Washington Pharmacy Advisory Committee Meeting

June 26, 2024

Nina Huynh, PharmD, BCPS

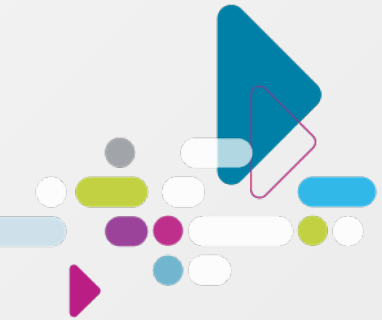
Umang Patel, PharmD

Agenda Topics

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

Disease Modifiers, T1DM

ANTIDIABETICS : CELLULAR THERAPY



Disease Modifiers, T1DM – Disease State Description

Type 1 Diabetes (T1DM)

- It is estimated that over 37 million Americans have diabetes mellitus (DM)
- Diabetes is responsible for increased morbidity and mortality and achieving adequate glycemic control is crucial to minimize chronic microvascular (e.g., blindness, renal dysfunction, neuropathy) and macrovascular (e.g., cardiovascular disease [CVD]) complications
- Misclassification of T1DM in adults is common and over 40% of those diagnosed with T1DM after the age of 30 years were initially thought to have T2DM
- Distinguishing features of T1DM includes younger age at diagnosis (< 35 years), lower body mass index (BMI; < 25 kg/m^2), unintended weight loss, ketoacidosis, and glucose > 360 mg/dL
  - A family history of T1DM or a history of autoimmune disease may also be present

- **American Diabetes Association (ADA) Standards of Medical Care in Diabetes, 2023**
  - Advises that most adults and children with T1DM be treated with multiple daily insulin injections of prandial and basal insulin, or continuous subcutaneous (SC) insulin infusion
  - Rapid-acting insulin analogs are typically used to reduce hypoglycemia risk
  - Continuous glucose monitoring (CGM) should be considered in most patients
    - Automated insulin delivery systems are recommended to improve glycemic control and reduce hypoglycemia
    - The rapid-acting insulins, insulin aspart (Fiasp, Novolog, generic), insulin glulisine (Apidra), insulin lispro (Admelog, Humalog U-100, generic), insulin lispro-aabc (Lyumjev), and insulin lispro/protamine lispro (Humalog Mix 50/50 and 75/25, generic) are approved for use with insulin pumps

Disease Modifiers, T1DM

Lantidra (donislecel-jujn)

- June 2023
  - FDA approved donislecel-jujn, the first pancreatic islet cellular therapy made from deceased donor cells, for the treatment of adults with T1DM who are unable to approach target HbA1c because of current repeated episodes of severe hypoglycemia despite intensive diabetes management and education
- FDA Indication
  - Treatment of adults with Type 1 diabetes who are unable to approach target HbA1c because of current repeated episodes of severe hypoglycemia despite intensive diabetes management and education
- Warnings
  - Risks from Concomitant Immunosuppression: Increased risk of severe infections including opportunistic infections, malignancy, and severe anemia
  - Procedural Complications: Liver laceration, hemorrhage and intra-abdominal bleeding have occurred with portal administration
- Dosage
  - Individualized dosage is based on tissue volume
    - The recommended minimum dose is 5,000 equivalent islet number (EIN)/kg for initial infusion and 4,500 EIN/kg for subsequent infusion in the same recipient
    - The maximum dose per infusion is dictated by the estimated tissue volume, which should not exceed 10 mL per infusion, and the total EIN present in the infusion bag (up to a maximum of 1×10^6 EIN per bag)
  - Second or third infusion may be performed within 1 year of the previous infusion or within 1 year of losing independence from exogenous insulin
  - Pre-infusion induction immunosuppression is required
- Availability
  - Approved as cellular suspension administered as an IV infusion into the hepatic portal vein
  - Each infusion uses one lot of Lantidra which consists of islets manufactured from the pancreas of a single deceased donor
  - The dosage strength is represented by the total EIN in a single preparation and varies between product batches

Cardiovascular, Other

CARDIOVASCULAR AGENTS : MISC

Cardiovascular, Other – Disease State Description

Cardiovascular disease

- Between 2013 and 2019, the American College of Cardiology (ACC) and the American Heart Association (AHA), in combination with the National Heart, Lung, and Blood Institute (NHLBI), released 4 new consensus guidelines regarding cholesterol management, cardiovascular (CV) risk assessment, obesity, and lifestyle
  - Obesity is associated with increased risk in cardiovascular disease (CVD) mortality
- In 2018, ACC and AHA emphasizes lifestyle modification including a reduced calorie diet and aerobic physical activity, as a critical component of atherosclerotic cardiovascular disease (ASCVD) risk reduction, both prior to and in conjunction with cholesterol-lowering drug therapies
- In June 2021, AHA published a scientific statement on physical activity as a crucial component in the first-line treatment for increased blood pressure and cholesterol
  - The statement details mild- to moderate-risk patient groups appropriate for lifestyle-only treatment of increased cholesterol as well as a description of the recommendations, usual effects, and considerations for lifestyle management with physical activity
- In 2023, AHA also published a scientific statement which reports that resistance training has a favorable but modest effect on total cholesterol (TC), triglycerides (TG), and high-density lipoprotein cholesterol (HDL-C)
  - Evidence for the effect of resistance training on low-density lipoprotein cholesterol (LDL-C) is more variable

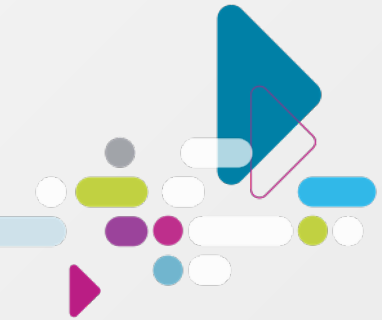
Cardiovascular, Other

Lodoco (colchicine)

- June 2023
  - FDA approved colchicine 0.5 mg tablets to reduce the risk of MI, stroke, coronary revascularization, and CV death in adults with established atherosclerotic disease or with multiple risk factors for CV disease
- FDA Indications
  - Reduce the risk of myocardial infarction (MI), stroke, coronary revascularization, and cardiovascular death in adult patients with established atherosclerotic disease or with multiple risk factors for cardiovascular disease
- Warnings
  - Blood dyscrasias: myelosuppression, leukopenia, granulocytopenia, thrombocytopenia, pancytopenia, and aplastic anemia
  - Neuromuscular toxicity: Myotoxicity including rhabdomyolysis may occur, especially in combination with other drugs known to cause this effect; consider temporary interruption or discontinuation
  - Contraindications: Pre-existing blood dyscrasias, renal failure, and severe hepatic impairment
- Dosage
  - Recommended dose is 0.5 mg once daily
- Availability
  - Tablets: 0.5 mg

Stem Cell Mobilizers

HEMATOPOIETIC AGENTS : STEM CELL MOBILIZERS



Stem Cell Mobilizers – Disease State Description

Multiple Myelomas (MM)

- Multiple myeloma is a malignant neoplasm of plasma cells that accumulate in the bone marrow leading to bone destruction and marrow failure
- In addition, patients with symptomatic MM must have ≥ 1 myeloma-defining event which may include hypercalcemia, renal insufficiency, anemia, or lytic bone lesions
- Multiple myeloma accounts for approximately 1.8% of all malignancies and 18% of all hematologic malignancies in the US
- The median age of diagnosis is 69 years
- Multiple myeloma is sensitive to a variety of agents, but the disease is not considered curable with currently available drug therapies
- The clinical course of MM usually involves initial responses to chemotherapy, but these responses may be transient; thus, re-treatment with multiple rounds of therapy with different agents may be required to treat relapse
- The 5-year relative survival rate is 57.9%, and overall survival now is estimated to be 8 to 10 years among patients with standard-risk disease, but it is significantly lower in patients that exhibit high-risk features

- **The NCCN guidelines, 2022**
  - States a preference for 3-drug regimens over 2-drug regimens as the standard of care for primary treatment
    - Patients who could not be considered for initiation of treatment with a 3-drug regimen can be started with a 2-drug regimen, with a third drug added once performance status improves
    - For transplant-eligible patients, the 3-drug regimen of bortezomib/lenalidomide/dexamethasone is the preferred initial therapy (category 1)
    - For patients who are non-transplant candidates, recommendations for primary therapy include bortezomib/lenalidomide/dexamethasone and daratumumab/lenalidomide/dexamethasone (both designated category 1)
  - Single-agent lenalidomide is the NCCN category 1, preferred oral drug treatment for maintenance therapy of MM, regardless of the transplant eligibility status of the patient.
    - Bortezomib/lenalidomide with or without dexamethasone for transplant eligible patients is listed as useful in certain circumstances (category 2A), and bortezomib/lenalidomide is listed as useful in certain circumstances for non-transplant candidates

Stem Cell Mobilizers – Disease State Description

Aphexda (motixafortide)

- **September 2023:**
  - A hematopoietic stem cell mobilizer indicated in combination with filgrastim (G-CSF) to mobilize hematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in patients with multiple myeloma
- **FDA Indication**
  - In combination with filgrastim (G-CSF) to mobilize hematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in patients with multiple myeloma
- **Warnings**
  - Anaphylactic Shock and Hypersensitivity Reactions: Premedicate all patients with a combination of an H1-antihistamine, an H2 blocker, and a leukotriene inhibitor prior to each dose. Administer in a setting where personnel and therapies are available for immediate treatment. Observe for signs and symptoms and manage promptly.
  - Injection Site Reactions: The addition of analgesic premedication (e.g., acetaminophen) is recommended
  - Tumor Cell Mobilization in Patients with Leukemia: may mobilize leukemic cells and should not be used in leukemia patients
  - Leukocytosis: Monitor white blood cell counts during use
- **Dosage**
  - Initiate after filgrastim has been administered daily for 4 days
  - Recommended dosage is 1.25 mg/kg actual body weight SC 10 to 14 hours prior to initiation of apheresis
  - A second dose can be administered 10 to 14 hours prior to a third apheresis
- **Availability**
  - 62 mg lyophilized powder in a SDV for reconstitution

Thrombopoiesis Stimulating Proteins

HEMATOPOIETIC AGENTS : THROMBOPOIESIS (TPO) STIMULATING PROTEINS

Thrombopoiesis Stimulating Proteins – Disease State Description

Immune thrombocytopenia (ITP)

- An immune-mediated disorder in which platelets are opsonized by autoreactive antibodies and prematurely destroyed by the reticuloendothelial system
- In children, ITP is usually an acute, self-limiting disease that often occurs weeks after viral infection or immunization
  - Spontaneous remission in children typically occurs within ≤ 2 months in 80% of usual cases
  - Although treatment does not impact the likelihood for chronic ITP, it can shorten the duration of thrombocytopenia in some patients
- In adults, ITP has an insidious onset with no preceding viral or other illness and typically has a chronic course
  - A complete blood count (CBC) shows isolated thrombocytopenia; if anemia and/or neutropenia are found, it indicates the potential for other conditions
  - Signs and symptoms of ITP are highly variable and range from asymptomatic with mild bruising or mucosal bleeding to frank hemorrhage from any site
  - Severity of ITP in adults is dependent on the presence of active bleeding, as well as platelet count, patient age, patient lifestyle related to risk of bleeding, and presence of additional risk factors for bleeding, such as uremia or chronic liver diseases (CLD)
- Secondary causes of ITP include drug-induced, autoimmune diseases such as systemic lupus erythematosus (SLE), and viral infections such as human immunodeficiency virus (HIV) and hepatitis C virus (HCV)

- **American Society of Hematology (ASH), 2019**
  - For newly-diagnosed adults who are asymptomatic or have minor mucocutaneous bleeding, ASH suggests treatment with corticosteroids over observation only if the platelet count is < 30 × 10^9/L (conditional recommendation, very low certainty evidence) and recommends management with observation rather than corticosteroid use if the platelet count is ≥ 30 x 10^9/L (very low certainty)
  - Treatment decisions should consider the severity of thrombocytopenia, comorbid conditions, use of antiplatelet or anticoagulant drugs, upcoming procedures, and the patient's age
  - For the management of adults with newly diagnosed ITP:
    - Shorter courses of corticosteroids (such as prednisone 0.5 to 2 mg/kg/day or dexamethasone 40 mg/day for 4 days for a total of ≤ 6 weeks) are recommended over longer courses of corticosteroids (> 6 weeks) (very low certainty
    - Corticosteroids alone are suggested as initial therapy in these patients rather than rituximab and corticosteroids

Thrombopoiesis Stimulating Proteins – Disease State Description

Aplastic anemia

- Caused by bone marrow failure
- Most cases of aplastic anemia have an acquired cause; this can include idiopathic factors, infections, exposure to ionizing radiation/toxic chemicals, pregnancy, and other conditions
- Initial presentation is often related to anemia or bleeding; however, fever or infections may occur
- Symptoms include dyspnea, fatigue, swelling of the feet, gingival bleeding, petechial rashes, infection, headache, and pallor color
- The major causes of morbidity and mortality from aplastic anemia include infection and bleeding
- Severe or very severe aplastic anemia should be treated promptly
- Nonpharmacologic treatment includes blood transfusions and hematopoietic cell transplant
- Pharmacotherapy includes:
  - Immunosuppressive agents (e.g., cyclosporine, methylprednisolone, equine or rabbit antithymocyte globulin, cyclophosphamide, alemtuzumab; all off-label use [except antithymocyte globulin [(Atgam]), which is indicated for the treatment of moderate to severe aplastic anemia in patients unsuitable for bone marrow transplantation])
    - Approximately 25% to 30% of patients fail to respond to immunosuppressive therapy
  - Hematopoietic growth factors (eltrombopag, sargramostim [off-label], filgrastim [off-label]), and the antineoplastic agent fludarabine (off-label)
    - Monotherapy with hematopoietic growth factors (e.g., recombinant human erythropoietin [rHuEPO], granulocyte colony-stimulating factor [G-CSF]) is not recommended for newly diagnosed patients
  - Chelating agents (deferoxamine, deferasirox) may be required in patients chronically transfused due to elevated serum ferritin levels

Thrombopoiesis Stimulating Proteins

Alvaiz (eltrombopag)

- November 2023
  - FDA has approved a new formulation of eltrombopag (Alvaiz), a thrombopoietin receptor agonist, indicated for:
    1. Treatment of thrombocytopenia in patients ≥ 6 years old with persistent or chronic immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy (should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increase the risk for bleeding)
    2. Treatment of thrombocytopenia in adults with chronic hepatitis C to allow the initiation and maintenance of interferon (IFN)-based therapy (should be used only in patients with chronic hepatitis C whose degree of thrombocytopenia prevents the initiation of IFN-based therapy or limits the ability to maintain interferon-based therapy)
    3. Treatment of adults with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy
- FDA Indication
  - Treatment of thrombocytopenia in adult and pediatric patients 6 years and older with persistent or chronic immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. Alvaiz should be used only inpatients with ITP whose degree of thrombocytopenia and clinical condition increase the risk for bleeding
  - Treatment of thrombocytopenia in adult patients with chronic hepatitis C to allow the initiation and maintenance of interferon-based therapy. Alvaiz should be used only in patients with chronic hepatitis C whose degree of thrombocytopenia prevents the initiation of interferon-based therapy or limits the ability to maintain interferon-based therapy
  - Treatment of adult patients with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy
- Warnings
  - BBW: Risk of hepatic decompensation in patients with chronic hepatitis C and risk of hepatotoxicity
  - Safety and efficacy not established in combination with direct-acting antiviral agents used w/o IFN for treatment of chronic hep C infection
  - Not indicated for treatment of patients with myelodysplastic syndrome (MDS): Increased risk of death and progression of myelodysplastic syndromes to acute myeloid leukemia
- Dosage
  - Persistent or chronic ITP: Initiate at 36 mg daily; Dose reductions are needed for patients with hepatic impairment and some patients of East-/Southeast-Asian ancestry. Adjust to maintain platelet count greater than or equal to 50 x 10^9/L. Do not exceed 54 mg per day
  - Chronic Hepatitis C-associated thrombocytopenia: Initiate at 18 mg daily for all patients. Adjust to achieve target platelet count required to initiate antiviral therapy. Do not exceed 72 mg per day
  - Refractory Severe Aplastic Anemia: Initiate at 36 mg daily. Reduce initial dose in patients with hepatic impairment or patients of East-/Southeast-Asian ancestry. Adjust to maintain platelet count greater than 50 x 10^9/L. Do not exceed 108 mg per day
- Availability
  - Oral tablets: 9 mg, 18 mg, 36 mg, and 54 mg

Immunomodulators, Asthma

ASTHMA AND COPD AGENTS : MONOCLONAL ANTIBODIES

Immunomodulators, Asthma – Disease State Description

Asthma

- Annually, there are > 1 million emergency department visits in the United States (US) attributable to asthma
- An estimated 8.7% of adults and 6.2% of children (over 24.9 million Americans total) have asthma with > 39% reporting at least 1 asthma attack in the last year
- Asthma is typically characterized by chronic airway inflammation and hyperresponsiveness and is diagnosed based on history of respiratory symptoms (e.g., wheeze, shortness of breath, cough) and evidence of variable expiratory airflow limitation

- **Global Initiative for Asthma (GINA), 2023**
  - The GINA Evidence-based report offers a management plan to adjust therapy in a continuous cycle of assessment, treatment, and review of the patient's response as it relates to symptom control, future risk of exacerbations, and side effects
  - During this continuous cycle, a stepwise treatment approach is used to achieve control using the patient's current level of control as the baseline
  - If the patient is not controlled on the current regimen, treatment should be stepped up until control is achieved
  - Patients in steps 1 and 2 are considered to have mild asthma, patients well-controlled in steps 3 to 4 have moderate asthma, and asthma that remains uncontrolled despite optimized treatment with high dose ICS-long-acting beta-agonist (LABA) or requires high dose ICS-LABA to maintain control is considered to be severe
  - Treatment regimens are laid out in 2 tracks depending on the medication chosen by the patient for relief of breakthrough symptoms (as-needed reliever medication)
    - Track 1 outlines the treatment approach when the reliever is low dose ICS-formoterol and is the preferred approach due to demonstrated efficacy in reducing severe exacerbations and the simplicity of having one medication for both maintenance and as-needed treatment
    - Track 2 provides an alternative approach when the chosen reliever medication is a short-acting beta agonist (SABA) or ICS-SABA
    - To control asthma, treatment may be stepped up or down within a track while using the same reliever medication or switching between tracks

Immunomodulators, Asthma – Disease State Description

Stepwise Approach to Asthma Control from 2023 GINA Guidelines – Controller and Reliever Therapy in Patients ≥ 12 Years Old

Step	Track 1	Track 2	Other Controller Options
Reliever			
1 – 5	▪ As-needed low dose ICS-formoterol*	▪ As-needed SABA or ICS-SABA	--
Controller			
1	▪ As-needed low dose ICS-formoterol	▪ Low dose ICS whenever SABA is taken	--
2	▪ As-needed low dose ICS-formoterol	▪ Low dose maintenance ICS	▪ Low dose ICS whenever SABA is taken ▪ Daily LTRA ▪ Add HDM SLIT
3	▪ Low dose maintenance ICS-formoterol	▪ Low dose maintenance ICS-LABA	▪ Medium dose ICS ▪ Add LTRA or HDM SLIT
4	▪ Medium dose maintenance ICS-formoterol	▪ Medium/high dose maintenance ICS-LABA	▪ Add LAMA or LTRA or HDM SLIT ▪ High dose ICS
5	▪ Add LAMA ▪ Refer for phenotypic assessment ▪ Consider high dose ICS-formoterol ± anti-IgE (omalizumab), anti-IL5/5R (benralizumab, mepolizumab, reslizumab), anti-IL4R (dupilumab), anti-TSLP (tezepelumab) ▪ Consider treatment guided by sputum eosinophil count	▪ Add LAMA ▪ Refer for phenotypic assessment ▪ Consider high dose ICS-LABA ± anti-IgE (omalizumab), anti-IL5/5R (benralizumab, mepolizumab, reslizumab), anti-IL4R (dupilumab), anti-TSLP (tezepelumab) ▪ Consider treatment guided by sputum eosinophil count	▪ Add azithromycin (adults) or LTRA ▪ Add low dose OCS (consider adverse effects)

HDM SLIT = house dust mite sublingual immunotherapy; ICS = inhaled corticosteroid; IgE = Immunoglobulin E; IL-4R = Interleukin-4 receptor; IL-5/5R = interleukin-5/IL-5 receptor; LABA = long-acting beta$_2$-agonist; LAMA = long-acting muscarinic antagonist; LTRA = leukotriene receptor antagonist; SABA = short acting beta$_2$-agonist

* The data supporting the use of low-dose ICS/formoterol as a reliever medication are primarily derived from budesonide-formoterol.

Stepwise Approach to Asthma Control from 2023 GINA Guidelines – Controller and Reliever Therapy in Patients 6 to 11 Years Old

Step	Preferred Controller	Other Controller Options	Reliever*
1	▪ Low dose ICS whenever SABA is taken	▪ Daily low dose ICS	▪ As needed SABA
2	▪ Daily low dose ICS	▪ Daily LTRA ▪ Low dose ICS whenever SABA is taken	▪ As needed SABA
3	▪ Low dose ICS-LABA ▪ Medium dose ICS ▪ Very low dose ICS-formoterol MART	▪ Low dose ICS + LTRA	▪ As needed SABA (or ICS/formoterol for MART)
4	▪ Medium dose ICS-LABA ▪ Low dose ICS-formoterol MART ▪ Refer for expert advice	▪ Add tiotropium or LTRA	▪ As needed SABA (or ICS/formoterol for MART)
5	▪ Refer for phenotypic assessment ± higher dose ICS-LABA or add-on therapy (e.g., anti-IgE [omalizumab], anti-IL4R [dupilumab], anti-IL-5 [mepolizumab])	▪ Add low dose OCS as a last resort (consider adverse effects)	▪ As needed SABA

ICS = inhaled corticosteroid; IgE = Immunoglobulin E; IL-5 = interleukin-5; LABA = long acting beta$_2$-agonist; LTRA = leukotriene receptor antagonist; MART = maintenance and reliever therapy; OCS = oral corticosteroid; SABA = short acting beta$_2$-agonist

* The data supporting the use of low-dose ICS/formoterol as a reliever medication are primarily derived from budesonide-formoterol.

Immunomodulators, Asthma – Disease State Description

Food Allergy

- An estimated 32 million people in the US have food allergies, including 5.6 million children
- It is now estimated that peanut allergies specifically affect almost 1 million children in the US, and only 20% will outgrow their allergy
- It is estimated that allergic reactions to food cause 4 to 10 deaths annually in the US, and peanut allergies specifically were associated with food allergy deaths in 35 of 91 people from 2010 to 2019
- Previously, food allergy treatments primarily consisted of avoiding the allergen and promptly treating any accidental exposure
- Reaction to peanut exposure varies from mild skin and/or gastrointestinal symptoms to severe angioedema and anaphylaxis
- When accidental peanut exposure occurs, antihistamines can manage mild to moderate reactions, but patients must carry an epinephrine auto-injector to treat severe reactions

Immunomodulators, Asthma

Xolair (Omalizumab)

- **February 2024:**
  - **FDA approved new indication for IgE-mediated food allergy in adult and pediatric patients ≥ 1 year old for reduction of allergic reactions (Type I), including anaphylaxis, that may occur with accidental exposure to one or more foods, used in conjunction with food allergen avoidance**
  - **Limitation of use stating not indicated for the emergency treatment of allergic reactions, including anaphylaxis**
- **FDA Indication**
  - Moderate to severe persistent asthma in adults and pediatric patients 6 years of age and older with a positive skin test or in vitro reactivity to a perennial aeroallergen and symptoms that are inadequately controlled with inhaled corticosteroids
  - Chronic rhinosinusitis with nasal polyps (CRSwNP) in adult patients 18 years of age and older with inadequate response to nasal corticosteroids, as add-on maintenance treatment
  - **IgE-mediated food allergy in adult and pediatric patients aged 1 year and older for the reduction of allergic reactions (Type I), including anaphylaxis, that may occur with accidental exposure to one or more foods. To be used in conjunction with food allergen avoidance**
  - Chronic spontaneous urticaria (CSU) in adults and adolescents 12 years of age and older who remain symptomatic despite H1 antihistamine treatment
- **Warnings**
  - **BBW**: Anaphylaxis, presenting as bronchospasm, hypotension, syncope, urticaria, and/or angioedema of the throat or tongue
- **Dosage**

Indication	Dosage
Asthma	75 to 375 mg SC every 2 or 4 weeks
Chronic Rhinosinusitis with Nasal Polyps	75 to 600 mg SC every 2 or 4 weeks
IgE-Mediated Food Allergy	**75 mg to 600 mg SC every 2 or 4 weeks**
Chronic Spontaneous Urticaria	150 or 300 mg SC every 4 weeks

- **Availability**
  - Single-dose prefilled syringe: 75 mg/0.5 mL, 150 mg/mL, and 300 mg/2 mL solution
  - Single-dose prefilled autoinjector: 75 mg/0.5 mL, 150 mg/mL and 300 mg/2 mL solution
  - Single-dose vial for reconstitution: 150 mg lyophilized powder

Immunomodulators, Asthma

Fasenra (benralizumab)

- **April 2024:**
  - **Indication as add-on maintenance treatment of patients with severe asthma & with an eosinophilic phenotype has been expanded to include pediatrics aged 6 to 11 years old. Fasenra was previously approved for patients ≥ 12 years old for this indication**
- **FDA Indication**
  - **Add-on maintenance treatment of patients aged 6 years and older with severe asthma, and with an eosinophilic phenotype**
- **Dosage**
  - **Fasenra should only be administered by a caregiver or Health Care Practitioner (HCP) for patients aged 6 to 11 years old**
  - **Recommended dosage for patients 6 to 11 years old is based on body weight**
    - **< 35 kg: 10 mg (one injection) SC every 4 weeks for the first 3 doses, then every 8 weeks thereafter**
    - **≥ 35 kg: 30 mg (one injection) SC every 4 weeks for the first 3 doses, then every 8 weeks thereafter**
  - Recommended dosage for adult and adolescent patients 12 years of age and older is 30 mg every 4 weeks for first 3 doses followed by once every 8 weeks thereafter
- **Warnings**
  - Hypersensitivity reactions: anaphylaxis, angioedema, urticaria, rash
- **Availability**
  - **10 mg/0.5 mL solution in a single-dose prefilled syringe**
  - **30 mg/mL solution in a single-dose prefilled syringe**
  - **30 mg/mL solution in a single-dose autoinjector pen**

Stimulants & Related Agents:

ADHD / ANTI-NARCOLEPSY : DOPAMINE AND NOREPINEPHRINE REUPTAKE INHIBITORS (DNRIS)

ADHD / ANTI-NARCOLEPSY : NON-STIMULANTS

ADHD / ANTI-NARCOLEPSY : STIMULANTS - LONG ACTING

ADHD / ANTI-NARCOLEPSY : STIMULANTS - MISC

ADHD / ANTI-NARCOLEPSY : STIMULANTS - SHORT ACTING

Stimulants & Related Agents - Disease State Description

Attention Deficit Hyperactivity Disorder (ADHD)

- The most common use of stimulants is for the treatment of ADHD, for which they are considered first-line therapy
- ADHD been diagnosed in approximately 9.8% of children 3 to 17 years of age and about estimated to range from 2% to 7% of adults
- It is a chronic condition with core symptoms of inattention, hyperactivity, and difficulty controlling behavior
- It may also be accompanied by internalized disorders, such as depression and anxiety, as well as conduct and disruptive behavior disorders, autism spectrum disorder, and tics
- The 3 main types of ADHD are primary hyperactive, primary inattentive, and combine

- **American Academy of Pediatrics (AAP), 2019**
  - Recommend parent- and/or teacher-administered behavior therapy as first-line treatment for children 4 to 5 years of age
  - Methylphenidate (MPH) may be prescribed if the behavior interventions do not provide significant improvement and there continues to be moderate to severe disturbance in the child's function
  - For children 6 to 11 years of age, the evidence is particularly strong for FDA-approved stimulant use for ADHD, and sufficient, but less compelling for non-stimulants in the following order: atomoxetine (Strattera), guanfacine ER (Intuniv) and clonidine ER (Kapvay)
  - Medication therapy in addition to behavioral therapy is recommended
  - For patients 12 to 18 years of age, the AAP recommends FDA-approved medications, with the adolescent's assent, and behavior therapy as treatment for ADHD; preferably both

Stimulants & Related Agents - Disease State Description

Binge-eating disorder (BED)

- BED is the most common eating disorder in the United States (US) with an estimated lifetime prevalence of 0.85%
- BED is characterized by uncontrolled eating of a large amount of food, not associated with inappropriate compensatory behavior, occurring at least once every week for 3 months and ≥ 3 of the following behaviors: eating rapidly, eating until uncomfortably full, eating when not hungry, eating alone due to embarrassment, and/or feelings of guilt after eating

- **American Psychiatric Association (APA), 2023**
  - Suggests treatment with an antidepressant or lisdexamfetamine for patients seeking pharmacologic therapy, noting that lisdexamfetamine has been associated with modest short-term effects and caution should be exercised in those with cardiac disease, psychotic symptoms, or bipolar disorder due to potential adverse events
  - Lisdexamfetamine dimesylate (Vyvanse) is the first and only FDA-approved product for moderate to severe BED in adults

Stimulants & Related Agents

New Generic

- **amphetamine ER ODT- July 2023**
  - FDA approved the first generic for Adzenys XR-ODT (amphetamine ER ODT) by Actavis
- **lisdexamfetamine dimesylate – September 2023**
  - FDA approved first-time generic for Vyvanse capsules and chewable tablets by several manufacturers, indicated for ADHD in patients ≥ 6 years old, and for moderate to severe binge-eating disorder (BED) in adults

Antipsychotics

ANTIPSYCHOTICS / ANTIMANIC AGENTS : ANTIPSYCHOTICS - 2ND GENERATION

ANTIPSYCHOTICS / ANTIMANIC AGENTS : ANTIPSYCHOTICS - COMBINATIONS

ANTIPSYCHOTICS / ANTIMANIC AGENTS : PARKINSONS PSYCHOTIC DISORDER

ANTIPSYCHOTICS / ANTIMANIC AGENTS : COMBINATION PSYCHOTHERAPEUTICS

Antipsychotics – Disease State Description

Schizophrenia

- The most common psychotic illness is schizophrenia, which affects 1% of the population
- Between 20% and 40% of schizophrenic patients attempt suicide, and 4 to 5% of patients succeed in their attempt
- Symptoms of schizophrenia can be subcategorized as positive, negative, cognitive, and mood
- Symptoms include delusions, hallucinations, disorganized speech, disorganized or catatonic behavior

- **American Psychiatric Association (APA), 2020**
  - Recommends that patients with schizophrenia be treated with an antipsychotic, including monitoring for both safety and efficacy
  - An antipsychotic should be continued in patients whose symptoms improve, with the APA suggesting continuation of the same antipsychotic after stabilization
  - Recommends clozapine specifically in patients with treatment-resistant schizophrenia and in patients with a significant risk of suicide. They also suggest clozapine for patients with aggressive behavior despite other treatments
  - In addition, there is no preference for first-generation antipsychotics (FGAs) or second-generation antipsychotics (SGAs), although clinically meaningful distinctions, such as tolerability, do occur
  - Except for clozapine, no antipsychotic has demonstrated superior efficacy when compared to other agents within the class
  - APA also state that there is no reliable strategy to predict response; thus, initial treatment choice is often individualized and includes several patient-specific factors
  - The guideline also details management of adverse effects, such as acute dystonia, parkinsonism, akathisia, and tardive dyskinesia, some of which may warrant a switch to an alternative antipsychotic treatment

Antipsychotics – Disease State Description

Bipolar Disorder

- Lifelong prevalence estimates of bipolar disorder range from 0.9% to 2.1% of the population
- Characterized by episodes of mania, depression, or a mixed state
- Criteria used to diagnose bipolar I disorder:
  1. The presence of a manic episode (persistent elevated, expansive, or irritable mood for at least 1 week with increased energy/activity) **OR**
  2. A mixed features specifier (rapidly alternating polarity of mood, sadness, irritability, and mania for at least 1 week), **AND**
  3. 3 or more other characteristic symptoms (inflated self-esteem or grandiosity, decreased need for sleep, more talkative than usual or pressured speech, flight of ideas or feelings of racing thoughts, distractibility, increase in goal-directed activity or psychomotor agitation, and excessive involvement in risky, pleasurable activities)
- There is no cure for bipolar disorder, but the appropriate pharmacological treatment can decrease morbidity and mortality

- **American Psychiatric Association (APA), 2002**
  - First-line pharmacological treatment for more severe manic or mixed episodes requires the initiation of lithium or valproate plus an antipsychotic agent
  - SGAs are preferred over the FGAs due to their more tolerable adverse effect profile
  - For a bipolar manic episode with less severity, monotherapy with lithium, valproate, or an antipsychotic may be sufficient
  - Use of standard antidepressants as monotherapy can precipitate a manic episode in bipolar patients
  - During maintenance treatment, recommendations suggest to first optimize the medication dose in patients with bipolar disorder, especially in patients experiencing a breakthrough manic episode, and then consider adding another first-line agent
  - A Guideline Watch supplement was published in 2005 and included additional data on the use of SGAs (e.g., aripiprazole, olanzapine, quetiapine, risperidone, ziprasidone) as monotherapy or adjunctive therapy and an extended-release formulation of carbamazepine for the acute treatment of manic or mixed episodes and stated that these provide clinicians with additional treatment options

Antipsychotics

Fanapt (iloperidone)

- **April 2024:**
  - **FDA approved new indication for acute treatment of manic or mixed episodes associated with bipolar I disorder in adults**
- **FDA Indication**
  - **Acute treatment of manic or mixed episodes associated with bipolar I disorder in adults**
  - Treatment of schizophrenia in adults
- **Warnings**
  - BBW: Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Not approved for the treatment of patients with dementia-related psychosis
  - Cerebrovascular Adverse Reactions in Elderly Patients with Dementia-Related Psychosis: Increased incidence of cerebrovascular adverse reactions (e.g., stroke, transient ischemic attack)
  - Pregnancy: May cause extrapyramidal and/or withdrawal symptoms in neonates with third trimester exposure
- **Dosage**
  -

Indication	Starting Dosage	Recommended Dosage
Bipolar mania	**1 mg twice daily**	**12 mg twice daily**
Schizophrenia	1 mg twice daily	6 mg to 12 mg twice daily

- **Availability**
  - Oral Tablet: 1 MG, 2 MG, 4 MG, 6 MG, 8 MG, 10 MG, 12 MG

Antipsychotics

Risvan (risperidone ISM)

- **April 2024:**
  - Atypical antipsychotic FDA-approved for the treatment of schizophrenia in adults
  - Prolonged-release injectable risperidone that provides immediate and sustained plasma drug levels and does not require loading doses or supplementation with oral risperidone
- **FDA Indication**
  - Schizophrenia in adults
- **Warnings**
  - BBW: Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Not approved for the treatment of patients with dementia-related psychosis
  - Cerebrovascular Adverse Reactions in Elderly Patients with Dementia-Related Psychosis: Increased incidence of cerebrovascular adverse reactions (e.g., stroke, transient ischemic attack)
  - Pregnancy: May cause extrapyramidal and/or withdrawal symptoms in neonates with third trimester exposure
- **Dosage**
  - Risvan may be initiated at a dosage of 75 mg or 100 mg once monthly after establishing tolerability with oral risperidone
  - Administered by intramuscular (IM) injection in the gluteal or deltoid muscle by Health Care Practitioners
  - Risvan 75 mg IM monthly corresponds to 3 mg/day oral risperidone and 100 mg IM monthly corresponds to 4 mg/day oral risperidone
  - Patients who are on stable on oral risperidone doses < 3 mg/day or > 4 mg/day may not be candidates for Risvan
  - Do not administer more than one dose per month
- **Availability**
  - For extended-release injectable suspension: 75 mg and 100 mg

Bone Resorption Inhibitors;
Bone Resorption Suppression and Related Agents

BONE DENSITY REGULATORS : RANK LIGAND INHIBITORS

Bone Density Regulators

FDA Communication

❖ **Prolia (denosumab) – January 2024**

- FDA released a Drug Safety Communication to warn that denosumab increases the risk of severe hypocalcemia in patients with advanced Chronic Kidney Disease (CKD) including dialysis-dependent patients
  - Cases of serious harm, including hospitalization, life-threatening events, and death have been reported
- Severe hypocalcemia is more common in patients with CKD who also have mineral and bone disorder (CKD-MBD)

Anti-Allergens, Oral
ALLERGY : ALLERGENIC EXTRACTS / BIOLOGICALS - ORAL

COPD Agents
ASTHMA AND COPD AGENTS : ANTICHOLINERGICS
ASTHMA AND COPD AGENTS : LONG ACTING MUSCARINIC AGENT / LONG ACTING BETA AGONIST COMBINATIONS
ASTHMA AND COPD AGENTS : LONG ACTING MUSCARINIC AGENTS
ASTHMA AND COPD AGENTS : PHOSPHODIESTERASE 4 INHIBITORS

Glucocorticoids, Inhaled
ASTHMA AND COPD AGENTS : INHALED CORTICOSTEROID COMBINATIONS
ASTHMA AND COPD AGENTS : INHALED CORTICOSTEROIDS

Growth Factors
ENDOCRINE AND METABOLIC AGENTS : GROWTH HORMONE RELEASING HORMONES (GHRH)

Erythropoiesis Stimulating Proteins
HEMATOPOIETIC AGENTS : ERYTHROID MATURATION AGENTS
HEMATOPOIETIC AGENTS : ERYTHROPOIESIS-STIMULATING AGENTS (ESAS)
HEMATOPOIETIC AGENTS : HYPOXIA-INDUCIBLE FACTOR PROLYL HYDROXYLASE INHIBITORS

Oncology, Oral - Prostate
ONCOLOGY AGENTS : ANDROGEN BIOSYNTHESIS INHIBITORS – ORAL
ONCOLOGY AGENTS : ANTIANDROGENS - ORAL

Oncology, Oral - Breast
ONCOLOGY AGENTS : CYCLIN DEPENDENT KINASES (CDK) INHIBITORS - ORAL
ONCOLOGY AGENTS : ANTIESTROGENS - ORAL

Oncology, Oral - Skin
ONCOLOGY AGENTS : HEDGEHOG PATHWAY INHIBITORS - ORAL

Oncology, Oral - Hematologic
ONCOLOGY AGENTS : HEDGEHOG PATHWAY INHIBITORS - ORAL
ONCOLOGY AGENTS : RETINOIDS - ORAL

Oncology, Oral – Renal Cell Carcinoma
ONCOLOGY AGENTS : MTOR KINASE INHIBITORS – ORAL

Oncology, Oral – Lung
ONCOLOGY AGENTS : TOPOISOMERASE INHIBITORS - ORAL

Oncology, Oral – Other
ONCOLOGY AGENTS : IMIDAZOTETRAZINES – ORAL

Idiopathic Pulmonary Fibrosis
RESPIRATORY AGENTS : PULMONARY FIBROSING AGENTS

Smoking Cessation Agents
SMOKING DETERRENTS : MISC - OTHER