 2019 Update

- All NOACs are now preferred over warfarin in NOAC-eligible patients with AF; exceptions to this are patients with moderate-to-severe mitral stenosis or a mechanical heart valve
  - In NOAC-eligible patients, NOACs were shown to be at least noninferior to warfarin in preventing stroke and systemic embolism and have a lower risk of bleeding
  - Apixaban is preferred in patients with end-stage renal disease or on dialysis while the other NOACs are not recommended in this population due to lack of evidence
  - Edoxaban is now included in the guidelines as an option for stroke prevention
  - The anticoagulant reversal agents idarucizumab (Praxbind) and andexanet alfa (Andexxa) are recommended in the event of life-threatening bleeding or an urgent procedure

# Guidelines- Diabetes Mellitus

- American Diabetes Association (ADA), 2020

- For diabetes technology, an automated insulin delivery system should be considered in adults with T1DM who have the skills to use the device in order to improve time in range and reduce A1C and hypoglycemia (A-rated recommendation)
  - These systems may also be useful to improve glycemia in children (B-rated recommendation)
- Regarding obesity management, ADA states that lorcaserin should no longer be used, as the FDA requested its market withdrawal
- For pharmacologic T2DM therapy, ADA advises to interrupt SGLT2 inhibitor therapy before scheduled surgery to avoid diabetic ketoacidosis, this aligns with label revisions for SGLT2 inhibitors
- For management of CVD in patients with T2DM, ADA advises to consider an SGLT2 inhibitor in patients with Heart Failure (HF) with reduced ejection fraction to reduce risk of worsening HF and CV death

# Guidelines- Diabetes Mellitus

- American College of Cardiology, 2020

- The ACC published an expert consensus decision pathway for CV risk reduction in patients with T2DM
- They identify opportunities to initiate an SGLT2 inhibitor or GLP-1RA with demonstrated CV or renal benefit in patients with T2DM
  - A medication from either class may be initiated in any patient with T2DM and ASCVD at the time of diagnosis of T2DM or ASCVD or any time after diagnosis, including at hospital discharge for ASCVD
  - An agent from either class can also be started in patients with T2DM without established ASCVD but who are at high risk of ASCVD
- In addition, initiation of an SGLT2 inhibitor with demonstrated CV or renal benefit is recommended in patients with Heart Failure and/or diabetic kidney disease
- A GLP-1RA is an alternative in patients with  $eGFR < 30 \text{ ml/min/1.73 m}^2$

- Kidney Disease: Improving Global Outcomes (KDIGO), 2020

- Published its first guidelines on managing diabetes in patients with chronic kidney disease (CKD)
- Key recommendations include:
  - Patients with diabetes, hypertension, and albuminuria should start treatment with an ACEI or ARB
  - Monitor glycemic control using HbA1c in patients with diabetes and CKD
    - Target HbA1c range from  $< 6.5\%$  to  $< 8\%$  in those not on dialysis depending on hypoglycemia risk
  - Metformin and a SGLT2 inhibitor are recommended in patients with  $eGFR \geq 30 \text{ mL/min/1.7 m}^2$ 
    - If glycemic targets are not met, then a long-acting GLP-1 agonist is recommended