Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Washington Pharmacy Advisory Committee Meeting

February 19th, 2020

Umang Patel, Pharm.D.

Agenda Topics

- Overview of Disease State
- Indications
- Dosage & Formulations
- Guideline Updates

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Incretin Mimetics/Enhancer & SGLT2 Inhibitors

Disease State Description - Diabetes Mellitus

- It is estimated that 30 million Americans have diabetes mellitus (DM)
  - Of which, nearly 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

American Diabetes Association, 2018

Guidelines- Diabetes Mellitus

American Diabetes Association (ADA), 2019

- In 2019, ADA Standards of Medical Care in Diabetes continued to include the SGLT2 inhibitors in the management algorithm for T2DM
  - Glycemic Goals
    - The position statement recommends HbA1c < 7% as a reasonable target for most non-pregnant adult patients
    - A target HbA1c of 6% to 6.5% is recommended in most pregnant women
    - **Relaxed HbA1c goals are recommended in some older patients (≥ 65 years) to reduce the risk of hypoglycemia, particularly in those with chronic comorbidities, cognitive impairment, or functional dependence**
    - **Based on a diabetes care decision cycle designed to prevent complications and optimize quality of life, therapy should be individualized based on HbA1c target, impact on weight and hypoglycemia, side effects, the frequency and mode of administration, patient adherence, patient preference, and cost**
  - Antidiabetic therapy for Type 2 Diabetes Mellitus
    - Start with metformin, unless contraindicated
    - In patients *without* atherosclerotic cardiovascular disease (ASCVD), if monotherapy with metformin at a maximum tolerated dose does not achieve or maintain the HbA1c target over 3 months, an oral agent (e.g., sulfonylurea [SU], thiazolidinedione [TZD], dipeptidyl peptidase-4 [DPP-4] inhibitor, sodium-glucose cotransporter-2 [SGLT2] inhibitor), a glucagon-like peptide 1 (GLP-1) receptor agonist, or basal insulin should be added
    - In patients *with* ASCVD, the addition of an agent with known cardiovascular (CV) risk reduction (empagliflozin or liraglutide, class A recommendation; canagliflozin, class C recommendation) is preferred
    - In newly diagnosed T2DM patients with markedly symptomatic and/or elevated blood glucose levels (≥ 300 mg/dL) or HbA1c (≥ 10%), basal insulin therapy, typically plus metformin with or without additional noninsulin agents, should be considered from the beginning
      - If target HbA1c is not achieved after 3 months, then the addition of a rapid-acting mealtime insulin or a GLP-1 agonist, or change to premixed insulin should be considered. Insulin therapy is the treatment of choice for T1DM and T2DM in pregnancy
    - In general, the ADA advises that prescribers use SGLT2 inhibitors with caution in patients at risk for bone fracture

Guidelines- Diabetes Mellitus

American Diabetes Association (ADA), 2019

- Key revisions include for patients with T2DM who require an injectable drug, a GLP-1 receptor agonist is preferred over insulin
- Routine glucose self-monitoring is of limited additional benefit for patients with T2DM not on insulin
- 10-year ASCVD risk should be part of a patient's overall risk assessment
- Criteria for the diagnosis of diabetes was changed to include two abnormal test results from the same sample (e.g., fasting plasma glucose and A1C from same sample)
- Stress the importance of a diabetes care team; revisions to lifestyle management recommendations; a recommendation was added to reevaluate glycemic targets over time; new section on diabetes technology
- Changes made to align with ADA-EASD consensus report

American Diabetes Association (ADA) and European Association for the Study of Diabetes (EASD), 2018

- A decision cycle for patient-centered glycemic management of T2DM to prevent complications and optimize quality of life
  - It includes factors that impact treatment choice, including HbA1c target, the agent's impact on weight and hypoglycemia and its side effect profile, the frequency and mode of administration, and probability of patient adherence
- Additional focus is placed on lifestyle management and diabetes self-management education and support
- Efforts targeting weight loss, including lifestyle, medication, and surgical interventions, are recommended for those with obesity
- The first injectable medication recommended is a GLP-1 receptor agonist
- Patients with CVD
  - A SGLT2 inhibitor or GLP-1 receptor agonist with proven CV benefit is recommended
- CKD or Clinical Heart Failure
  - A SGLT2 inhibitor with proven benefit is recommended
  - If contraindicated, a GLP-1 receptor agonist shown to reduce CKD progression should be used

Disease State Description- Diabetes Mellitus

American Academy of Clinical Endocrinologists (AACE) and American College of Endocrinology (ACE), 2019

- Glycemic Goals
  - Recommend diabetes treatment with a goal HbA1c ≤ 6.5% if it can be reached without substantial hypoglycemia or other adverse effects
  - For patients with concurrent illness and who are at risk of hypoglycemia, a goal HbA1c > 6.5% is appropriate
- Antidiabetic Therapy
  - The initial choice of antidiabetic agent should be based on glycemic profile, HbA1c, body weight, and presence of comorbidities
  - Patients with T2DM and an HbA1c < 7.5%
    - Start with monotherapy, preferably with metformin; monotherapy with a TZD or SU should be used with caution
    - Alternatives to metformin as initial therapy include, GLP-1 receptor agonists, SGLT2 inhibitors, DPP-4 inhibitors, α-glucosidase inhibitors (AGI)
  - Patients withT2DM and an HbA1c ≥ 7.5%
    - Begin with dual therapy with metformin (unless contraindicated) plus a second agent, including a GLP-1 agonist, SGLT2 inhibitor, DPP-4 inhibitor, TZDs, or basal insulin
    - TZDs, basal insulin, and sulfonylureas should be used with caution
  - Patients with an HbA1c > 9% and no symptoms of hyperglycemia
    - Start with maximum doses of 2 antihyperglycemic agents
  - Patients with an HbA1c > 9% with symptoms
    - Begin insulin therapy with or without other agents
  - Pregnant women
    - Preferred treatment for postprandial hyperglycemia in pregnant women is regular or rapid-acting insulin analogs; basal insulin needs can be met with the use of rapid-acting insulin via infusion pump or long-acting insulin
  - The HbA1c should be reassessed every 3 months and failure to improve glycemic control may warrant additional complementary therapy for optimal glycemic control

Disease State Description- Diabetes Mellitus

American Academy of Clinical Endocrinologists (AACE) and American College of Endocrinology (ACE), 2019

- Antidiabetic Therapy (Continued)
  - **Additionally, dapagliflozin demonstrated reduced all-cause mortality and the composite of CV death and HF hospitalization; however, it did not significantly lower the combined risk of CV death and nonfatal MI and stroke**
  - **AACE/ACE also acknowledges the risk of initial renal impairment, hypotension, syncope, and falls due to dehydration related to increased diuresis with SGLT2 inhibitors, and in clinical trials, canagliflozin and dapagliflozin were associated with increased incidence of bone fracture**
  - **Guidelines recommend stopping SGLT2 inhibitor therapy 24 hours before scheduled surgeries and expected metabolically stressful activities, such as extreme sports**
  - **Avoid therapy with SGLT2 inhibitors with insulin in patients on a very low carbohydrate diet or with excess alcohol intake**

Disease State Description- Diabetes Mellitus

American Academy of Clinical Endocrinologists (AACE) and American College of Endocrinology (ACE), 2018

- Insulin Recommendations
  - Insulin is required in all patients with T1DM
  - Advise that insulin therapy can be considered for patients with T2DM, when HbA1c > 8%, or therapy with 2 or more oral antidiabetic agents or GLP-1 therapy fails to achieve target glycemic control
  - When insulin therapy is indicated in patients with T2DM, therapy with long-acting basal insulin analogs (degludec, glargine, and detemir) should be the initial choice in most cases
    - Basal insulin analogs (degludec, detemir, glargine) are preferred over intermediate-acting neutral protamine Hagedorn (NPH) because basal insulin analog provide a relatively flat serum insulin level and are associated with less hypoglycemia
    - Rapid-acting insulin analogs (aspart, glulisine, lispro, inhaled insulin) are preferred over regular insulin for postprandial hyperglycemia because they have a more rapid onset and offset of action and result in less hypoglycemia
  - Basal-bolus insulin therapy is flexible and is recommended for intensive insulin therapy

American College of Physicians (ACP), 2018

- Developed a statement to guide clinicians in selecting targets for pharmacologic treatment of T2DM, including recommending a goal HbA1c level between 7% and 8% in most patients
- State that clinicians should consider deintensifying pharmacologic therapy in patients who achieve HbA1c levels < 6.5%, treat patients to minimize symptoms related to hyperglycemia, and avoid targeting an HbA1c level in patients with a life expectancy < 10 years due to advanced age because the harms outweigh the benefits in this population

World Health Organization (WHO), 2018

- In 2018, the World Health Organization (WHO) released guidelines for treatment intensification in patients with T2DM
- Recommend introduction of human insulin in patients with T2DM who do not achieve glycemic control with metformin and/or a sulfonylurea (SU)
- In adults with T1DM, or adults with T2DM for whom insulin is indicated, human insulin should be used to manage blood glucose; long-acting insulin analogues should be considered for T1DM or adults with T2DM who experience frequent, severe hypoglycemia with human insulin.
- They recommend addition of a DPP-4 inhibitor, a SGLT2 inhibitor, or a TZD if insulin is unsuitable in patients with T2DM who do not achieve glycemic control with metformin and/or a sulfonylurea

Incretin Mimetics/Enhancers - Indications

Drugs	Generic	Indications
Amylin Analogue		
pramlintide (Symlin)	---	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)
Dipeptidyl Peptidase-4 (DPP-4) Enzyme Inhibitors		
alogliptin (Nesina)	---	Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (T2DM)
alogliptin/metformin (Kazano)	---	
alogliptin/pioglitazone (Oseni)	---	
linagliptin (Tradjenta)	---	Adjunct to diet and exercise to improve glycemic control in adults with T2DM
linagliptin/empagliflozin (Glyxambi)	---	Adjunct to diet and exercise to improve glycemic control in adults with T2DM when treatment with both empagliflozin and linagliptin is appropriate Empagliflozin is indicated to reduce the risk of cardiovascular death in adults with T2DM and established cardiovascular disease (CVD); however, effectiveness of linagliptin/empagliflozin on reducing the risk of CV death in adults with T2DM and CVD has not been established
linagliptin/metformin (Jentadueto)	---	Adjunct to diet and exercise to improve glycemic control in adults with T2DM when treatment with both linagliptin and metformin is appropriate
linagliptin/metformin ER (Jentadueto XR)	---	
saxagliptin (Onglyza)	---	Adjunct to diet and exercise to improve glycemic control in adults with T2DM
saxagliptin/dapagliflozin (Qtern)	---	Adjunct to diet and exercise to improve glycemic control in adults with T2DM
saxagliptin/metformin ER (Kombiglyze XR)	---	Adjunct to diet and exercise to improve glycemic control in adults with T2DM when treatment with both saxagliptin and metformin is appropriate
sitagliptin (Januvia)	---	Adjunct to diet and exercise to improve glycemic control in adults with T2DM
sitagliptin/ertugliflozin (Steglujan)	---	Adjunct to diet and exercise to improve glycemic control in adults with T2DM when treatment with both ertugliflozin and sitagliptin is appropriate
sitagliptin/metformin (Janumet)	---	Adjunct to diet and exercise to improve glycemic control in adults with T2DM when treatment with sitagliptin and metformin is appropriate
sitagliptin/metformin ER (Janumet XR)	---	Adjunct to diet and exercise to improve glycemic control in adults with T2DM when treatment with both sitagliptin and metformin ER is appropriate

Incretin Mimetics/Enhancers - Indications

Drugs	Generic	Indications
Glucagon-like Peptide-1 (GLP-1) Receptor Agonists		
dulaglutide (Trulicity)	---	Adjunct to diet and exercise to improve glycemic control in adults with T2DM
exenatide (Byetta)	---	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 T2DM who are not achieving adequate glycemic control on insulin glargine alone
exenatide ER (Bydureon, Bydureon BCise)	---	Adjunct to diet and exercise to improve glycemic control in adults with T2DM
liraglutide (Victoza)	---	Adjunct to diet and exercise to improve glycemic control in adult and pediatric patients ≥ 10 years of age with T2DM Reduce the risk of major adverse cardiovascular events in adults with T2DM and established cardiovascular disease (CVD)
liraglutide/insulin degludec (Xultophy)	---	Adjunct to diet and exercise to improve glycemic control in adults with T2DM
lixisenatide (Adlyxin)	---	Adjunct to diet and exercise to improve glycemic control in adults with T2DM
lixisenatide/insulin glargine (Soliqua)	---	Adjunct to diet and exercise to improve glycemic control in adults with type T2DM
semaglutide (Ozempic)	---	Adjunct to diet and exercise to improve glycemic control in adults with T2DM

Disease State Description - Diabetes Mellitus

- 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

- Studies evaluating the impact of SGLT2 inhibitors on macrovascular complications, (e.g., cardiovascular outcomes) include the EMPA-REG OUTCOME and CANVAS/CANVAS-R
  - **The EMPA-REG OUTCOME trial** reported approximately a one-third relative risk reduction for cardiovascular death, hospitalization due to heart failure, and all-cause death with use of empagliflozin (**Jardiance**) as compared to placebo
  - **The CANVAS and CANVAS-R trials** demonstrated a 14% risk reduction (hazard ratio [HR], 0.86 [95% CI, 0.75 to 0.97]) in first occurrence of major adverse cardiovascular event (MACE) in patients with T2DM treated with canagliflozin (**Invokana**)
  - **Based on the DECLARE–TIMI 58 trial**, **dapagliflozin** did not result in a lower rate of MACE compared to placebo; however, it did lead to a lower incidence of HF-related hospitalizations

American Diabetes Association, 2018

Hypoglycemics, SGLT2 Inhibitors

- FDA MedWatch, August 2018
  - A new MedWatch Safety Alert: SGLT2 (sodium-glucose cotransporter-2) Inhibitors for Diabetes
    - FDA is warning that cases of necrotizing fasciitis of the perineum (Fournier's gangrene) have been reported with SGLT2 inhibitors based on results of a case series
    - Between March 2013 and May 2018, 12 cases of Fournier's gangrene were found in patients taking an SGLT2 inhibitor, resulting in significant medical care needed and 1 death
    - A new warning will be added to the PI of all SGLT2 inhibitors regarding this risk
    - Health Care Practitioners should assess patients for Fournier's gangrene if they present with symptoms consistent with this diagnosis; patients should be treated accordingly immediately

- **Black Box Warnings**
  - **Canagliflozin Containing Products (Invokana, Invokamet, and Invokamet XR)**
    - In patients with type 2 diabetes who have established cardiovascular disease (CVD) or at risk for CVD, canagliflozin has been associated with lower limb amputations, most frequently of the toe and midfoot; some also involved the leg.
    - Before initiating, consider factors that may increase the risk of amputation
    - Monitor patients receiving canagliflozin for infections or ulcers of the lower limbs, and discontinue if these occur

SGLT2 Inhibitors- Indications

Drugs	Generic	Indications
canagliflozin (Invokana)	---	▪ Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (T2DM) ▪ To reduce the risk of major adverse cardiovascular events (MACE) in adults with T2DM and established cardiovascular disease (CVD) ▪ To reduce the risk of end-stage kidney disease, doubling of serum creatinine, cardiovascular death, and hospitalization for heart failure in adults T2DM and diabetic nephropathy with albuminuria > 300 mg/day
canagliflozin/ metformin (Invokamet)	---	▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM when treatment with both canagliflozin and metformin is appropriate ▪ To reduce the risk of MACE in adults with T2DM and established CVD
canagliflozin/ metformin (Invokamet XR)	---	▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM when treatment with both canagliflozin and metformin is appropriate ▪ To reduce the risk of MACE in adults with T2DM and established CVD*
dapagliflozin (Farxiga)	---	▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM ▪ To reduce the risk of hospitalization for heart failure in adults with T2DM and established CVD or multiple cardiovascular (CV) risk factors
dapagliflozin/ metformin ER (Xigduo XR)	---	▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM when treatment with both dapagliflozin and metformin is appropriate ▪ Dapagliflozin is indicated to reduce the risk of hospitalization for heart failure in adults with T2DM and established CVD or multiple CV risk factors.
empagliflozin (Jardiance)	---	▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM ▪ To reduce the risk of cardiovascular death in adults with T2DM and established CVD
empagliflozin/ metformin (Synjardy)	---	▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM when treatment with both empagliflozin and metformin is appropriate ▪ To reduce the risk of cardiovascular death in adults with T2DM and established CVD
empagliflozin/ metformin ER (Synjardy XR)	---	▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM when both empagliflozin and metformin is appropriate ▪ To reduce the risk of cardiovascular death in adults with T2DM and established CVD
ertugliflozin (Steglatro)	---	▪ Adjunct to diet and exercise to improve glycemic control in adults T2DM
ertugliflozin/ metformin (Segluromet)	---	▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM who are not adequately controlled on a regimen containing ertugliflozin or metformin, or in patients who are already treated with both ertugliflozin and metformin

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Insulin and Related Agents

Disease State Description - Diabetes Mellitus

- 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

- The World Health Organization (WHO), 2018
  - Released guidelines regarding diabetes treatment intensification
  - WHO recommends introduction of human insulin in patients with T2DM who do not achieve glycemic control with metformin and/or a sulfonylurea (SU)
  - In adults with T1DM, or adults with T2DM for whom insulin is indicated, human insulin should be used to manage blood glucose; long-acting insulin analogues should be considered for T1DM or adults with T2DM who experience frequent, severe hypoglycemia with human insulin

Insulin & Related Agents - Indications

Drugs	Generic	Indications
Rapid-Acting Insulins		
human insulin inhalation powder (Afrezza)	---	To improve glycemic control in adults with diabetes mellitus
insulin aspart (Fiasp)	---	To improve glycemic control in adults with diabetes mellitus
insulin aspart (Novolog)	---	To improve glycemic control in adults and children with diabetes mellitus
insulin glulisine (Apidra)	---	To improve glycemic control in adults and children with diabetes mellitus
insulin lispro (Admelog, Humalog, Humalog Junior)	X	To improve glycemic control in adults and children 3 years of age and older with T1DM and adults with T2DM
Regular (R) Insulins		
human insulin (Humulin R)	---	To improve glycemic control in adults and children with diabetes mellitus Human insulin 500 U/mL (Humulin R U-500) is for use in patients requiring daily doses > 200 units
human insulin (Novolin R)	---	
Intermediate (N) Insulins		
human insulin NPH (Humulin N)	---	To improve glycemic control in adults and children with diabetes mellitus
human insulin NPH (Novolin N)	---	
Long-Acting Insulins		
insulin degludec (Tresiba)	---	To improve glycemic control in patients 1 year of age or older with diabetes mellitus‡
insulin detemir (Levemir)	---	To improve glycemic control in adults and children with diabetes mellitus
insulin glargine U-100§ (Basaglar)	---	To improve glycemic control in adults and children with T1DM and adults with T2DM
insulin glargine U-100 (Lantus)	---	
insulin glargine U-300 (Toujeo)	---	To improve glycemic control in adults with diabetes mellitus
Rapid/Intermediate-Acting Combination Insulins		
insulin aspart 70/30 (Novolog Mix)	---	To improve glycemic control in patients with diabetes mellitus
insulin lispro 50/50, 75/25 (Humalog Mix)	---	For the treatment of patients with diabetes mellitus for the control of hyperglycemia
Regular/Intermediate-Acting Combination Insulins		
human insulin 70/30 (Humulin)	---	To improve glycemic control in adults with diabetes mellitus
human insulin 70/30 (Novolin)	---	

Insulin & Related Agents

- FDA Statement, December 2019
  - The FDA has published a statement regarding the pathway for approval of "chemically synthesized polypeptides"
  - In March 2020, the majority of protein products (including all current insulin products) will have the potential for biosimilar and interchangeable products to increase competition through FDA approval under abbreviated pathways
  - However, products that are deemed "chemically synthesized polypeptides" are not eligible for the abbreviated approval pathways utilized for biosimilar or interchangeable products
  - The statement addresses how removal of this exclusion would allow for chemically synthesized follow-on insulins and other products to become approved through abbreviated pathways as well
- FDA Safety Communication, September 2019
  - The FDA issued a Safety Communication regarding the use of pen needles when injecting medicine
  - The FDA has received reports of patients using standard pen needles to administer insulin without removing the inner needle cover, resulting in the insulin not being injected and the risk for hyperglycemia
    - This included 1 case that resulted in hospitalization and death
  - The FDA advised healthcare providers (HCP) to instruct patients on the proper use of pen needles for medication delivery and ensure that the patient can demonstrate proper technique
    - At time of dispensing, HCPs should remind patients of the type of pen needle and how to use it
- FDA Safety Communication, May 2019
  - The FDA also issued a Safety Communication regarding the use of devices for diabetes management that are unauthorized for sale in the US. Devices that are unauthorized have not received FDA review and approval to assure their safety and efficacy
  - As a result, use of these devices could lead to incorrect blood glucose level measurements and/or an improper dose of insulin which could result in serious or potentially life-threatening medical complications
  - In addition, combining devices not appropriate for use with other devices also should be avoided
  - The FDA recommends that patients only use diabetes management devices that have received authorization from the FDA for sale in the US

Antidiabetics

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

Antidiabetics

- **Recommendation:**
  - All products in the drug class listed on slide 19 are considered safe and efficacious for their medically accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA.
  - Products in this class may require prior authorization to determine medical necessity.
  - All non-preferred products require a trial of two preferred products before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.

Antidiabetics

- **Motion:** I move that all products in the drug classes listed on slide 19 are considered safe and efficacious for their medically accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA. Products in this class may require prior authorization to determine medical necessity. All non-preferred products require a trial of two preferred products before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.
- **Motion: Huynh**
- **2nd: Park**

Antidiabetics: Insulin

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

Antidiabetics: Insulin

- **Recommendation:**
  - All products in the drug class listed on slide 22 are considered safe and efficacious for their medically accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA.
  - Products in this class may require prior authorization to determine medical necessity.
  - All non-preferred products require a trial of two preferred products before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.

Antidiabetics: Insulin

- **Motion:** I move that all products in the drug classes listed on slide 22 are considered safe and efficacious for their medically accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA. Products in this class may require prior authorization to determine medical necessity. All non-preferred products require a trial of two preferred products before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.
- **Motion: Storhaug**
- **2nd: Flatebo**

Antidiabetics: SGLT2 Inhibitors

- **Recommendation:**
  - All products in the Antidiabetics: SGLT2 Inhibitors drug class are considered safe and efficacious for their medically accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA.
  - All non-preferred products require a trial of two preferred products with the same indication before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.

Antidiabetics: SGLT2 Inhibitors

- **Motion:** I move that all products in the Antidiabetics: SGLT2 Inhibitors drug class are considered safe and efficacious for their medically accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA. All non-preferred products require a trial of two preferred products with the same indication before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.
- **Motion: Flatebo**
- **2nd: Huynh**

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Thiazolidinediones (TZDs)

Thiazolidinediones (TZDs) – Indications, Dosing & Availability

Drugs	Generic	Indications
TZDs		
pioglitazone (Actos)	X	Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (T2DM)
rosiglitazone (Avandia)	---	Adjunct to diet and exercise to improve glycemic control in adults with T2DM
TZDs and glimepiride		
pioglitazone/ glimepiride (Duetact)	X	Adjunct to diet and exercise to improve glycemic control in adults with T2DM who are already treated with a thiazolidinedione and sulfonylurea combination or who are not adequately controlled on either agent alone
TZDs and metformin		
pioglitazone/ metformin (Actoplus Met)	X	Adjunct to diet and exercise to improve glycemic control in adults with T2DM who are already treated with a thiazolidinedione and metformin combination or who are not adequately controlled on either agent alone
pioglitazone/ metformin extended-release (Actoplus Met XR)	---	Adjunct to diet and exercise to improve glycemic control in adults with T2DM who are already treated with a thiazolidinedione and metformin combination or who are not adequately controlled on either agent alone

Drugs	Initial Dose	Maintenance Dose	Availability
TZDs			
pioglitazone (Actos)	15 mg to 30 mg daily	15 mg to 45 mg daily	15 mg, 30 mg, 45 mg tablets
rosiglitazone (Avandia)	4 mg daily OR 2 mg twice daily	2 mg to 4 mg twice daily OR 8 mg daily	2 mg, 4 mg tablets
TZDs and glimepiride			
pioglitazone/ glimepiride (Duetact)	Prior therapy with glimepiride or pioglitazone: 30/2 mg or 30/4 mg once daily with the first meal of the day Maximum daily dose: 45/8 mg		30/2 mg, 30/4 mg tablets
TZDs and metformin			
pioglitazone/ metformin (Actoplus Met)	15/500 mg or 15/850 mg tablets once or twice daily with food Max daily dose: 45 mg/2,550 mg administered in divided doses with food		15/500 mg, 15/850 mg tablets
pioglitazone/ metformin extended-release (Actoplus Met XR)	15/1,000 mg or 30/1,000 mg tablets once daily with evening meal Max daily dose: 45/2,000 mg administered once daily with evening meal		15/1,000 mg, 30/1,000 mg tablets

Thiazolidinediones (TZDs)

- FDA Safety Communication - Bladder Cancer Risk
  - In 2016, the FDA issued an updated safety communication concluding that all pioglitazone-containing products may be linked to an increase risk of bladder cancer
    - This is a follow-up to the initial FDA safety announcement in 2010 that reported a possible increased risk of bladder cancer with pioglitazone when used for over 1 year
  - The FDA urged patients taking pioglitazone to contact a medical professional if they experience signs or symptoms associated with bladder cancer such as blood in urine or pain while urinating
  - Also, in 2016 the results from an observational cohort study of over 145,000 patients initiated on antidiabetic medications over a 13 year period suggest that the risk of bladder cancer increases with duration of time and the amount or dose of pioglitazone used
    - However, an increased risk of bladder cancer was not associated with rosiglitazone use
  - Consequently, use of pioglitazone is not recommended in patients with active bladder cancer and should be used with caution in those with a prior history of bladder cancer, considering the benefits of glycemic control versus unknown risks for cancer recurrence

Antidiabetics: Thiazolidinediones

- **Recommendation:**
  - All products in the Antidiabetics: Thiazolidinediones drug class are considered safe and efficacious for their medically accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA.
  - All non-preferred products require a trial of two preferred products with the same indication before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.

Antidiabetics: Thiazolidinediones

- **Motion:** I move that all products in the Antidiabetics: Thiazolidinediones drug class are considered safe and efficacious for their medically accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA. All non-preferred products require a trial of two preferred products with the same indication before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.
- **Motion: Park**
- **2nd: Huynh**

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Pancreatic Enzymes

Disease State Description – Pancreatic Enzymes

- Pancreas
  - The exocrine functions of the pancreas include the secretion of pancreatic enzymes necessary for digestion
  - Pancreatic secretions also neutralize gastric acid in the duodenum and achieve an appropriate pH for maintaining the activity of the enzymes
  - When this pancreatic function is lost, supplementation of the pancreatic enzymes is needed
  - Conditions such as cystic fibrosis (CF), chronic pancreatitis, pancreatic tumors, and absence of all or a part of the pancreas are associated with a lack of pancreatic enzymes in the body

- Cystic Fibrosis
  - Reduced pancreatic enzyme effects occur due to thickened secretions in the gastrointestinal (GI) tract, specifically the pancreas
  - Pancreatic enzymes are unable to move into the duodenum, leading to malabsorption of nutrients and malnutrition
  - This is the main cause of poor growth, fatty diarrhea, and deficiency in fat-soluble vitamins in this population

- Pancreatic Enzymes
  - Supplemental pancreatic enzymes are available in a variety of formulations and strengths
  - All formulations are measured by their content of amylase, lipase, and protease
  - In order to avoid gastric inactivation, enteric coatings and buffering may be used to deliver enzymes to the intestine
  - Historically, pancreatic enzyme products were available over-the-counter (OTC)
    - However, due to reports of problems associated with their use, such as intestinal stricture and lack of therapeutic effect, the Food and Drug Administration (FDA) announced that all exocrine pancreatic insufficiency drug products are new drugs and announced the conditions for continued marketing of these drug products

Pancreatic Enzymes - Indications

Product	Generic	Formulation	Amylase (Units)	Lipase (Units)	Protease (Units)	Notes
Creon 3,000	---	Capsule (EC, DR)	15,000	3,000	9,500	For infants, capsule contents may be administered directly to the mouth or with a small amount of applesauce
Creon 6,000			30,000	6,000	19,000	Capsule can be opened for patients unable to swallow
Creon 12,000			60,000	12,000	38,000	
Creon 24,000			120,000	24,000	76,000	
Creon 36,000			180,000	36,000	114,000	
Pancreaze	---	Capsule (DR)	10,850	2,600	6,200	Capsule can be opened for patients unable to swallow For infants, capsule contents may be administered directly to the mouth or with a small amount of acidic food such as applesauce. Contents should be followed by breast milk or formula but may not be administered directly into breast milk or formula
			24,600	4,200	14,200	
			61,500	10,500	35,500	
			98,400	16,800	56,800	
			83,900	21,000	54,700	
Pertzye 4,000	---	Capsule (DR)	15,125	4,000	14,375	Only pancreatic enzyme containing bicarbonate-buffered enteric-coated microspheres Capsule can be swallowed whole; for patients unable to swallow capsules can be opened and administered orally or via a gastrostomy tube Pertzye 400 (infants up to 12 months): For infants, capsule contents may be administered directly to the mouth or with a small amount of acidic food with a pH ≤ 4.5, such as applesauce. Contents should be followed by breast milk or formula but may not be administered directly into breast milk or formula.
Pertzye 8,000			30,250	8,000	28,750	
Pertzye 16,000			60,500	16,000	57,500	
Pertzye 24,000			90,750	24,000	86,250	

Pancreatic Enzymes - Indications

Product	Manufacturer	Formulation	Amylase (Units)	Lipase (Units)	Protease (Units)	Notes
Viokace 10,440	---	Tablet	39,150	10,440	39,150	Tablets should be swallowed whole and not crushed Should not be used in pediatric patients; may result in tablet degradation in the gastric environment which may result in suboptimal growth
Viokace 20,880			78,300	20,880	78,300	
Zenpep 3,000	---	Capsule (EC,DR)	14,000	3,000	10,000	For infants, capsule contents may be administered directly to the mouth or with a small amount of acidic food with a pH ≤ 4.5 such as applesauce
Zenpep 5,000			24,000	5,000	17,000	Capsule can be opened for patients unable to swallow
Zenpep 10,000			42,000	10,000	32,000	
Zenpep 15,000			63,000	15,000	47,000	
Zenpep 20,000			84,000	20,000	63,000	
Zenpep 25,000			105,000	25,000	79,000	
Zenpep 40,000			168,000	40,000	126,000	

Digestive Aids: Pancreatic Enzymes

- **Recommendation:**
  - All products in the Digestive Aids: Pancreatic Enzymes drug class are considered safe and efficacious for their medically accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA.
  - All non-preferred products require a trial of two preferred products with the same indication before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.

Digestive Aids: Pancreatic Enzymes

- **Motion:** I move that all products in the Digestive Aids: Pancreatic Enzymes drug class are considered safe and efficacious for their medically accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA. All non-preferred products require a trial of two preferred products with the same indication before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.
- **Motion: Huynh**
- **2nd: Schwilke**

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Growth Hormones

Disease State Description and Guidelines - Growth Hormone

- 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

Pediatric Endocrine Society, 2017

- Prader-Willi syndrome (PWS)
  - A genetic disorder in which several genes on chromosome 15 are missing or unexpressed on the paternal chromosome
  - PWS is characterized by hyperphagia and food preoccupations, as well as small stature and mental retardation
  - The major manifestations of PWS are neurobehavioral and endocrine abnormalities, hypothalamic obesity, hypotonia, short stature, developmental delay, and aspects of hypothalamic endocrine dysfunction and pubertal delay or absence
  - In some cases, the impaired GH secretion (which can persist into adulthood) may be the result of hypothalamic dysfunction
  - Daily growth hormone injections support linear growth, increase muscle mass, and may lessen food preoccupation and weight gain in patients with PWS

Prader-Willi Syndrome Association (USA), 2011

Disease State Description and Guidelines - Growth Hormone

- Chronic Renal Insufficiency
  - Children with CRI may have difficulty attaining a normal height and weight for several reasons, including malnutrition, renal osteodystrophy, electrolyte, calcium and vitamin D imbalances, inadequate use of protein by the body, and abnormalities in the growth hormone (GH)-insulin-like growth factor (IGF)-1 axis
- Babies born small for gestational age (SGA)
  - Defined as babies with birth weights that fall below the tenth percentile for that gestational age. Typically, intrauterine growth retardation is the causative factor
  - Although the majority of these children catch up in height to normal range during the first 2 years of life, approximately 10% of SGA children fail to exhibit catch-up growth by age 2 years
  - Growth hormone levels in these children may be low or within normal range. Decreased growth may be due to insensitivity to growth hormone as well as low IGF-1 levels
  - It is thought that administering exogenous GH may overcome GH insensitivity
- Short stature homeobox gene (SHOX)
  - A gene on the X and Y chromosomes that control the formation of many body structures, including the growth and maturation of bones in the arms and legs
  - Patients with SHOX deficiency (gene mutation or present in only 1 copy) may present with a broad phenotypic spectrum ranging from isolated short stature with no distinguishing clinical features to short stature with moderate to severe skeletal dysplasia
  - Approximately 1% to 4% of patients with clinical features consistent with idiopathic short stature may test positive for SHOX deficiency

Disease State Description and Guidelines - Growth Hormone

- Turner syndrome (TS)
  - In patients with TS, female sexual characteristics are present but are underdeveloped due to several chromosomal abnormalities
  - At least 95% of all patients with TS have short stature
  - Short stature in patients with TS is characterized by mild intrauterine growth retardation, slow growth during infancy, delayed onset of the childhood component of growth, and growth failure during childhood and adolescence
  - These factors lead to a diminished final height which can be positively affected by growth hormone therapy

Endocrine Society, 2003

- Idiopathic short stature (ISS)
  - A condition in which the height of an individual is more than a 2 standard deviation score (SDS) below the corresponding mean height for a given age, sex, and population group without evidence of systemic, endocrine, nutritional, or chromosomal abnormalities
  - The PES defines ISS as height standard deviation score ≤ -2.25 with a predicted adult height less than the normal range (63 inches in men; 59 inches in women)
  - Specifically, children with ISS have normal birth weight and are GH sufficient

Pediatric Endocrine Society, 2008

Disease State Description and Guidelines - Growth Hormone

- Short Bowel Syndrome (SBS)
  - A malabsorption disorder caused by either the surgical removal of the small intestine or the loss of its absorptive function due to various diseases. Intestinal mucosa contains receptors for growth hormone and for IGF-1, which is known to mediate many of the cellular actions of growth hormone
  - In human clinical studies, the administration of growth hormone enhanced the transmucosal transport of water, electrolytes, and nutrients
  - Zorbtive is indicated for the treatment of SBS in patients receiving specialized nutritional support

- Noonan Syndrome
  - A congenital disorder that includes heart malformation, short stature, indentation of the chest, learning disabilities, impaired blood clotting, and a certain configuration of facial features
  - Short stature is present in as many as 80% of patients
  - Growth hormone has been used successfully to correct short stature associated with the disorder

Pediatric Endocrine Society, 2008

Growth Hormone - Indications

Drug	Generic	Indication(s)				
		GHD (Pediatric/ Adult)	Turner Syndrome	SGA	ISS	Other
Genotropin	---	X	X	X	X	PWS
Humatrope	---	X	X	X	X	SHOX
Norditropin	---	X	X	X	X	Noonan Syndrome, PWS
Nutropin AQ NuSpin	---	X	X	--	X	CRI
Omnitrope	---	X	X	X	X	PWS
Saizen	---	X	--	--	--	--
Serostim	---	--	--	--	--	HIV wasting or cachexia to increase lean body mass and weight, and improve physical endurance
Zomacton	---	X	X	X	X	SHOX
Zorbtive	---	--	--	--	--	SBS

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Growth Factors

Overview of Disease State – Growth Factors

- Growth hormone insensitivity or insulin-like growth factor-1 (IGF-1) deficiency refers to a variety of disorders characterized by the resistance to growth hormone
  - Growth hormone insensitivity can be defined by a deficiency in the production of growth hormone or peripheral action of IGF-1 on linear growth
  - Severe primary IGF-1 deficiency is due to a mutation of the growth hormone receptor or post-growth hormone receptor signaling
  - Severe primary IGF-1 deficiency is also characterized by the development of growth hormone inactivating antibodies in pediatric patients with growth hormone gene deletion
    - Patients are considered to have severe primary IGF-1 deficiency when the following criteria are met: height standard deviation score ≤ -3, basal IGF-1 standard deviation score ≤ -3, and normal or elevated growth hormone

- HIV Lipodystrophy
  - Soon after combination antiretroviral therapy was found effective in treating HIV infected patients, adverse side effects from the medications were reported, including metabolic changes, morphological abnormalities and lipodystrophy
  - HIV lipodystrophy is found in patients on highly active anti-retroviral therapy (HAART)
  - Patients with HIV lipodystrophy were described as having a loss of subcutaneous fat in limbs, face, and buttocks and an accumulation of fat in other areas of the body including the abdominal viscera
  - Patients who have increased visceral abdominal fat and waist circumference are at an increased risk for metabolic syndrome, cardiovascular disease, atherosclerosis, and diabetes mellitus

Growth Factors – Indications, Dosing, & Availability

Drugs	Generic	Indications
mecasermin [rDNA origin] injection (Increlex)	---	Treatment for growth failure in children with severe primary IGF-1 deficiency or with growth hormone (GH) gene deletion who have developed neutralizing antibodies to GH
tesamorelin (Egrifta)	---	Growth hormone releasing factor (GRF) analog indicated for the reduction of excess abdominal fat in HIV-infected patients with lipodystrophy

Drugs	Dosage	Availability
mecasermin [rDNA origin] injection (Increlex)	Recommended dose: 0.04 to 0.08 mg/kg twice daily given subcutaneously If tolerated well after 1 week, the dose may be increased by 0.04 mg/ kg per dose to a maximum of 0.12 mg/kg given twice daily	Solution for injection: 40 mg/vial (10 mg per mL)
tesamorelin (Egrifta)	Recommended dose: 2 mg injected subcutaneously once daily	Lyophilized powder for injection: 1 mg tesamorelin/vial Diluent (sterile water for injection, USP 10 ml)

Growth Factors – Guidelines

- Severe IGF-1 Deficiency/Growth Hormone Gene Deletion
  - Increlex is the only available product approved for the indication of long-term treatment of growth failure in pediatric patients with severe primary IGF-1 deficiency or with growth hormone gene deletion with development of neutralizing antibodies to growth hormone
  - Patients with diagnoses that are not growth hormone deficient and will not respond well to exogenous growth hormone
  - Likewise, mecasermin (Increlex) should not be used as a substitute for patients who require growth hormone therapy
  - Increlex should not be used in patients with secondary forms of IGF-1 deficiency and all thyroid and nutritional issues should be corrected prior to initiating Increlex therapy
  - Increlex should not be used for weight loss management

- HIV Lipodystrophy
  - Recombinant human growth hormone (rhGH) has been used with success in patients with AIDS-related wasting syndrome since it has been shown to improve muscle mass
  - However, studies have shown rhGH causes a reduction in visceral adiposity but supra-physiologic levels of IGF-1 and symptoms of excess growth hormone occurred causing treatment cessation
  - Egrifta offers a specific treatment option for the reduction of excessive abdominal fat in HIV patients with lipodystrophy as it appears to target the visceral fat compartment with little effect on subcutaneous fat or fat in the limbs

Endocrine and Metabolic Agents

- Growth Hormones
- Growth Hormone Releasing Hormones (GHRH)

- **Recommendation:**
  - All products in the drug classes listed above are considered safe and efficacious for their medically accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA.
  - Products in this class may require prior authorization to determine medical necessity.
  - All non-preferred products require a trial of two preferred products with the same indication before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.

Endocrine and Metabolic Agents

- Growth Hormones
- Growth Hormone Releasing Hormones (GHRH)

- **Motion:** All products in the drug classes listed above are considered safe and efficacious for their medically accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA. Products in this class may require prior authorization to determine medical necessity. All non-preferred products require a trial of two preferred products in their respective class before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.
- **Motion: Flatebo**
- **2nd: Lee**

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Ulcerative Colitis

Disease State Description - Ulcerative Colitis

- Ulcerative colitis (UC) is a chronic inflammatory disease primarily affecting the colon and rectum

- UC affects approximately 1,000,000 people in the United States (US) and the incidence continues to increase worldwide. The Center for Disease Control and Prevention (CDC) estimates the current prevalence of UC at 238 per 100,000 adults
  - UC may present at any age, but onset typically peaks between 15 and 30 years of age

- The disease is characterized by superficial infiltration of the bowel wall by inflammatory white cells, resulting in multiple mucosal ulcerations and crypt abscesses

- The predominant symptom of UC is diarrhea, which is usually associated with blood in the stool
  - Additional symptoms may include pain in the lower quadrant or rectum along with systemic features, including fever, malaise, and weight loss (which are more common if a greater portion of the colon is affected)
  - The initial attack of UC may be fulminant with bloody diarrhea, but the disease more commonly begins indolently, with non-bloody diarrhea progressing to bloody diarrhea
  - UC can present initially with any extent of anatomic involvement ranging from disease confined to the rectum to the entire large intestine (pancolitis)
  - Most commonly, UC follows a chronic intermittent course with long periods of quiescence interspersed with acute attacks lasting weeks to months. However, a significant percentage of patients suffer a chronic continuous course

Centers for Disease Control and Prevention, 2015

Disease State Description - Ulcerative Colitis

- Aminosalicylates remain first-line treatment options for mild to moderate active UC with 90% of patients treated with this class shortly after disease diagnosis
  - Mesalamine agents currently are available in oral and rectal formulations
  - The rectal products achieve high luminal concentrations of the active component, 5-aminosalicylic acid (5-ASA, mesalamine), while minimizing adverse events from systemic absorption
  - Several aminosalicylates are available and differ only in mode of distribution throughout the small intestine and colon
- Second-line therapy with a course of oral or rectal steroids, such as budesonide (Uceris), is indicated for induction therapy in patients with mild to moderate disease who do not respond to oral and rectal mesalamine agents or in patients with moderate to severe disease
  - Oral and rectal corticosteroids are not intended for maintenance therapy and can lead to serious adverse effects with long-term use
- For active ulcerative proctitis, an effective and rapid-acting approach is nightly administration of mesalamine retention enemas or suppositories, often supplemented with an oral aminosalicylate
  - Corticosteroid enemas can also be used
  - Another approach to proctitis is administration of an oral aminosalicylate alone, although therapeutic response may not be evident for 3 to 4 weeks
- In patients with severe or refractory UC symptoms, oral corticosteroids are indicated
  - Corticosteroids, while highly efficacious in short-term use, have numerous adverse effects, especially in the elderly, which preclude long-term use
  - Patients who respond to oral prednisone and can be fully withdrawn from the drug over a period 60 days and should be maintained on an aminosalicylate
- Patients with corticosteroid-dependent or corticosteroid-refractory disease, immunosuppression with azathioprine or mercaptopurine may prevent colectomy
  - Several injectable tumor necrosis factor (TNF)-inhibitors (infliximab [Remicade], adalimumab [Humira], and golimumab [Simponi Aria]) are approved for inducing and maintaining clinical response/remission in patients with moderate to severe active UC who fail conventional therapy or who are considered at high-risk for colectomy
  - Vedolizumab (Entyvio) is an intravenous (IV) integrin receptor antagonist approved for inducing and improving clinical response/remission in patients with moderate to severe active UC who showed an inadequate response to or were intolerant of treatment with a TNF-inhibitor, immunomodulator, or corticosteroid
  - The oral Janus kinase inhibitor tofacitinib (Xeljanz, Xeljanz XR) is also indicated for moderately to severely active UC

Treatment Guidelines- ACG, 2019

The 2019 American College of Gastroenterology (ACG)

- Clinical guidelines state treatment selection for UC should be based on not only inflammatory activity but also disease prognosis
- In patients with:
- Mildly active proctitis and distal UC are treated with rectal 5-ASA
    - Oral 5-ASA agents are used if needed as add-on for distal UC or to treat extensive disease
- Mildly active UC who are intolerant or nonresponsive to 5-ASA, oral budesonide MMX is recommended to induce remission
- Moderately active UC should be treated with oral 5-ASA or budesonide MMX
- Moderately to severely active UC, the ACG recommends induction of remission using systemic corticosteroids, anti-TNF therapy, vedolizumab, or tofacitinib
    - With the exception of corticosteroids, the medication used to induce remission should be continued as maintenance therapy
    - The ACG states that complimentary therapies such as probiotics, curcumin, and fecal microbiota transplantation (FMT) require further study and clarification of treatment/end points

Treatment Guidelines- AGA, 2019

The 2019 American Gastroenterology Association (AGA)

- Treatment of mild to moderate UC recommend standard-dose mesalamine (2 to 3 g/day) or diazo-bonded 5-ASA (balsalazide and olsalazine) for induction and maintenance treatment
- High-dose oral mesalamine combined with rectal 5-ASA may be required for patients with suboptimal response to standard-dose therapy, or in those with moderate or extensive disease
  - Oral prednisone or budesonide MMX may be added in those refractory to optimized oral and rectal 5-ASA
- Proctosigmoiditis or proctitis can be treated with topical mesalamine rather than oral 5-ASA
  - In patients with suboptimal response or intolerance to rectal mesalamine, rectal corticosteroids (enema or foam) may be used
- Patients who do not respond adequately to the therapies as outlined above may need to escalate to systemic corticosteroids, immunomodulators, or biologic therapies
- The guidelines make no recommendations regarding the use of probiotics, curcumin, and FMT
  - While they appear to be safe, their use could delay initiation of proven efficacious treatments and potentially lead to worsening symptoms or complications

Treatment Guidelines- AAFP, 2013

- American Academy of Family Physicians (AAFP)
  - State that the incidence of colon cancer is increased with UC and achieving remission is critical in order to reduce a patient's lifetime risk
  - First-line treatment
    - Recommend 5-ASA (mesalamine) via suppository or enema for patients with proctitis or proctosigmoiditis, respectively
      - If unable to tolerate rectally administered 5-ASA therapy, may try oral preparations, although response times and remission rates are not as favorable. Oral 5-ASA is effective in patients with active mild to moderate UC extending from the proximal to the sigmoid colon
      - A topical 5-ASA may be added if an oral formulation alone is inadequate
      - A short-term course of oral corticosteroids may be appropriate if oral plus topical 5-ASA therapy is not effective or if a more rapid response is desired
      - Prednisone is given in dosages of 40 to 60 mg per day, with the full-dose continued until symptoms are completely controlled (usually 10 to 14 days) followed by a gradual taper
      - Long-term steroid use is not recommended for chronic maintenance due to significant side effects
  - To prevent relapse
    - Oral probiotics (*Lactobacillus* GG and *Escherichia coli* Nissle 1917) have been shown to be effective
    - The agent that is used to maintain remission is usually the same as that used to achieve remission
  - Symptoms refractory to oral mesalamine or oral corticosteroids may be treated with intravenous infliximab (Remicade)
  - Azathioprine is generally not recommended for active UC; however, it may be considered in patients who require corticosteroids or cyclosporine to induce remission
  - Budesonide (Uceris) was first FDA approved in January 2013 and is not specifically addressed in these guidelines

Ulcerative Colitis Agents - Indications

Drug	Generic	Indication(s)	
		Treatment	Maintenance
Oral Prodrug Forms			
balsalazide (Colazal)	**X**	Mild to moderately active ulcerative colitis (UC) in patients ≥ 5 years	---
balsalazide (Giazo)	**---**	Mild to moderately active UC in male patients ≥ 18 years	---
olsalazine (Dipentum)	**---**	---	Maintenance of remission of UC in patients intolerant of sulfasalazine
sulfasalazine (Azulfidine, Azulfidine EN-tabs)	**X**	Mild to moderately active UC Adjunctive therapy in severe UC	Maintenance of remission of UC
		Other: Enteric-coated tablets are indicated in patients with UC who cannot take uncoated sulfasalazine tablets because of gastrointestinal (GI) intolerance Treatment of rheumatoid arthritis that has not responded adequately to salicylates or other nonsteroidal anti-inflammatory agents (NSAIDs) Treatment of pediatric patients with polyarticular juvenile rheumatoid arthritis who have not responded adequately to salicylates or other NSAIDs	

Ulcerative Colitis Agents - Indications

Drug	Generic	Indication(s)	
		Treatment	Maintenance
Oral Delayed-Release Forms			
mesalamine delayed-release tablets (Asacol HD)	X	Moderately active UC	---
mesalamine delayed-release capsules (Delzicol)	---	Mild to moderately active UC in patients ≥ 5 years	Maintenance of remission of UC in adults
mesalamine MMX delayed-release tablets (Lialda)	X	Mild to moderately active UC	Maintenance of remission of UC
mesalamine extended-release capsules (Pentasa)	---	Mild to moderately active UC	--
mesalamine extended-release capsules (Apriso)	---	--	Maintenance of remission of UC in adults
Rectal Forms			
budesonide rectal foam (Uceris)	---	Mild to moderate active UC extending 40 cm from the anal verge	--
mesalamine enemas (Rowasa)	X	Mild to moderately active distal UC, proctosigmoiditis, or proctitis	--
mesalamine enemas sulfite-free (sfRowasa)	---	Mild to moderately active distal UC, proctosigmoiditis, or proctitis	--
mesalamine suppositories (Canasa)	X	Active ulcerative proctitis	--
Oral Corticosteroids			
budesonide extended-release tablets (Uceris)	X	Mild to moderately active UC	--

Gastrointestinal Agents: Inflammatory Bowel Agents

- **Recommendation:**
  - All products in the Gastrointestinal Agents: Inflammatory Bowel Agents drug class are considered safe and efficacious for their medically accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA.
  - All non-preferred products require a trial of two preferred products with the same indication before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.

Gastrointestinal Agents: Inflammatory Bowel Agents

- **Motion:** I move that all products in the Gastrointestinal Agents: Inflammatory Bowel Agents drug class are considered safe and efficacious for their medically accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA. All non-preferred products require a trial of two preferred products with the same indication before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.
- **Motion: Brown**
- **2nd: Flatebo**

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Cystic Fibrosis, Oral

Disease State Description - Cystic Fibrosis

- Cystic Fibrosis (CF) is a serious autosomal recessive multiorgan disorder
- Affects ~30,000 children and adults in the U.S. and is the most common fatal genetic disease in Caucasians
  - Children are anticipated to live to approximately 40 years of age with current treatments
  - In 2017, adults comprised approximately 53.5% of the CF population, while in 1987, they comprised approximately 29.8%
- 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, 2018

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
- Treatment of CF is mainly dependent on the type and severity of CF symptoms, and this can differ widely from person to person
  - Medication therapy for respiratory complications primarily includes antibiotics (oral, intravenous [IV], inhaled) as well as other treatments for airway clearance (e.g., bronchodilators, anti-inflammatory agents, and mucolytics, such as dornase alfa [Pulmozyme])
  - CFTR modulators (potentiators or correctors) are the newest class of medications available for this disease and improve chloride ion transport abnormalities
    - The FDA approved ivacaftor (Kalydeco) in 2012, lumacaftor/ivacaftor (Orkambi) in 2015, and tezacaftor/ivacaftor (Symdeko) in 2018. Each agent is approved for different CFTR genotypes
    - If a patient's genotype is unknown, an FDA-approved CF mutation test should be used to detect the presence of a CFTR mutation
    - This should be followed by verification, if needed, based on the results of the mutation test
    - Use of these agents does not eliminate the need for other symptomatic and preventative therapy; rather, their use is intended to improve the functionality of the CFTR protein

Guidelines - Cystic Fibrosis

- 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 lease one *G551d CFTR* mutation to improve lung function and quality of life and to reduce exacerbations
  - Ivacaftor had not received approval in younger patients or the additional mutations at the time of publication. Likewise, lumacaftor/ivacaftor and tezacaftor/ivacaftor were not approved in 2013. The CFF has also published guidelines on newborn screening, diagnosis, nutritional care, gastrointestinal (GI) related issues, other respiratory care, infection control, and general clinical care by age group (e.g., infants, preschool-aged children, and adults)
  - The CFF recommends use of ivacaftor in preschoolers with specific gating mutations (e.g., *G551D*, *G1244E*, *G1349D*, *G178R*, *G551S*, *S1251N*, *S1255P*, *S549N*, and *S549R*) and *R117H* mutations
    - Other treatments recommended in this age group for select individuals include oral, intravenous, and/or inhaled antibiotics for exacerbations, hypertonic saline, dornase alfa, and inhaled antipseudomonal antibiotics
    - No agent in this class is approved for the treatment of children < 12 months with CF
  - Notably, ivacaftor has received approval for an expanded number of mutations since this recommendation as well

- Clinical Pharmacogenetics Implementation Consortium (CPIC), 2014
  - Recommend ivacaftor therapy based on *CFTR* genotype in CF patients ≥ 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
  - Like the CFF guidelines, CPIC developed these guidelines prior to the approval of lumacaftor/ivacaftor, tezacaftor/ivacaftor, and the expanded indication (additional mutations, younger age) of ivacaftor; however, following ivacaftor's expanded approval, the CPIC Allele Definition Table has been updated with the additional variants

Cystic Fibrosis - Indications

Drug	Generic	Indication(s)
ivacaftor (Kalydeco)	---	• Treatment of cystic fibrosis (CF) in patients aged ≥ 6 months who have 1 mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene that is responsive to ivacaftor based on clinical and/or in vitro assay data
lumacaftor/ivacaftor (Orkambi)	---	• Treatment of CF in patients aged ≥ 2 years who are homozygous for the F508del mutation in the CFTR gene • Limitation of use: safety and efficacy have not been established in patients with CF other than those homozygous for the F508del mutation
tezacaftor/ivacaftor (Symdeko)	---	• Treatment of patients with CF aged ≥ 6 years who are homozygous for the F508del mutation or who have ≥ 1 mutation in the CFTR gene that is responsive to tezacaftor/ivacaftor based on in vitro data and/or clinical evidence†
elexacaftor/ivacaftor/tezacaftor (Trikafta)	---	• Treatment of cystic fibrosis (CF) in patients aged 12 years and older who have at least one F508del mutation in the CFTR gene

Cystic Fibrosis

- ivacaftor (Kalydeco)
  - **In May 2019, FDA expanded the indication for ivacaftor (Kalydeco) for use in patients as young as 6 months to 11 years who have 1 CFTR gene mutation that is responsive to ivacaftor potentiation based on clinical and/or in vitro assay data**
  - **Indication**
    - **Treatment of cystic fibrosis (CF) in patients aged ≥ 6 months who have 1 mutation in the *cystic fibrosis transmembrane conductance regulator* (*CFTR*) gene that is responsive to ivacaftor based on clinical and/or *in vitro* assay data**
  - **Limitation**
    - Elevated transaminases have been observed in patients with CF treated with Symdeko. ALT and AST should be assessed at baseline, every 3 months during the first year of treatment, and annually thereafter
    - A dosing adjustment of tezacaftor/ivacaftor (Symdeko) is required in patients using concomitant strong CYP3A inhibitors
  - **Dosage**
    - Adults and children ≥ 6 years of age: one 150 mg tablet orally every 12 hours (300 mg/day)
    - **Children 6 months to < 6 years old and 7 kg to < 14 kg: one 50 mg packet (oral granules) every 12 hours**
    - **Children 6 months to < 6 years old and 5 kg to < 7 kg: one 25 mg packet (oral granules) every 12 hours**
  - **Availability**
    - 150 mg tablets
    - **25 mg,** 50 mg, 75 mg oral granules in unit-dose packets

Cystic Fibrosis

- tezacaftor/ivacaftor (Symdeko)
  - **In June 2019, FDA expanded approval of Symdeko to include pediatric patients aged ≥ 6 years old with cystic fibrosis who have certain genetic mutations; previously, it was approved only in pts ≥ 12 years old with those same genetic mutations**
  - **Indication**
    - **Treatment of patients with CF aged ≥ 6 years who are homozygous for the F508del mutation or who have at least 1 mutation in the *CFTR* gene that is responsive to tezacaftor/ivacaftor based on *in vitro* data and/or clinical evidence**
  - **Limitation**
    - Elevated transaminases have been observed in patients with CF treated with Symdeko. ALT and AST should be assessed at baseline, every 3 months during the first year of treatment, and annually thereafter
    - A dosing adjustment of tezacaftor/ivacaftor (Symdeko) is required in patients using concomitant strong CYP3A inhibitors
  - **Dosage**
    - **Pediatric patients age 6 to less than 12 years weighing < 30 kg:**
      - **One tablet (containing tezacaftor 50 mg/ivacaftor 75 mg) in the morning and one tablet (containing ivacaftor 75 mg) in the evening**
    - Adults and pediatric patients age 12 years and older or pediatric patients age 6 to less than 12 years weighing ≥ 30 kg or more:
      - One tablet (containing tezacaftor 100 mg/ivacaftor 150 mg) in the morning and one tablet (containing ivacaftor 150 mg) in the evening
    - **All doses should be administered with fat-containing food**
  - **Availability**
    - **Tablets:**
      - **50/75 mg tezacaftor/ivacaftor + 75 mg ivacaftor**
      - 100/150 mg tezacaftor/ivacaftor + 150 mg ivacaftor

Cystic Fibrosis

- elexacaftor/tezacaftor/ivacaftor (Trikafta)
  - On October 21, 2019, FDA approved Trikafta
  - Indication
    - The treatment of cystic fibrosis (CF) in patients aged 12 years and older who have at least one *F508del* mutation in the *CFTR* gene
    - 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
  - Limitation
    - Should not be used in patients with severe hepatic impairment
    - Use not recommended in patients with moderate hepatic impairment unless the benefit exceeds the risk
    - Liver function tests (ALT, AST, and bilirubin) should be assessed prior to initiating, every 3 months during the first year of treatment, and annually thereafter
  - Dosage
    - Adults and pediatric patients aged 12 years and older:
      - Morning dose: two elexacaftor 100 mg, tezacaftor 50 mg and ivacaftor 75 mg tablets
      - Evening dose: one ivacaftor 150 mg tablet
      - Morning and evening dose should be taken approximately 12 hours apart with fat-containing food
  - Availability
    - Tablets: fixed dose combination containing elexacaftor 100 mg, tezacaftor 50 mg and ivacaftor 75 mg

Respiratory Agents: Cystic Fibrosis Agents

- **Recommendation:**
  - All products in the Respiratory Agents: Cystic Fibrosis Agents drug class are considered safe and efficacious for their medically accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA.
  - Products in this class may require prior authorization to determine medical necessity.
  - All non-preferred products require a trial of two preferred products with the same indication before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.

Respiratory Agents: Cystic Fibrosis Agents

- **Motion:** I move that all products in the Respiratory Agents: Cystic Fibrosis Agents drug class are considered safe and efficacious for their medically accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA. Products in this class may require prior authorization to determine medical necessity. All non-preferred products require a trial of two preferred products with the same indication before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.
- **Motion: Storhaug**
- **2nd: Park**

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Antibiotics, Inhaled

Disease State Description
Mycobacterium avium complex (MAC) lung disease

- *Mycobacterium avium* complex (MAC) is the most common nontuberculous mycobacterial (NTM) lung infection
- Treatment is continued until sputum cultures are consecutively negative for at least 12 months; typical duration exceeds 18 months
  - Eradication is difficult, and recurrence and relapse are common
- The timing of treatment depends on the type of disease and the risk of progression
  - While fibrocavitary disease has a rapid progression and warrants prompt treatment, a course of observation may be reasonable for patients with nodular bronchiectasis disease, if the patient has minimal symptoms or radiographic findings or the patient has comorbid conditions that are considered to be more serious than the MAC lung infection
  - During observation, sputum cultures are generally monitored every 2 to 3 months, and repeat imaging occurs after approximately 6 months
  - Signs of disease progression (e.g., increased bacterial load, development of cavitation or worsening nodularity) indicate the need for antibiotic therapy

Up to Date, 2018

Mycobacterium avium complex (MAC) lung disease – Guidelines

- American Thoracic Society (ATS) and Infectious Diseases Society of America (IDSA), 2007
  - A diagnosis of NTM lung disease should be based on a minimum of chest radiography or chest high-resolution computed tomography (HRCT) scan, ≥ 3 sputum specimens for acid-fast bacilli (AFB) analysis, and exclusion of other conditions (e.g., tuberculosis, lung malignancy)
    - Bronchoscopy or lung biopsy is not usually required
  - Due to the long therapy duration and potential for intolerance, treatment should only be considered in patients who meet the clinical, radiographic, and microbiologic criteria for the diagnosis of NTM
  - The currently recommended treatment for NTM includes a macrolide (clarithromycin or azithromycin), rifampin, and ethambutol
    - An intravenous (IV) aminoglycoside (amikacin, streptomycin) is added to treat rapidly progressing disease, extensive cavitary MAC, or after failure of standard multi-drug therapy
    - For infections that are macrolide-resistant, a regimen of rifabutin, ethambutol, plus a parenteral aminoglycoside is recommended
    - The ATS and IDSA are in the process of revising their statement

- Cystic Fibrosis Foundation (CFF) and European Cystic Fibrosis Society (CFS), 2016
  - Recommend susceptibility testing for MAC infections on isolates recovered prior to initiation of treatment, and sputum samples are recommended for culture every 4 to 8 weeks for the duration of treatment
    - Intravenous amikacin is recommended in select patients
    - A daily oral antibiotic regimen containing a macrolide (preferably azithromycin), rifampin, and ethambutol is recommended for clarithromycin-sensitive *M. avium* complex pulmonary disease
    - Monotherapy with a macrolide or other antimicrobial should never be used for MAC pulmonary disease
    - Treatment is recommended for 12 months beyond culture conversion (e.g., 3 consecutive negative cultures following the date of the first of the 3 cultures) if no positive cultures are obtained during these 12 months

Antibiotics, Inhaled - Indications

Drug	Generic	Indication(s)
amikacin liposome (Arikayce)	---	• For the treatment of Mycobacterium avium complex (MAC) lung disease as part of a combination antibacterial drug regimen in patients who do not achieve negative sputum cultures after a minimum of 6 consecutive months of a multidrug background regimen therapy • Limited Population: only indicated in adults who have limited or no alternative treatment options • Limitation of Use: has only been studied in patients with refractory MAC lung disease defined as patients who did not achieve negative sputum cultures after a minimum of 6 consecutive months of a multidrug background regimen therapy; use is not recommended for patients with non-refractory MAC lung disease
aztreonam (Cayston)	---	• For the improvement of respiratory symptoms in cystic fibrosis patients with Pseudomonas aeruginosa and a forced expiratory volume in 1 second (FEV1) between 25% and 75% predicted • Safety and effectiveness have not been established in pediatric patients < 7 years of age, patients with FEV1 <25% or >75% predicted, or patients colonized with Burkholderia cepacia
tobramycin (Bethkis)	---	• For the management of cystic fibrosis in adults and pediatric patients ≥ 6 years of age with P. aeruginosa and a FEV1 between 40% and 80% predicted, and patients with B. cepacia
tobramycin (Kitabis Pak)	---	• For the management of cystic fibrosis in adults and pediatric patients ≥ 6 years of age with P. aeruginosa • Safety and efficacy have not been demonstrated in patients < 6 years of age, patients with FEV1 < 25% or > 80% predicted, or patients colonized with B. cepacia
tobramycin (TOBI)	---	• For the management of cystic fibrosis patients with P. aeruginosa and a FEV1 between 25% and 75% predicted • Safety and efficacy have not been demonstrated in patients < 6 years of age, patients with FEV1 < 25% or > 75% predicted, or patients colonized with B. cepacia
tobramycin (TOBI Podhaler)	---	• For the management of cystic fibrosis patients with P. aeruginosa and a FEV1 between 25% and 80% predicted • Safety and efficacy have not been demonstrated in patients < 6 years of age, patients with FEV1 < 25% or > 80% predicted, or patients colonized with B. cepacia

Cystic Fibrosis – CFTR Potentiator

- amikacin liposome inhalation suspension (Arikayce)
  - **In November 2018, FDA approved Arikayce for CF (previously approved for treatment of *Mycobacterium avium* complex (MAC) lung disease as part of a combination antibacterial drug regimen**
  - **Indication**
    - **For the treatment of Mycobacterium avium complex (MAC) lung disease as part of a combination antibacterial drug regimen in patients who do not achieve negative sputum cultures after a minimum of 6 consecutive months of a multidrug background regimen therapy**
    - **Limited Population: only indicated in adults who have limited or no alternative treatment options**
    - **Limitation of Use: has only been studied in patients with refractory MAC lung disease defined as patients who did not achieve negative sputum cultures after a minimum of 6 consecutive months of a multidrug background regimen therapy; use is not recommended for patients with non-refractory MAC lung disease**
  - **Limitation**
    - **Contraindicated in patients with a known aminoglycoside hypersensitivity**
    - **Aminoglycoside use, including amikacin liposome, can result in ototoxicity, nephrotoxicity, neuromuscular blockade, and bilateral congenital deafness in pediatric patients exposed in utero**
  - **Dosage**
    - **Adults: 590 mg once daily**
    - **Administer 1 vial using the Lamira Nebulizer System**
  - **Availability**
    - **590 mg/8.4 mL (1 vial) inhalation suspension**

Antibiotics: Aminoglycosides - Inhaled

- **Recommendation:**
  - All products in the Antibiotics: Aminoglycosides-Inhaled drug class are considered safe and efficacious for their medically accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA.
  - Products in this class may require prior authorization to determine medical necessity.
  - All non-preferred products require a trial of two preferred products with the same indication before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.

Antibiotics: Aminoglycosides - Inhaled

- **Motion:** I move that all products in the Antibiotics: Aminoglycosides-Inhaled drug class are considered safe and efficacious for their medically accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA. Products in this class may require prior authorization to determine medical necessity. All non-preferred products require a trial of two preferred products with the same indication before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.
- **Motion: Flatebo**
- **2nd: Park**

Antibiotics: Monobactams - Inhaled

- **Recommendation:**
  - All products in the Antibiotics: Monobactams-Inhaled drug class are considered safe and efficacious for their medically accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA.
  - Products in this class may require prior authorization to determine medical necessity.
  - All non-preferred products require a trial of two preferred products with the same indication before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.

Antibiotics: Monobactams - Inhaled

- **Motion:** I move that all products in the Antibiotics: Monobactams-Inhaled drug class are considered safe and efficacious for their medically accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA. Products in this class may require prior authorization to determine medical necessity. All non-preferred products require a trial of two preferred products with the same indication before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.
- **Motion: Lee**
- **2nd: Huynh**

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Anticoagulants

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_2DS_2-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

The American Society of Hematology (ASH), 2019- Clinical Practice Guidelines on the Management of VTE

- Recommendations included prophylaxis for medical patients, VTE diagnosis, management of anticoagulation therapy, heparin-induced thrombocytopenia (HIT), VTE in pregnancy, and pediatric VTE treatment
- When anticoagulants are used for VTE prophylaxis, the guidelines prefer LMWH over UFH or direct acting anticoagulants
  - They also note that managing anticoagulation therapy is complex; therefore, in order to optimize management of anticoagulation therapy, ASH suggests patients should receive care from specialized anticoagulation management service centers versus primary care physicians whenever possible
- Additionally, for patients at low to moderate risk of recurrent VTE who require interruption of VKA therapy for invasive procedures, ASH recommends against periprocedural bridging with LMWH or UHF
- In patients with acute HIT, suggested treatment options include argatroban, bivalirudin, danaparoid, fondaparinux, or a direct oral anticoagulant
- Additional guidance on DVT/PE treatment, VTE in cancer patients, thrombophilia, and VTE in surgical patients is anticipated in the near future

Treatment Guidelines

The American Society of Clinical Oncology (ASCO) Guidelines, 2019

- State that cancer patients are significantly more likely to develop VTE than people without cancer
- Additionally, cancer patients exhibit increased rates of VTE recurrence and more bleeding complications during VTE treatment
- Both prophylaxis and treatment regimens are generally more aggressive in cancer patients than in other populations
  - For example, most patients hospitalized for any condition who also have an active malignancy should receive anticoagulation therapy as prophylaxis unless there is active bleeding or another contraindication
  - In the outpatient setting, routine thromboprophylaxis is not recommended for cancer patients.
  - However, the use of apixaban, rivaroxaban or LMWH as prophylaxis may be indicated for certain high-risk patients, including those with a Khorana score of 2 or higher prior to starting a new systemic chemotherapy regimen
- Patients with multiple myeloma receiving thalidomide or lenalidomide-based regimens with chemotherapy and/or dexamethasone should be offered prophylaxis with either aspirin or LMWH dependent on risk assessment
- Cancer patients undergoing major surgery should have anticoagulation continued for at least 7 to 10 days postoperatively and possible extended prophylaxis with a LMWH for up to 4 weeks for select high risk patients undergoing pelvic or abdominal surgery
- Initial anticoagulation for treatment of VTE in patients with cancer may include LMWH, UFH, fondaparinux or rivaroxaban
- Per ASCO guidelines, for patients initiating VTE treatment with parenteral anticoagulation, LMWH is preferred over UFH for the initial 5 to 10 days unless the patient has severe renal impairment
- There is strong evidence to support a recommendation for long-term anticoagulation with a LMWH, edoxaban or rivaroxaban for at least 6 months rather than a VKA

Treatment Guidelines

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 (CHA2DS2VASc ≥ 0 in males or ≥ 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 CHA2DS2VASc stroke risk factor are suggested to receive oral anticoagulation while patients considered at high risk of stroke (e.g., CHA2DS2VASc ≥ 2 in males or ≥ 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

Treatment Guidelines

AHA/ACC/HRS Guidelines, 2019 Update

- There is consensus throughout the published guidelines that all AF patients with mechanical heart valves should be treated with warfarin
  - Dabigatran (Pradaxa) is contraindicated in patients with mechanical heart valves due to an increased risk of bleeding
- Patients with AF and end-stage chronic kidney disease (CKD) (creatinine clearance [CrCl] < 15 mL/min) or those receiving hemodialysis should be treated with warfarin (Class IIa; Level B)
  - Dabigatran (Pradaxa) and rivaroxaban (Xarelto) should not be used in patients with end-stage CKD or receiving hemodialysis due to lack of evidence regarding the balance between risks and benefits (Class III; Level C)
  - Dosage recommendations are available for the use of dabigatran (Pradaxa), apixaban (Eliquis), and rivaroxaban (Xarelto) in patients with moderate to severe CKD and a CHA_2DS_2-VASc score > 2; however, safety and efficacy have not been established (Class IIb; Level C)
- Bridging therapy with UFH or LMWH for patients who require interruption of oral anticoagulant therapy should be contemplated
  - Considerations include the oral anticoagulant being interrupted, whether or not the patient has a mechanical heart valve, and the duration of time a patient will not be anticoagulated
  - These decisions should balance the risks of stroke and bleeding (Class I; Level C)

Treatment Guidelines

Stroke

- According to the Centers for Disease Control and Prevention (CDC), stroke is the fifth leading cause of death behind heart disease, cancer, chronic lower respiratory diseases, and accidents

American Academy of Neurology (AAN) guidelines, 2014 (reaffirmed in 2017), for the prevention of stroke in NVAF

- Dabigatran (Pradaxa) 150 mg twice daily is likely more effective than warfarin with a decreased risk for intracranial hemorrhage
- Rivaroxaban (Xarelto) is probably as effective as warfarin in preventing stroke or systemic embolism with a lesser frequency of intracranial hemorrhage and fatal bleeding
- Apixaban (Eliquis) 5 mg twice daily has been shown to result in a reduced mortality compared to warfarin due to a decreased risk of bleeding, including intracranial bleeding, rather than its effect on reduction of cerebral or systemic embolism compared to warfarin
- These guidelines also provide comparisons between the effectiveness and safety of the oral anticoagulants to antiplatelet agents, such as aspirin and clopidogrel
- Edoxaban (Savaysa) and betrixaban (Bevyxxa) were not available at the time the 2014 AAN guidelines were published; they are therefore not included in the AAN review
- Unresolved issues surrounding the use of the new anticoagulants in the setting of NVAF include the lack of data comparing these drugs to 1 another (all were compared only to warfarin) and the short duration of follow-up given the long-term real-world indication
- In addition, drug activity cannot be assessed in routine clinical practice which may lead to under- or over-treatment of patients, questionable safety of treatment for an acute ischemic stroke with a thrombolytic agent in patients receiving apixaban (Eliquis), dabigatran (Pradaxa), rivaroxaban (Xarelto), or edoxaban (Savaysa), and the lack of an antidote in the setting of acute hemorrhage
    - However, some of these issues are being addressed
    - In October 2015, the FDA approved idarucizumab (Praxbind), a humanized monoclonal antibody fragment, to reverse anticoagulation for emergency or urgent procedures and life-threatening or uncontrolled bleeding in patients treated with dabigatran (Pradaxa)

Treatment Guidelines

The American College of Cardiology (ACC), 2017 published a Consensus Decision Pathway on Management of Bleeding in Patients on Oral Anticoagulants

- For major bleeding, anticoagulants should be interrupted and, for most patients, an anticoagulant reversal agent is recommended if available
- Laboratory evaluation to identify residual anticoagulant activity is recommended in patients with severe renal impairment, particularly those taking dabigatran, which is 80% to 85% renally excreted
    - Use of an antifibrinolytic agent (tranexamic acid, epsilon aminocaproic acid) may be considered
- Platelet transfusion may be considered in select patients, particularly after other measures, such as oral anticoagulant reversal, have failed
- For nonmajor bleeding, ACC does not recommend routine reversal of an oral anticoagulant; however, interruption of oral anticoagulant therapy until the patient is clinically stable may be advised depending on individual patient characteristics, nature of the bleed, and the anticoagulation intensity
- The patient's current underlying bleeding risk and relevant medical comorbidities should also be considered

ACC/AHA Guidelines, 2016 – Management of PAD or CAD

- Guidelines focus on 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
- In October 2018, rivaroxaban (Xarelto) became the first oral anticoagulant approved for use in combination with low-dose aspirin to reduce the risk of major CV events (CV death, MI, and stroke) in patients with chronic CAD or PAD

Anticoagulants - Indications

Drug	Generic	DVT Prophylaxis				DVT Treatment
		Hip Replacement	Knee Replacement	Hip Fracture Surgery	Abdominal Surgery	
apixaban (Eliquis)	---	X	X	---	---	X
betrixaban (Bevyxxa)	---	---	---	---	---	-
dabigatran (Pradaxa)	---	X	---	---	---	X
edoxaban (Savaysa)	---	---	---	---	---	X
rivaroxaban (Xarelto)	---	X	X	---	---	X
warfarin (Coumadin, Jantoven)	X	---	---	---	---	X

Anticoagulants - Indications

Other Indications

- ***dalteparin (Fragmin)***
  - Prophylaxis of ischemic complications of unstable angina and non-Q-wave myocardial infarction (MI) when concurrently administered with aspirin
  - Deep vein thrombosis (DVT) prophylaxis for immobile medical patients who are at risk for thromboembolic complications
  - Extended treatment of symptomatic venous thromboembolism (VTE) (proximal DVT and/or pulmonary embolism [PE]), to reduce the recurrence of VTE in patients with cancer
  - Treatment of symptomatic VTE to reduce the recurrence of VTE in pediatric patients 1 month of age and older
- ***enoxaparin (Lovenox)***
  - For the prophylaxis of ischemic complications of unstable angina and non-Q-wave myocardial infarction in conjunction with aspirin
  - DVT prophylaxis to prevent thromboembolic complications in medical patients with severely restricted mobility during acute illness
  - Treatment of acute ST-segment elevation myocardial infarction (STEMI) managed medically or with subsequent percutaneous coronary intervention (PCI)
- ***fondaparinux (Arixtra)***
  - Treatment of acute PE when initial therapy is administered in the hospital and with warfarin
- ***apixaban (Eliquis)***
  - To reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation (NVAF)
  - For the treatment of PE
  - To reduce the risk of recurrent DVT and PE following initial therapy
- ***betrixaban (Bevyxxa)***
  - For the prophylaxis of VTE in adult patients hospitalized for acute medical illness who are at risk for thromboembolic complications due to moderate or severely restricted mobility and other risk factors for VTE
- ***dabigatran (Pradaxa)***
  - To reduce the risk of stroke and systemic embolism in patients with NVAF
  - To reduce the risk of recurrence of DVT and PE following initial therapy

Anticoagulants - Indications

Other Indications (Continued)

- ***edoxaban (Savaysa)***
  - To reduce the risk of stroke and systemic embolism in patients with NVAF
- ***rivaroxaban (Xarelto)***
  - To reduce the risk of stroke and systemic embolism in patients with NVAF
  - For the treatment of PE
  - For the reduction in the risk of recurrence of DVT and of PE for patients at continued risk for recurrent DVT and/or PE following initial 6-months treatment for DVT and/or PE
  - To reduce the risk of major cardiovascular (CV) events (CV death, MI, and stroke) in patients with chronic coronary artery disease (CAD) or peripheral artery disease (PAD) when used in combination with aspirin
  - For the prophylaxis of VTE and VTE related death during hospitalization and post-hospital discharge in adult patients admitted for an acute medical illness who are at risk for thromboembolic complications due to moderate or severe restricted mobility and other risk factors for VTE and not at high risk of bleeding
- ***warfarin (Coumadin)***
  - Prophylaxis and/or treatment of the thromboembolic complications associated with atrial fibrillation (AF) and/or cardiac valve replacement
  - Reduce the risk of death, recurrent myocardial infarction, and thromboembolic events, such as stroke or systemic embolization, after myocardial infarction
  - Prophylaxis and/or treatment of venous thrombosis and its extension, and pulmonary embolism (PE)

Anticoagulants – Dosing & Availability

Drug	DVT Prophylaxis			
	Patients with Nonvalvular Atrial Fibrillation	Prophylaxis of DVT/PE for Knee or Hip Replacement Surgery	Treatment of DVT/PE	To Prevent Recurrence of DVT/PE
apixaban (Eliquis)	5 mg twice daily	2.5 mg twice daily	10 mg twice daily x 7 days; 5 mg twice daily thereafter	2.5 mg twice daily
betrixaban (Bevyxxa)	--	--	--	--
dabigatran (Pradaxa)	150 mg twice daily	110 mg on first day, then 220 mg once daily	150 mg twice daily after 5 to 10 days of parenteral anticoagulant	150 mg twice daily
edoxaban (Savaysa)	60 mg once daily	--	60 mg once daily after 5 to 10 days of parenteral anticoagulant	--
rivaroxaban (Xarelto)	20 mg once daily	10 mg once daily	15 mg twice daily for 21 days; 20 mg once daily thereafter	10 mg daily after at least 6 months of standard treatment
warfarin (Coumadin, Jantoven)	typical dose may be 2 mg to 10 mg once daily but dose must be individualized based on INR	typical dose may be 2 mg to 10 mg once daily but dose must be individualized based on INR	typical dose may be 2 mg to 10 mg once daily but dose must be individualized based on INR	typical dose may be 2 mg to 10 mg once daily but dose must be individualized based on INR

Anticoagulants: Factor Xa and Thrombin Inhibitors

- **Recommendation:**
  - All products in the Anticoagulants: Factor Xa and Thrombin Inhibitors drug class are considered safe and efficacious for their medically accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA.
  - All non-preferred products require a trial of two preferred products with the same indication before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.

Anticoagulants: Factor Xa and Thrombin Inhibitors

- **Motion:** I move that all products in the Anticoagulants: Factor Xa and Thrombin drug class are considered safe and efficacious for their medically accepted indications and are eligible for preferred status and grandfathering at the discretion of HCA. All non-preferred products require a trial of two preferred products with the same indication before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.
- **Motion: Park**
- **2nd: Flatebo**

Appendices

Incretin Mimetics/Enhancers – Dosing & Availability

Drugs	Dosing	Time of Administration Related to Mealtime	Availability
Amylin Analogue			
pramlintide (Symlin)	T1DM: initiate at 15 mcg SC injection, titrate to 30 or 60 mcg by 15 mcg increments T2DM: initiate at 60 mcg SC injection, titrate to 120 mcg as tolerated	Prior to major meals, concurrently with insulin; decrease insulin doses 50% initially, then adjust only after reaching the target dose of pramlintide	1.5 mL, 2.7 mL pens (1 mg/mL)
DPP-4 Enzyme Inhibitors			
alogliptin (Nesina)	25 mg once daily	Take with or without food	6.25 mg, 12.5 mg, 25 mg tablets
alogliptin/metformin (Kazano)	1 tablet twice daily; adjust dose based on effectiveness and tolerability; Do not exceed 25 mg/2000 mg per day	Administer with food	12.5/500 mg,12.5/1,000 mg tablets
alogliptin/pioglitazone (Oseni)	1 tablet once daily; do not exceed 25 mg/45 mg per day	Take with or without food	12.5/15 mg, 12.5/30 mg, 12.5/45 mg, 25/15 mg, 25/30 mg, 25/45 mg tablets
linagliptin (Tradjenta)	5 mg once daily	Take with or without food	5 mg tablet
linagliptin/empagliflozin (Glyxambi)	5 mg/10 mg once daily in the morning; may increase to 5 mg/25 mg once daily	Take with or without food	5/10 mg, 5/25 mg tablets
linagliptin/metformin (Jentadueto)	Starting dose is 2.5 mg/500 mg twice daily for patients not already taking metformin or 2.5 mg linagliptin; may increase gradually to 2.5 mg/1,000 mg twice daily to minimize GI adverse events For patients already taking linagliptin and metformin, no dosage adjustment is needed when switching to the combination tablet	Take with meals	2.5/500 mg, 2.5/850 mg, 2.5/1,000 mg tablets

Incretin Mimetics/Enhancers – Dosing & Availability

Drugs	Dosing	Time of Administration Related to Mealtime	Availability
DPP-4 Enzyme Inhibitors (Continued)			
linagliptin/metformin ER (Jentadueto XR)	Starting dose In patients not already taking metformin: 5 mg linagliptin/1,000 mg metformin ER once daily In patients already taking metformin: 5 mg linagliptin and a similar total daily dose of metformin once daily In patients already taking linagliptin and metformin or Jentadueto: switch to Jentadueto XR containing 5 mg linagliptin and a similar total daily dose of metformin once daily Do not exceed total daily dose of linagliptin 5 mg and metformin 2,000 mg	Take with a meal	2.5/1,000 mg, 5/1,000 mg tablets
saxagliptin (Onglyza)	2.5 mg to 5 mg daily by mouth	Take with or without food	2.5 mg, 5 mg tablets
saxagliptin/dapagliflozin (Qtern)	1 tablet once daily, beginning with the 5/5 mg formulation for those not already taking dapagliflozin; otherwise, initial and subsequent dosing is based on tolerability and efficacy	Take in the morning Take with or without food Do not split, crush, or chew tablets	5/5 mg, 5/10 mg tablet
saxagliptin/metformin ER (Kombiglyze XR)	1 tablet once daily; maximum per day: 5 mg saxagliptin, 2,000 mg metformin	Take with evening meal	2.5/1,000 mg, 5/500 mg, 5/1,000 mg tablets
sitagliptin (Januvia)	100 mg once daily by mouth	Take with or without food	25 mg, 50 mg, 100 mg tablets
sitagliptin/ertugliflozin (Steglujan)	Starting dose is 100/5 mg once; may increase to 100/15 mg once daily	Take in the morning Take with or without food	100/5 mg, 100/15 mg tablets
sitagliptin/metformin (Janumet)	1 tablet twice daily by mouth maximum per day: 100 mg sitagliptin, 2,000 mg metformin	Take with food Do not split, crush, or chew tablets	50/500 mg, 50/1,000 mg tablets
sitagliptin/metformin ER (Janumet XR)	Dosage based on patient's current sitagliptin and/or metformin regimens up to a maximum of 100 mg sitagliptin and 2,000 mg metformin daily In patients not currently on metformin: 100 mg sitagliptin and 1,000 mg metformin ER per day In patients already treated with metformin, the recommended starting dose is sitagliptin 100 mg	Once daily with a meal preferably in the evening	50/500 mg, 50/1,000 mg, 100/1,000 mg tablets

Incretin Mimetics/Enhancers – Dosing & Availability

Drugs	Dosing	Time of Administration Related to Mealtime	Availability
GLP-1 Receptor Agonists			
dulaglutide (Trulicity)	0.75 mg SC once weekly; may increase to a maximum of 1.5 mg once weekly	Administer at any time of day without regard to meals	0.75 mg/0.5 mL and 1.5 mg/0.5 mL single-dose pens
exenatide (Byetta)	5 mcg SC injection twice daily; dose can be increased to 10 mcg twice daily after 1 month	Administer at any time within the 60-minute period before the morning and evening meals preferably at least 6 hours apart	1.2 mL (5 mcg/dose), 2.4 mL (10 mcg/dose) prefilled pen containing 250 mcg/mL solution
exenatide ER (Bydureon, Bydureon BCise)	2 mg SC injection administered once weekly	Administer at any time without regard to meals	Bydureon: 2 mg vial containing powdered exenatide with a 0.65 mL prefilled syringe containing diluents; 2 mg single-dose pen Bydureon BCise: 2 mg auto-injector
liraglutide (Victoza)	Adults: 0.6 mg once daily SC for 1 week; increase dose to 1.2 mg once daily; may increase to 1.8 mg daily, if needed, after ≥ 1 week of 1.2 mg dose Pediatrics: 0.6 mg once daily SC for 1 week; after ≥ 1 week may increase dose to 1.2 mg once daily; may increase to 1.8 mg daily, as needed, after ≥ 1 week of 1.2 mg dose	Administer once daily at any time of day independent of meals	Prefilled multidose pens that deliver 0.6 mg, 1.2 mg, and 1.8 mg doses; Pens contain 6 mg/mL (3 mL)
liraglutide/insulin degludec (Xultophy)	In patients naïve to basal insulin or a GLP-1 agonist: initial dose is 10 units SC once daily. In patients currently on basal insulin or a GLP-1 agonist: initial dose is 16 units SC once daily; discontinue insulin or GLP-1 agonist prior to starting liraglutide/insulin degludec	Administer at the same time each day with or without food.	Prefilled multidose pen that delivers 10 to 50 units/injection Pen contains 3.6 mg/mL liraglutide and 100 units/mL insulin degludec (3 mL)
lixisenatide (Adlyxin)	10 mcg once daily SC for 14 days; on day 15 increase to 20 mcg once daily	Administer once daily within 1 hour before the first meal of the day	Starter Pak: 1 Prefilled multidose pen that deliver 14 doses of 10 mcg (50 mcg/mL) and 1 pen of 20 mcg (100 mcg/mL) per dose Maintenance Pak: 2 prefilled multidose pens that deliver 20 mcg/dose (100 mcg/mL in 3 mL)
lixisenatide/insulin glargine (Soliqua)	In patients naive to basal insulin or to a GLP-1 receptor agonist, currently on a GLP-1 receptor agonist, or currently on < 30 units of basal insulin daily: initial dose of lixisenatide/insulin glargine is 15 units SC once daily; discontinue basal insulin or GLP-1 agonist prior to starting lixisenatide/insulin In patients currently on 30 to 60 units of basal insulin daily, with or without a GLP-1 agonist: initial dose of lixisenatide/insulin glargine is 30 units SC once daily; discontinue basal insulin or GLP-1 agonist prior to starting lixisenatide/insulin glargine	Administer once daily within 1 hour before the first meal of the day	Prefilled multidose pen that deliver 15 to 60 units per dose Pen contains lixisenatide 33 mcg and insulin glargine 100 units per mL (3 mL)
semaglutide (Ozempic)	Initial dose is 0.25 mg SC once weekly for 4 weeks; the 0.25 mg dose is not effective for glycemic control and is intended only for initiation of treatment After 4 weeks, increase to 0.5 mg once weekly; after an additional 4 weeks, may increase to 1 mg once weekly Maximum recommended dose is 1 mg once weekly	Administer on the same day each week, at any time of the day, without regard to meals If the administration day of the week is changed, at least 48 hours should be allowed between 2 doses	Prefilled multidose pens in 2 dosing increment options: one that delivers 0.25 mg or 0.5 mg per injection and another that delivers 1 mg per injection Pens contain semaglutide 2 mg/1.5 mL

Insulin & Related Agents – Dosing & Availability

Drugs	Dosing	Time of Administration related to mealtime	Availability
Rapid-Acting Insulins			
human insulin inhalation powder (Afrezza)	Dosing should be titrated to glycemic control in combination with a long acting insulin	At the beginning of the meal	Cartridge: 4 units, 8 units, and 12 units packaged as: ▪ 90 x 4-unit cartridges ▪ 90 x 8-unit cartridges ▪ 90 x 12-unit cartridges ▪ 90 x 4-unit + 90 x 8-unit cartridges ▪ 90 x 8-unit + 90 x 12-unit cartridges ▪ 60 of each 4-unit/8-unit/12-unit 2 inhalers are contained in each package
insulin aspart (Fiasp)	Dosing should be titrated to glycemic control in combination with an intermediate- or long-acting insulin (and/or with oral antidiabetic agents for T2DM)	At start of a meal or within 20 minutes after starting a meal	100 units/mL: ▪ 10 mL vial ▪ 3 mL prefilled FlexTouch® pen ▪ 3 mL PenFill cartridges
insulin aspart (Novolog)		5 to 10 minutes before eating	100 units/mL: ▪ 10 mL vial ▪ 3 mL prefilled FlexPen® ▪ 3 mL cartridge
insulin glulisine (Apidra)		Within 15 minutes before a meal or within 20 minutes after starting a meal	100 units/mL: ▪ 10 mL vial ▪ 3 mL prefilled SoloStar pen
insulin lispro (Admelog, Humalog, Humalog Junior)	Dosing should be titrated to glycemic control in combination with an intermediate or long acting insulin (and/or with oral antidiabetic agents for T2DM)	No more than 15 minutes before a meal or immediately after a meal	100 units/mL: ▪ 3 mL vial (Admelog; Humalog) ▪ 10 mL vial (Admelog; Humalog)* ▪ 3 mL prefilled pen (Admelog SoloStar; Humalog KwikPen, Humalog Junior KwikPen) ▪ 3 mL cartridge (Humalog) U-200 (200 units/mL): ▪ 3 mL prefilled pen (Humalog KwikPen)*
human insulin (Humulin R, Novolin R)	Dosing should be titrated to glycemic control in combination with an intermediate or long acting insulin (and/or with oral antidiabetic agents for T2DM)	30 minutes prior to meal	100 units/mL: ▪ 3 mL vials (Humulin R U-100) ▪ 10 mL vials (Humulin R U-100; Novolin R U-100) 500 units/mL: ▪ 20 mL vials (Humulin R U-500) 500 units/mL:

Insulin & Related Agents – Dosing & Availability

Drugs	Dosing	Time of Administration related to mealtime	Availability
Intermediate (N) Insulins			
human insulin NPH (Humulin N, Novolin N)	Dosing should be titrated to glycemic control. Can be used in combination with an quick- or long-acting insulin (and/or with oral antidiabetic agents for T2DM); Total daily dose is given as 1 to 2 injections per day	30 to 60 minutes prior to meal or bedtime	100 units/mL: ▪ 3 mL vials (Humulin N) ▪ 10 mL vials (Humulin N; Novolin N) ▪ 3 mL prefilled pen (Humulin N KwikPen; Novolin FlexPen)
Long-Acting Insulins			
insulin degludec (Tresiba)	Dosing should be titrated to glycemic control in combination with an intermediate or long acting insulin (and/or with oral antidiabetic agents for T2DM) Dosing should be titrated to glycemic control in combination with an intermediate or long acting insulin (and/or with oral antidiabetic agents for T2DM)	Adults: Administer SC once daily at any time during the day There should be a minimum interval of 8 hours after the last injection Pediatrics: Administer SC once daily at the same time each day; for patients requiring < 5 units each day, use the U-100 vial	100 U/mL: ▪ 10 mL vial ▪ 3 mL FlexTouch pen U-200 (200 U/mL): ▪ 3 mL FlexTouch pen
insulin detemir (Levemir)		Once daily (with the evening meal or at bedtime) or twice daily (with the evening meal, at bedtime, or 12 hours after the morning dose)	100 units/mL: ▪ 10 mL vial ▪ 3 mL FlexTouch
insulin glargine (Basaglar)		Administer SC once daily at any time during the day, at the same time every day	100 units/mL: ▪ 3 mL prefilled KwikPen
insulin glargine (Lantus)			100 units/mL: ▪ 10 mL vial ▪ 3 mL SoloStar pen
insulin glargine (Toujeo)			300 units/mL: ▪ 1.5 mL SoloStar prefilled pen ▪ 3 mL Max SoloStar prefilled pen
Rapid/Intermediate-Acting Combination Products			
insulin aspart/ protamine aspart (Novolog Mix 70/30)	Dosing should be titrated to glycemic control	Within 15 minutes before meal initiation or immediately after a meal Typically dosed on a twice-daily basis (breakfast and dinner)	▪ 10 mL vial ▪ 3 mL prefilled FlexPen
insulin lispro/ protamine lispro (Humalog Mix 75/25, Humalog Mix 50/50)		Within 15 minutes before meal initiation or immediately after a meal	▪ 10 mL vial ▪ 3 mL prefilled KwikPen
human insulin (Humulin,	Dosing should be titrated to glycemic control in	30 to 60 minutes prior to meal	▪ 3 mL vials (Humulin 70/30)

SGLT2 Inhibitors- Dosing & Availability

Drugs	Parameters	Dosage	Availability
canagliflozin (Invokana)	Recommended starting dose	100 mg once daily taken before the first meal	100 mg, 300 mg tablet
	Patients tolerating canagliflozin 100 mg daily, requiring additional glycemic control, and have an eGFR ≥ 60 mL/min/1.73 m^2	300 mg once daily	
	Moderate renal impairment (eGFR 45 to 59 mL/min/1.73 m^2)	100 mg once daily	
canagliflozin/ metformin (Invokamet)	Recommended starting dose (Base initial dose on patient's current regimen)	For patients not on either metformin or canagliflozin: one 50/500 mg tablet twice daily For patients on metformin: switch to Invokamet containing canagliflozin 50 mg with a similar total daily dose of metformin taken twice daily with meals; For patients on canagliflozin: switch to Invokamet containing metformin 500 mg with a similar total daily dose of canagliflozin taken twice daily with meals; For patients on canagliflozin and metformin: switch to Invokamet containing the same total daily doses of each component taken twice daily with meals	50/500 mg, 50/1,000 mg, 150/500 mg, 150/1,000 mg immediate-release tablet
	Moderate renal impairment (eGFR 45 to 59 mL/min/1.73 m^2)	50 mg twice daily of the canagliflozin component	
canagliflozin/ metformin (Invokamet XR)	Recommended starting dose (Base initial dose on patient's current regimen)	For patients not on either metformin or canagliflozin: two 50/500 mg tablets once daily with the morning meal For patients on metformin: switch to 2 tablets of Invokamet XR containing a total of canagliflozin 100 mg with a similar total daily dose of metformin taken once daily with the morning meal; For patients on canagliflozin: switch to 2 tablets of Invokamet XR containing a total of metformin 1,000 mg with the current total daily dose of canagliflozin taken once daily with the morning meal; For patients on canagliflozin and metformin: switch to 2 tablets of Invokamet XR containing the same total daily doses of each component taken once daily with the morning meal	50/500 mg, 50/1,000 mg, 150/500 mg, 150/1,000 mg extended-release tablet
	Moderate renal impairment (eGFR 45 to 59 mL/min/1.73 m2)	100 mg/day of the canagliflozin component	
dapagliflozin (Farxiga)	Recommended starting dose to improve glycemic control	5 mg once daily, taken in the morning, with or without food	5 mg, 10 mg tablet
	Patients tolerating dapagliflozin 5 mg once daily who require additional glycemic control	10 mg once daily	
	To reduce the risk of hospitalization for heart failure	10 mg once daily	

SGLT2 Inhibitors- Dosing & Availability

Drugs	Parameters	Dosage	Availability
dapagliflozin/ metformin ER (Xigduo XR)	Recommended starting dose to improve glycemic control	5 mg once daily (if not already taking dapagliflozin), taken in the morning with food; Gradually escalate dosage to reduce gastrointestinal side effects due to metformin; Do not exceed 10 mg dapagliflozin/2,000 mg metformin per day; Swallow whole; do not crush, cut, or chew For patients needing a dose of Xigduo XR 5/2,000 mg, use two 2.5/1,000 mg ER tablets.	2.5/1,000 mg 5/500 mg, 5/1000 mg, 50/1,000 mg, 10/500 mg, 10/1,000 mg extended-release tablet
	To reduce the risk of hospitalization for heart failure	10 mg of the dapagliflozin component once daily	
empagliflozin (Jardiance)	Recommended starting dose	10 mg once daily in the morning, with or without food	10 mg, 25 mg tablet
	Patients tolerating empagliflozin 10 mg once daily who require additional glycemic control	25 mg once daily	
empagliflozin / metformin (Synjardy)	Recommended starting dose (Base initial dose on patient's current regimen)	For patients on metformin: switch to empagliflozin 5 mg with similar total daily dose of metformin; administer twice daily with meals; For patients on empagliflozin: switch to metformin 500 mg with a similar total daily dose of empagliflozin; administer twice daily with meals; Gradually escalate dosage to reduce gastrointestinal side effects due to metformin; Do not exceed 25 mg empagliflozin and 2,000 mg metformin per day	5/500 mg, 5/1,000 mg, 12.5/500 mg, 12.5/1,000 mg immediate-release tablet
empagliflozin / metformin ER (Synjardy XR)	Recommended starting dose (Base initial dose on patient's current regimen)	Base initial dose on patient's current regimen For patients on metformin: switch Synjardy XR containing a total of empagliflozin 10 mg with a similar total daily dose of metformin taken once daily with the morning meal; For patients on empagliflozin: switch to 2 tablets of Synjardy XR containing a total of metformin ER 1,000 mg with the current total daily dose of empagliflozin taken once daily with the morning meal; For patients on canagliflozin and metformin: switch Synjardy XR containing the same total daily doses of each component taken once daily with the morning meal Synjardy XR 5/1,000 mg and 12.5/1,000 mg tablets should be taken as 2 tablets together once daily Synjardy XR 10/1,000 mg and 25/1,000 mg tablets should be taken as a single tablet once daily	5/1,000 mg, 10/1,000 mg, 12.5/1,000 mg, 25/1,000 mg extended-release tablet
ertugliflozin (Steglatro)	Recommended starting dose	5 mg once daily in the morning, with or without food	5 mg, 15 mg tablet
	Patients tolerating ertugliflozin 5 mg once daily who require additional glycemic control	15 mg once daily	
ertugliflozin/ metformin (Segluromet)	Recommended starting dose (Base initial dose on patient's current regimen)	Administer twice daily with meals Do not exceed ertugliflozin 15 mg and metformin 2,000 mg daily For patients on metformin, switch to Segluromet containing 2.5 mg ertugliflozin, with a similar total daily dose of metformin. For patients on ertugliflozin, switch to Segluromet containing 500 mg metformin, with a similar total daily dose of ertugliflozin. For patients already treated with ertugliflozin and metformin, switch to Segluromet containing the same total daily dose of ertugliflozin and a similar daily dose of metformin.	2.5/500 mg, 2.5/1,000 mg, 7.5/500 mg, 7.5/1,000 mg tablet

Growth Hormone – Dosing & Availability

Drug	Dosage Forms	Dosage
Genotropin	Two chamber cartridge (for use with Pen or Mixer): 5 mg, 12 mg contains preservative MiniQuick® syringe device: 0.2 mg, 0.4 mg, 0.6 mg, 0.8 mg, 1 mg, 1.2 mg, 1.4 mg, 1.6 mg, 1.8 mg, 2 mg (SD) contains no preservative	Weekly doses should be divided into 6 or 7 SC injections given in the thigh, buttocks, or abdomen and must not be injected intravenously ▪ GHD (ped): 0.16 to 0.24 mg/kg/week ▪ GHD (adult): – weight-based dosing: not more than 0.04 mg/kg/week to start; may increase to maximum of 0.08 mg/kg/week at 4 to 8 week intervals – non-weight-based dosing: 0.15 to 0.3 mg/day to start; may increase every 1 to 2 months by increments of 0.1 to 0.2 mg/day ▪ ISS: up to 0.47 mg/kg/week ▪ PWS: 0.24 mg/kg/week ▪ SGA: up to 0.48 mg/kg/week ▪ TS: 0.33 mg/kg/week
Humatrope	Vials (with diluent): 5 mg (MD) Cartridge kits (with prefilled diluent syringes): 6 mg, 12 mg, 24 mg (MD)	Weekly doses should be divided into 6 or 7 SC injections given in the upper arm, thigh, buttocks, or abdomen ▪ GHD (ped): 0.18 to 0.3 mg/kg/week ▪ GHD (adult): – weight-based dosing: not more than 0.006 mg/kg/day to start; may increase to maximum of 0.0125 mg/kg/day – non-weight-based dosing: 0.15 to 0.3 mg/day to start; may increase every 1 to 2 months by increments of 0.1 to 0.2 mg/day ▪ ISS: up to 0.37 mg/kg/week ▪ SGA: up to 0.47 mg/kg/week ▪ SHOX: 0.35 mg/kg/week ▪ TS: up to 0.375 mg/kg/week

Growth Hormone – Dosing & Availability

Drug	Dosage Forms	Dosage
Norditropin	FlexPro® prefilled pens: 5 mg, 10 mg, 15 mg, 30 mg (MD)	Weekly doses should be divided into 6 or 7 SC injections given in the upper arm, thigh, buttocks, or abdomen ▪GHD (ped): 0.17 to 0.24 mg/kg/week ▪GHD (adult): – weight-based dosing: (not recommended for obese patients) not more than 0.004 mg/kg/day to start; may increase to maximum of 0.016 mg/kg/day – non-weight-based dosing: 0.15 to 0.3 mg/day to start; may increase every 1 to 2 months by increments of 0.1 to 0.2 mg/day ▪ISS: up to 0.47 mg/kg/week ▪Noonan Syndrome: up to 0.46 mg/kg/week a. PWS: 0.24 mg/kg/week ▪SGA: up to 0.47 mg/kg/week TS: up to 0.47 mg/kg/week
Nutropin AQ NuSpin	Pens: 5 mg, 10 mg, 20 mg (MD)	Weekly doses should be divided into 7 SC injections given in the upper arm, thigh, buttocks, or abdomen ▪GHD (ped): prepubertal: up to 0.3 mg/kg/week ▪GHD (ped): pubertal: up to 0.7 mg/kg/week ▪GHD (adult): – weight-based dosing: not more than 0.006 mg/kg/day to start; may increase to maximum of 0.025 mg/kg/day in patients ≤ 35 years old and 0.0125 mg/kg daily in patients > years old – non-weight-based dosing: 0.15 to 0.3 mg/day to start; may increase every 1 to 2 months by increments of 0.1 to 0.2 mg/day ▪CRI: up to 0.35 mg/kg/week ▪ISS: up to 0.3 mg/kg/week TS: up to 0.375 mg/kg/week divided into equal doses given 3 to 7 times per week

Growth Hormone – Dosing & Availability

Drug	Dosage Forms	Dosage
Omnitrope	Vials: 5.8 mg (MD) Cartridge: 5 mg/1.5 mL, 10 mg/1.5 mL (MD)	Weekly doses should be divided into 6 or 7 SC injections given in the thigh, buttocks, or abdomen ▪ GHD (ped): 0.16 to 0.24 mg/kg ▪ GHD (adult): – weight-based dosing: not more than 0.04 mg/kg/week to start, may increase every 1 to 2 months to maximum of 0.08 mg/kg/week – non-weight-based dosing: 0.15 to 0.3 mg/day to start; may increase every 1 to 2 months by increments of 0.1 to 0.2 mg/day ▪ ISS: up to 0.47 mg/kg/week ▪ PWS: 0.24 mg/kg/week ▪ SGA: up to 0.48 mg/kg/week ▪ TS: 0.33 mg/kg/week
Saizen	Vials (with diluent): 5 mg, 8.8 mg (MD) Click.easy® cartridge: 8.8 mg (MD) Saizenprep reconstitution device: 8.8 mg vial with 1 cartridge 1.51 mL diluent sterile water for injection	Weekly doses should be divided into 3 alternate days, 6 days, or 7 SC daily injections given in the upper arm, thigh, buttocks, or abdomen ▪ GHD (ped): 0.18 mg/kg/week ▪ GHD (adult): – weight-based dosing: not more than 0.005 mg/kg/day to start, may increase to maximum of 0.01 mg/kg/day after 4 weeks non-weight-based dosing: 0.15 to 0.3 mg/day to start; may increase every 1 to 2 months by increments of 0.1 to 0.2 mg/day
Serostim	Vials (with diluent): 5 mg, 6 mg (SD) Vials (with diluent): 4 mg (MD)	HIV/AIDS wasting or cachexia: 0.1 mg/kg SC daily at bedtime (up to a total dose of 6 mg) or 0.1 mg/kg every other day

Growth Hormone – Dosing & Availability

Drug	Dosage Forms	Dosage
Zomacton	Vials (with diluent): 5 mg, 10 mg (MD)	Weekly doses should be divided into 3, 6, or 7 SC injections given in the upper arm, thigh, buttocks, or abdomen ▪ GHD (ped): 0.18 to 0.3 mg/kg/week ▪ GHD (adult): – weight-based dosing (not recommended for obese patients): start at 0.006 mg/kg/day to start; may increase to maximum of 0.0125 mg/kg/day – non-weight-based dosing: 0.15 to 0.3 mg/day to start; may increase every 1 to 2 months by increments of 0.1 to 0.2 mg/day ▪ TS: Up to 0.375 mg/kg/week ▪ ISS: Up to 0.37 mg/kg/week ▪ SHOX: 0.35 mg/kg/week ▪ SGA: Up to 0.47 mg/kg/week
Zorbtive	Vials (with diluent): 8.8 mg (MD)	▪ SBS: 0.1 mg/kg/day SC, maximum of 8 mg daily; administration for > 4 weeks has not been adequately studied; Zorbtive is not indicated for patients < 18 years of age or in adults > 65 years of age

Ulcerative Colitis Agents – Dosing & Availability

Drug	Adults	Pediatrics	Availability
Oral Prodrug Forms			
balsalazide (Colazal)	2.25 g (3 capsules) 3 times daily with or without food for 8 to 12 weeks; total daily dose: 6.75 g	Children 5 to 17 years: 2.25 g (three 750mg capsules) 3 times daily for 8 weeks OR 750 mg (1 capsule) 3 times daily for 8 weeks*	750 mg capsule
balsalazide (Giazo)	3.3 g (3 tablets) twice daily with or without food for up to 8 weeks; total daily dose: 6.6 g	--	1.1 g tablet
olsalazine (Dipentum)	0.5 g (2 capsules) twice daily	--	250 mg capsule
sulfasalazine (Azulfidine, Azulfidine EN-tabs)	Initial: 3 to 4 g (6 to 8 tablets) daily in evenly divided doses with dosage intervals not exceeding 8 hours Maintenance: 2 grams daily	Children ≥ 6 years: Initial: 40 to 60 mg/kg/day divided into 3 to 6 doses Maintenance: 30 mg/kg per day divided into 4 doses	500 mg tablet 500 mg enteric coated delayed-release tablet
Oral Delayed-Release Forms			
mesalamine delayed-release tablets (Asacol HD)	1.6 g (2 tablets) 3 times daily for 6 weeks‡; total daily dose: 4.8 g; take on an empty stomach ≥ 1 hour before and 2 hours after a meal	--	800 mg delayed-release tablet
mesalamine delayed-release capsules (Delzicol)	Initial: 0.8 g (2 capsules) 3 times daily with or without food for 6 weeks Maintenance: 1.6 g (4 capsules) daily in 2 to 4 divided doses for 6 months§	Children ≥ 5 years: Initial: weight-based up to a maximum of 2.4 g/day with or without food; twice daily dosing for 6 weeks Maintenance: not indicated	400 mg delayed-release capsule
mesalamine MMX tablets (Lialda)	Initial Therapy: 2.4 g or 4.8 g (2 to 4 tablets) once daily with food for up to 8 weeks ¶ Maintenance: 2.4 g (2 tablets) once daily with food§	--	1.2 g delayed-release tablet

Ulcerative Colitis Agents – Dosing & Availability

Drug	Adults	Pediatrics	Availability
Oral Delayed-Release Forms *(continued)*			
mesalamine extended-release capsules (Pentasa)	1 g (2 to 4 capsules) 4 times a day for up to 8 weeks‖	--	250 mg, 500 mg extended-release capsules
mesalamine extended-release capsules (Apriso)	1.5 g (4 capsules) once daily in the morning with or without food**	--	0.375 g extended-release capsules
Rectal Forms			
budesonide rectal foam (Uceris)	1 metered dose (2 mg) rectally twice daily for 2 weeks followed by 1 metered dose once daily for 4 weeks	--	2 aerosol canisters each containing 14 metered doses delivering 2 mg per actuation with 28 PVC applicators
mesalamine enemas (Rowasa)	4 g (60 mL) rectally at bedtime (and retained for a minimum of 8 hours) for 3 to 6 weeks	--	4 g/60 mL enema (7 and 28 unit packages) Kits include the suspension and cleansing wipes
mesalamine enemas sulfite-free (sfRowasa)	4 g (60 mL) rectally at bedtime (and retained for a minimum of 8 hours) for 3 to 6 weeks	--	4 g/60 mL enema (7 and 28 unit packages)
mesalamine suppositories (Canasa)	1 g rectally at bedtime (and retained for a minimum of 1 to 3 hours) for 3 to 6 weeks	--	1,000 mg suppositories
Oral Corticosteroids			
budesonide ER tablets (Uceris)	9 mg once daily in the morning with or without food for up to 8 weeks	--	9 mg enteric coated delayed- and extended-release tablets

Cystic Fibrosis – Dosing & Availability

Drug	Dosing	Available Strengths
ivacaftor (Kalydeco)	Adults and children ≥ 6 years of age: one 150 mg tablet orally every 12 hours (300 mg/day) Children 12 months to < 6 years old and ≥ 14 kg: one 75 mg packet (oral granules) every 12 hours (150 mg/day) Children 12 months to < 6 years old and 7 kg to < 14 kg: one 50 mg packet (oral granules) every 12 hours (100 mg/day) All doses should be administered with fat-containing food Oral granules should be mixed with 5 mL of age-appropriate food or liquid and completely consumed within 1 hour at or below room temperature Reduce dose to once daily in patients with moderate to severe hepatic impairment and those taking concomitant moderate CYP3A inhibitors; reduce dose to twice weekly in patients taking concomitant strong CYP3A inhibitors	150 mg tablets; 50 mg, 75 mg oral granules in unit-dose packets
lumacaftor/ivacaftor (Orkambi)	Adults and children ≥ 12 years of age: two 200/125 mg tablets orally every 12 hours (800/500 mg/day) Children 6 to 11 years old: two 100/125 mg tablets orally every 12 hours (400/500 mg/day) Children 2 to 5 years old and ≥ 14 kg: one 150/188 mg granule packet orally every 12 hours (300/376 mg/day) Children 2 to 5 years old and < 14 kg: one 100/125 mg granule packet orally every 12 hours (200/250 mg/day) All doses should be administered with fat-containing food Oral granules should be mixed with 5 mL of age-appropriate food or liquid and completely consumed within 1 hour at or below room temperature Reduce dose in patients with moderate or severe hepatic impairment (throughout treatment) and when initiating lumacaftor/ivacaftor in patients already taking strong CYP3A inhibitors (first week only)	100/125 mg, 200/125 mg tablets 100/125 mg, 150/188 mg oral granules in unit-dose packets
tezacaftor/ivacaftor (Symdeko)	Adults and children ≥ 12 years of age: one tablet containing tezacaftor 100 mg/ivacaftor 150 mg orally in the morning and one tablet containing ivacaftor 150 mg in the evening, approximately 12 hours apart All doses should be administered with fat-containing food	100/150 mg tezacaftor/ivacaftor fixed-dose combination tablets co-packaged with 150 mg ivacaftor tablets
elexacaftor/ivacaftor/ tezacaftor (Trikafta)	The recommended dose is two combination tablets each containing 100 mg elexacaftor/50 mg tezacaftor/75 mg ivacaftor in the morning and one tablet of 150 mg ivacaftor in the evening, approximately 12 hours apart. Tablets should be swallowed whole and taken with fat-containing foods. Missed doses should be made up as soon as possible, but only if it has been ≤ 6 hours since the missed dose.	100 mg elexacaftor, 75 mg tezacaftor, and 50 mg ivacaftor co-packaged with 150 mg ivacaftor

Antibiotics, Inhaled – Dosing & Availability

Drug	Dose	Administration	Duration	Average Length of Treatment (minutes)	Availability
amikacin liposome (Arikayce)	Adults: 590 mg once daily	Administer 1 vial using the Lamira™ Nebulizer System	Variable; recommended for 12 months following negative sputum (generally 12 to 18 months)	≈14	590 mg/8.4 mL (1 vial) inhalation suspension
aztreonam (Cayston)	For adults and pediatric patients > 7 years old: 75 mg 3 times a day	Reconstitute 1 vial of powder with 1 ampule of saline immediately before use and administer dose only with Altera® Nebulizer System	28 days on treatment, followed by 28 days off	≈2 to 3	75 mg powder for inhalation solution (1 vial)
tobramycin (Bethkis)	For adults and pediatric patients > 6 years old: 300 mg twice a day	Administer 1 ampule by using a hand-held PARI LC® PLUS Reusable Nebulizer with a PARI Vios® Air compressor	28 days on treatment, followed by 28 days off	≈15	300 mg/4 mL (1 ampule) for nebulization
tobramycin (Kitabis Pak)	For adults and pediatric patients > 6 years old: 300 mg twice a day	Administer drug using PARI LC PLUS™ Reusable Nebulizer with a DeVilbiss® Pulmo-Aid® compressor as close to 12 hours apart as possible (not < 6 hours between doses)	28 days on treatment, followed by 28 days off	≈15	300 mg/5 mL (1 ampule) for nebulization
tobramycin (TOBI)	For adults and pediatric patients > 6 years old: 300 mg twice a day	Administer drug using PARI LC PLUS Reusable Nebulizer with a DeVilbiss Pulmo-Aid compressor and as close to 12 hours apart as possible (not < 6 hours between doses)	28 days on treatment, followed by 28 days off	≈15	300 mg/5 mL (1 ampule) for nebulization
tobramycin (TOBI Podhaler)	For adults and pediatric patients > 6 years old: 112 mg twice daily	Administered only with Podhaler device; capsules are inserted 1 at a time in the device and inhaled sequentially	28 days on treatment, followed by 28 days off	≈15	28 mg dry powder capsules for inhalation