Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Washington Pharmacy Advisory Committee Meeting

October 19th, 2022

Umang Patel, Pharm.D.

Agenda Topics

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

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Lipotropics, Other:

ANTIHYPERLIPIDEMICS : MICROSOMAL TRIGLYCERIDE TRANSFER PROTEIN (MTP) INHIBITOR
ANTIHYPERLIPIDEMICS : PCSK-9 INHIBITORS

Lipotropics, Other - Disease State Description

- National Health and Nutrition Examination Survey (NHANES) reported that in 2015 to 2018 approximately 11.4% of adults had high total cholesterol (≥ 240 mg/dL) and 18.4% had low HDL-C (< 40 mg/dL)
  - Higher prevalence in women (12.1%) compared to men (10.5%)

- Many clinical trials have demonstrated that a high serum concentration of low-density lipoprotein cholesterol (LDL-C) and low levels of high-density lipoprotein cholesterol (HDL-C) are major risk factors for coronary heart disease (CHD)

National Center for Health Statistics Data Brief, 2018

Lipotropics, Other - Guidelines

- American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology (ACE), 2020
  - Although CV outcome trials (CVOTs) with colesevelam or bempedoic acid (BA) are not published, outcome trials with statins and ezetimibe or a PCSK9 inhibitor suggest further reduction in LDL-C though any combination of drugs would provide ASCVD benefits
  - Thereby, the 2020 AACE/ACE algorithm advocates for progression of therapy intensity in order to reach LDL-C targets
  - The 2019 approval of icosapent ethyl marked the first FDA approval for a medication that lowers TGs and reduces ASCVD
  - As the REDUCE IT trial used for approval showed a TG decrease of only 18%, the 2020 AACE/ACE algorithm states the CV outcome benefit does not appear to be related to the reduction in TGs
  - For patients with hypertriglyceridemia who do not have established ASCVD or diabetes with ≥ 2 risk factors and are not at the TG goal of < 150 mg/dL with statin therapy, then a fibrate, omega-3 fatty acid, or niacin can be considered
  - In order to decrease the potential for acute pancreatitis, all patients with severe hypertriglyceridemia (> 500 mg/dL) should receive a fibrate, prescription-grade omega-3 fatty acid, and/or niacin

Lipotropics, Other - Disease State Description

- Endocrine Society, 2020
  - In 2020, the ES published a clinical practice guideline focusing on lipid management in patients with endocrine disorders with the objective of preventing CV events and TG-induced pancreatitis; it also addresses whether treatment of the endocrine disorder improves lipid abnormalities as well as CV outcomes
  - The 2020 guidance recommends drug therapy as an adjunct to diet and exercise to prevent pancreatitis in adults with fasting TG levels > 500 mg/dL
  - Statin therapy is recommended in addition to lifestyle changes to decrease the CV risk in adults with type 2 diabetes and other CV risk factors
  - Additional details on these recommendations and recommendations for type 1 diabetes mellitus, obesity, thyroid disease, excess glucocorticoids, growth hormone secretion disorders, polycystic ovary syndrome, and menopause/hormone replacement are also provided

- American College of Cardiology, 2021
  - The ACC published an expert consensus decision pathway for the management of ASCVD risk reduction in patients with persistent hypertriglyceridemia, defined as TG levels ≥ 175 mg/dL after a minimum of 4 to 12 weeks of lifestyle intervention, a stable dose of maximally tolerated statins when indicated, and management of secondary causes.
  - ACC emphasizes the necessary lifestyle interventions for hypertriglyceridemia and recommends a low-fat diet and consideration of fibrates and prescription grade omega 3 fatty acids
  - They also note that fibrates provide benefit as monotherapy but not when combined with statins.

Lipotropics, Other - Disease State Description

- American Heart Association, 2021
  - The AHA published a scientific statement on physical activity as a crucial component in the first-line treatment for increased blood pressure or 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
  - Guidance and resources are also provided for evaluating, prescribing, counseling, and referring to assist in increased physical activity

- American College of Cardiology (ACC), 2021
  - Published an expert consensus decision pathway (ECDP) for the management of ASCVD risk reduction in patients with persistent hypertriglyceridemia (defined as TG levels ≥ 175 mg/dl after a minimum of 4-12 weeks of lifestyle intervention, a stable dose of maximally tolerated statins when indicated, and management of secondary causes)
  - ACC emphasizes the necessary lifestyle interventions for hypertriglyceridemia and recommends a low-fat diet and consideration of fibrates and prescription grade omega 3 fatty acids
  - They also note that fibrates provide benefit as monotherapy but not when combined with statins

Lipotropics, Other

- **evolocumab (Repatha)**
  - **October 2021: The FDA approved an expanded indication for Repatha to reduce LDL-C, as an adjunct to diet and other LDL-C-lowering therapies, in pediatric patients ≥ 10 years old with HeFH and in adults and pediatric patients ≥ 10 years old with HoFH; previously, it was only approved in pediatric patients ≥ 13 years old with HoFH**
  - **Indications:**
    - In adults with established cardiovascular disease (CVD) to reduce the risk of myocardial infarction, stroke, and coronary revascularization
    - As an adjunct to diet, alone or in combination with other low-density lipoprotein cholesterol (LDL-C)-lowering therapies, in adults with primary hyperlipidemia, including heterozygous familial hypercholesterolemia (HeFH), to reduce LDL-C
    - As an adjunct to diet and other LDL-C-lowering therapies in pediatric patients aged 10 years and older with HeFH, to reduce LDL-C
    - **As an adjunct to other LDL-C-lowering therapies in adults and pediatric patients aged 10 years and older with homozygous familial hypercholesterolemia (HoFH), to reduce LDL-C**
  - **Dosage:**
    - **<u>In adults and pediatric patients aged 10 years and older with HoFH:</u>**
      - **The initial recommended dosage is 420 mg once monthly administered subcutaneously**
      - **The dosage can be increased to 420 mg every 2 weeks if a clinically meaningful response is not achieved in 12 weeks**
      - Patients on lipid apheresis may initiate treatment with 420 mg every 2 weeks to correspond with their apheresis schedule. Administer after the apheresis session is complete
    - See dosage for other indications in PI/TCR
  - **Formulations:**
    - Injection: 140 mg/mL solution single-dose prefilled syringe
    - Injection: 140 mg/mL solution single-dose prefilled SureClick autoinjector
    - Injection: 420 mg/3.5 mL solution single-dose Pushtronex system (on-body infusor with prefilled cartridge)

Lipotropics, Other

- **inclisiran (Leqvio)**
  - **December 2021: The FDA has approved inclisiran (Leqvio), a small interfering RNA (siRNA) directed to PCSK9 mRNA, indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with HeFH or clinical ASCVD, who require additional lowering of LDL-C; the effect of inclisiran on CV morbidity and mortality has not been established**
  - **Indications:**
    - **As an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (ASCVD), who require additional lowering of lowdensity lipoprotein cholesterol (LDL-C)**
    - **Limitations of Use: The effect of Leqvio on cardiovascular morbidity and mortality has not been determined**
  - **Precautions:**
    - **Discontinue when pregnancy is recognized**
    - **Renal Impairment: No dose adjustments are necessary for patients with mild, moderate, or severe renal impairment**
    - **Hepatic Impairment: No dose adjustment is necessary in patients with mild to moderate hepatic impairment. Has not been studied in patients with severe hepatic impairment**
  - **Dosage:**
    - **The recommended dosage, in combination with maximally tolerated statin therapy, is 284 mg administered as a single subcutaneous injection initially, again at 3 months, and then every 6 months**
    - **Should be administered by a healthcare professional**
  - **Formulations:**
    - **Injection: 284 mg/1.5 mL (189 mg/mL) in a single-dose prefilled syringe**

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Antivirals, Oral:

ANTIVIRALS : INFLUENZA AGENTS

Antivirals, Oral- Disease State Description

- Common illness affecting most people at least once in their lifetime
  - Uncomplicated illness typically resolves after 3 to 7 days
  - Often self-limiting
  - Persons at higher risk for influenza complications: < 2 years or ≥ 65 years old, immunocompromised patients, pregnant/postpartum patients, < 19 years old + long-term ASA therapy, American Indians/Alaska Natives, extremely obese patients, nursing homes/other chronic care facility patients, and patients with specific, chronic disease states

- Influenza vaccination is the primary method for preventing influenza
  - Inactivated influenza vaccines are available in quadrivalent and trivalent formulations, while recombinant influenza vaccine and LAIV4 are available in quadrivalent formulations
  - There is also a high-dose inactivated influenza vaccine and adjuvanted inactivated influenza vaccine available in trivalent formulations
  - For the 2021-2022 season, inactivated influenza vaccines, recombinant influenza vaccine, and live attenuated influenza vaccine (LAIV) are available
  - Virus strains included in the 2021-2022 US influenza vaccines contain hemagglutinin (HA) derived from an influenza A/Victoria/2570/2019 (H1N1)pdm09-like virus (for egg-based vaccines) or an influenza A/Wisconsin/588/2019 (H1N1)pdm09-like virus (for cell culture–based and recombinant vaccines), an influenza A/Cambodia/e0826360/2020 (H3N2)-like virus, an influenza B/Washington/02/2019 (Victoria lineage)-like virus, and an influenza B/Phuket/3073/2013 (Yamagata lineage)-like virus
  - Cell culture–based inactivated (ccIIV4) and recombinant (RIV4) influenza vaccines contain HA derived from an A/Hawaii/70/2019 (H1N1)pdm09-like virus, an A/Hong Kong/45/2019 (H3N2)-like virus, a B/Washington/02/2019 (Victoria lineage)-like virus, and a B/Phuket/3073/2013 (Yamagata lineage)-like virus

Centers for Disease Control and Prevention, 2021

Antivirals, Oral- Treatment Guidelines

- Centers for Disease Control and Prevention, 2020
  - There are 3 FDA-approved neuraminidase inhibitor antiviral drugs recommended by CDC for the 2020-2021 season:
    - oseltamivir (Tamiflu)
    - zanamivir (Relenza)
    - peramivir (Rapivab)
  - The fourth recommended FDA-approved product is the cap-dependent endonuclease inhibitor baloxavir marboxil (Xofluza)
    - Adamantanes (amantadine and rimantadine) are not recommended for use in the U.S. due to resistance to these drugs by many influenza A influenza B viruses
  - Empiric antiviral treatment, without waiting for laboratory confirmation, is recommended as early as possible for any patient with confirmed or suspected influenza who has severe, complicated, or progressive illness; is hospitalized; or is at high risk for influenza complications
  - In addition, empiric antiviral treatment of non-high-risk outpatients with suspected influenza can be started based on clinical judgement without an office visit
  - According to the CDC, oseltamivir (oral or enterically-administered) is the recommended antiviral for patients with severe, complicated, or progressive illness or who are hospitalized
  - Insufficient data for Relenza, Rapivab, or Xofluza in patients with severe influenza
  - Co-infection with influenza A or B viruses and SARS-CoV-2 can occur and should be considered, particularly in hospitalized patients with severe respiratory disease

Antivirals, Oral- Treatment Guidelines

- baloxavir marboxil (Xofluza)
  - **October 2021: Product labeling updated to include a new 80 mg tablet strength and the 40 mg tablet packaged as a 1-tablet single-dose (previously, a 2-tablet presentation); 20 mg tablet strength was removed**
  - **August 2022: FDA expanded indication to include those 5 to 11 years old for treatment of acute uncomplicated influenza in patients who have been symptomatic for no more than 48 hours and otherwise healthy and for those 5 to 11 years old for post-exposure prophylaxis of influenza; previously approved for patients ≥ 12 years old with acute uncomplicated influenza < 48 hours symptomatic who are otherwise healthy or at high-risk of influenza-related complications and for post-exposure prophylaxis in patients ≥ 12 years old**
  - **Indications**
    - Treatment of acute uncomplicated influenza in patients who have been symptomatic for no more than 48 hours and who are:
      - **Otherwise healthy adults and pediatric patients 5 years of age and older**, OR
      - Adults and pediatric patients 12 years of age and older who are at high risk of developing influenza-related complications
    - Post-exposure prophylaxis of influenza in patients 5 years of age and older following contact with an individual who has influenza
  - **Warnings and Precautions**
    - Co-administration of baloxavir marboxil (Xofluza) with polyvalent cation-containing laxatives, antacids, or oral supplements (e.g., calcium, iron, magnesium, selenium, or zinc) should be avoided
  - **Dosage**
    - Stratified by age and weight (See TCR/PI)
  - **Availability**
    - Tablets: 20 and 40 mg
    - For oral suspension: 40 mg/20 mL when constituted for final concentration of 2 mg/mL

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Sinus Node Inhibitors:

CARDIOVASCULAR AGENTS : SINUS NODE INHIBITORS

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Pituitary Suppressive Agents, LHRH:

ENDOCRINE AND METABOLIC AGENTS : PITUITARY SUPPRESSANTS
ONCOLOGY AGENTS : LHRH ANALOGS - INJECTABLE

Pituitary Suppressants - Disease State Description

- Prostate Cancer
  - From 2014 to 2018, the median age at diagnosis of prostate cancer in the US was 67 years
  - The estimated number of new cases of prostate cancer in the US in 2021 is 248,530 with estimated deaths at 34,130

- Treatment Options
  - Depend on several factors, such as the patient's assigned risk group at time of initial diagnosis, the patient's projected survival, based on age and comorbidities, and the benefits and potential side effects of treatment
  - Treatment options consist of active surveillance, radiation therapy, hormonal therapy, chemotherapy, surgery, or a combination of 2 or more of these
    - Active surveillance, also referred to as watchful waiting, is the monitoring of cancer progression before initiating treatment
    - Radiation therapy uses high-powered energy to kill the cells
    - Hormonal therapy, also called androgen deprivation therapy (ADT), is the mainstay of treatment for metastatic prostate cancer
    - ADT lowers androgen (testosterone and dihydrotestosterone) levels which causes the prostate tumor to shrink or grow more slowly
  - Luteinizing hormone-releasing hormone (LHRH) agonists prevent signaling of the testicles to make testosterone, therefore decreasing circulating testosterone levels
  - This class of drugs includes the GnRH agonists leuprolide (Camcevi), leuprolide acetate (Eligard, Lupron Depot), goserelin (Zoladex), triptorelin (Trelstar), and histrelin (Vantas), as well as the GnRH antagonists, degarelix (Firmagon) and relugolix (Orgovyx)
  - Anti-androgens, such as bicalutamide (Casodex), flutamide, and nilutamide (Nilandron), are given in conjunction with LHRH agonists
    - These drugs prevent testosterone from reaching the cancer cells
  - Chemotherapy treatment is used to kill rapidly growing cancer cells
  - Surgery involves the removal of the prostate gland (radical prostatectomy), some surrounding tissue, and a few lymph nodes

Pituitary Suppressants

- leuprolide mesylate (Camcevi)
  - **May 2021: The FDA approved Camcevi, a GnRH agonist, for the treatment of adult patients with advanced prostate cancer**
  - **Indication**
    - **A gonadotropin-releasing hormone (GnRH) agonist indicated for the treatment of adult patients with advanced prostate cancer**
  - **Warnings and Precautions**
    - **Tumor Flare: Transient worsening of bone pain, uretral obstruction, spinal cord compression, or the occurrence of additional signs and symptoms of prostate cancer may develop during the first few weeks of treatment. Monitor patients closely and manage symptoms**
    - **Hyperglycemia and Diabetes: Hyperglycemia and an increased risk of developing diabetes have been reported in men receiving GnRH agonists. Monitor blood glucose level and manage according to current clinical practice**
    - **Cardiovascular Diseases: Increased risk of myocardial infarction, sudden cardiac death, and stroke has been reported in men receiving GnRH agonists. Monitor for cardiovascular disease and manage according to current clinical practice**
    - **Embryo-Fetal Toxicity: May cause fetal harm**
  - **Dosage**
    - **Recommended Dosage: 42 mg subcutaneously every 6 months**
  - **Availability**
    - **Injectable emulsion: 42 mg**

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Ulcerative Colitis Agents:

GASTROINTESTINAL AGENTS : INFLAMMATORY BOWEL AGENTS

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

GI Motility, Chronic:

GASTROINTESTINAL AGENTS : IRRITABLE BOWEL SYNDROME (IBS) AGENTS / GI MOTILITY

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Phosphate Binders:

GASTROINTESTINAL AGENTS : PHOSPHATE BINDER AGENTS

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Bladder Relaxant Preparations:

GENITOURINARY AGENTS : OVERACTIVE BLADDER AGENTS

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

HAE Treatments:

HEMATOLOGICAL AGENTS : HEREDITARY ANGIOEDEMA AGENTS

Magellan Rx MANAGEMENT

Magellan Medicaid Administration

Potassium Binders:

MISCELLANEOUS THERAPEUTIC CLASSES : POTASSIUM REMOVING AGENTS

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Multiple Sclerosis Agents

Multiple Sclerosis Agents – Disease State Description

- Multiple sclerosis (MS) is a complex human autoimmune-type inflammatory disease of the central nervous system (CNS)
  - More than 2.3 million people worldwide have MS; 1 million people in the U.S.
  - Multiple sclerosis occurs most commonly in whites, with rare cases in African-Americans and Asian-Americans

- Although the etiology is predominantly unknown, MS is characterized pathologically by demyelination and subsequent axonal degeneration
  - The nerve degeneration associated with MS can result in a wide variety of symptoms, including sensory disturbances (numbness, paresthesias, burning, and pain) in the limbs, optic nerve dysfunction, ataxia, fatigue, and bladder, bowel, and sexual dysfunction
  - Severe cases may result in partial or complete paralysis
  - While cognitive impairment occurs in approximately 50% of people with MS, only 10% experience serious intellectual deterioration

- MS can be categorized as either relapsing-remitting MS (observed in 85% to 90% of patients) or primary progressive MS (observed in 10% of patients)
  - Relapses or “attacks” typically present subacutely, with symptoms developing over hours to several days, persisting for several days or weeks, and then gradually dissipating

National Medical Society, 2017

Multiple Sclerosis Agents – Disease State Description

- The clinical course of MS falls into 1 of the following categories, with the potential to progress from less severe to more serious types:
  - **Clinically isolated syndromes (CIS):** the first episode of neurologic symptoms due to inflammation or demyelination lasting at least 24 hours. Patients with MRI-detected brain lesions consistent with MS are at high risk of developing MS
  - **Relapsing-remitting MS (RRMS):** Clearly defined, self-limited attacks of neurologic dysfunction, followed by periods of remission without disease progression. Most patients experience a recovery of function that is often, but not always, complete
  - **Primary progressive MS (PPMS):** Nearly continuous worsening of disease not interrupted by distinct relapses; some of these individuals have occasional plateaus and temporary minor improvements
  - **Secondary progressive MS (SPMS):** Relapsing-remitting disease course at onset, followed by progression with or without occasional relapses, minor remissions, and plateaus; most patients eventually convert to progressive MS

National Medical Society, 2017

Multiple Sclerosis Agents

- fingolimod (Tascenso ODT)
  - **December 2021: The FDA has approved a new formulation of fingolimod (Tascenso ODT), a sphingosine 1-phosphate receptor modulator, indicated for the treatment of relapsing forms of MS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in pediatric patients ≥ 10 years old and weighing ≤ 40 kg**
  - **Indication**
    - **Treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in pediatric patients 10 years of age and older and weighing less than or equal to 40 kg**
  - **Limitation**
    - Malignancies: Suspicious skin lesions should be evaluated
    - Fetal Risk: May cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use an effective method of contraception during treatment and for 2 months after stopping treatment
    - Vaccines: Avoid live attenuated vaccines during, and for 2 months after stopping treatment
  - **Dosage**
    - Recommended dosage for pediatric patients (10 years of age and older) weighing ≤ 40 kg: 0.25 mg orally once daily, with or without food
  - **Availability**
    - Orally disintegrating tablets: 0.25 mg

Multiple Sclerosis Agents

- **FDA Communication**
  - **Glatiramer acetate (Copaxone; Glatopa)- August 2022**
    - **FDA is warning that autoinjector devices that are optional for use with glatiramer acetate injection may not be compatible for use across FDA-approved glatiramer acetate injection drug products and has resulted in missed and partial doses**
    - **There are currently 3 FDA-approved glatiramer acetate injection drug products (Copaxone, Glatopa, generic) on the market—all available in a single-dose prefilled syringe with an attached needle for SC administration**
    - **Patients may administer the dose using only the syringe or by inserting the syringe into an autoinjector**
    - **The autoinjectors are reusable and are available by prescription separately**
    - **FDA has requested that drug product manufacturers update their labeling to instruct users to confirm the autoinjector is compatible before using it to inject glatiramer acetate**

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Opiate Dependence Treatments:

SUBSTANCE USE DISORDER : AGENTS FOR OPIOID WITHDRAWAL
SUBSTANCE USE DISORDER : OPIOID ANTAGONISTS
SUBSTANCE USE DISORDER : OPIOID PARTIAL AGONISTS – SUBCUTANEOUS
SUBSTANCE USE DISORDER : OPIOID PARTIAL AGONISTS - TRANSMUCOSAL

Opiate Dependence Treatment – Disease State Description

- Prescription and illicit opioid abuse and misuse has reached national interest and was declared a National Public Health Emergency by the Department of Health and Human Services (DHHS) Acting Secretary in 2017

- The 2020 National Survey on Drug Use and Health (NSDUH) reported there was an estimated 37.3 million Americans aged 12 years and older who were current (past month) illicit drug users
  - There were approximately 9.4 million people aged 12 or older in the United States (US) who misused opioids in the past year
  - Approximately 40.3 million people aged 12 or older in 2020 were considered to have a substance use disorder (SUD) in the past year, including 28.3 million people with an alcohol use disorder, 18.4 million people with an illicit drug use disorder, and 2.7 million had an opioid use disorder

- In 2020, the US Preventive Services Task Force issued a final recommendation statement on screening for unhealthy drug use. For adults, they recommended screening implemented when services for accurate diagnosis, effective treatment, and appropriate care can be offered or referred. For adolescents, the current evidence is insufficient to determine the benefits and harms of screening for unhealthy drug use

Opiate Dependence Treatment – Guidelines

- American Society of Addiction Medicine (ASAM), 2020
  - State that the choice of medication (e.g., buprenorphine, methadone, naltrexone) should be a shared decision between the clinician and patient and should consider patient preferences, treatment history, concomitant medical conditions, and treatment setting
  - Additionally, all FDA-approved medications should be available options to all patients with individual needs taken into consideration for deciding between buprenorphine, methadone, and naltrexone, in conjunction with psychosocial treatment services, although they do provide some additional context for treatment selection
    - There is no recommended time limit for the pharmacological treatment of opioid use disorder
    - Methadone is recommended for patients who may benefit from additional supervision in an opioid treatment program (OTP), buprenorphine may be dispensed in OTP or in office-based opioid treatment (OBOT), while naltrexone may be prescribed in any setting
      - Oral naltrexone requires special attention to medication adherence and may require observed administration for some patients
    - The combined use of benzodiazepines and sedative-hypnotics increases the risk of serious adverse effects when administered with methadone and buprenorphine; however, the harm of untreated opioid use disorder may outweigh the risk
    - Buprenorphine and methadone are the standard treatment options for managing the acute withdrawal from opioids
      - When buprenorphine is selected for managing opioid withdrawal, buprenorphine should not be initiated until there are objective signs of opioid withdrawal and at a dose to suppress the withdrawal symptoms
      - ASAM notes that methadone and buprenorphine are more effective in decreasing symptoms and aiding in the completion in withdrawal
    - Additionally, the group states that alpha-2 adrenergic agonists, such as clonidine (not approved for this use) and lofexidine are safe and effective to manage opioid withdrawal
    - The focused update also includes recommendations for special populations (e.g., pregnant women patients suffering from pain, adolescents, patients with co-occurring psychiatric conditions, patients in the criminal justice system) because this may impact drug selection, psychosocial services offered, and overall care planning
    - ASAM recommends that naloxone, for the reversal of opioid overdose, and training for patients and significant others should be provided to patients being treated for or with a history of opioid use disorder

Opiate Dependence Treatment – Guidelines

- World Health Organization (WHO) in partnership with the United Nations Office on Drugs and Crime (UNODC), 2020
  - Updated their International Standards for the Treatment of Drug Use Disorders
  - They recommend tapered doses of opioid agonists (methadone or buprenorphine) for opioid withdrawal, although alpha-2 adrenergic agonists may also be used
  - Naloxone should be on hand for people with opioid dependence and their families for use in the event of an opioid overdose, and they should be trained to manage opioid overdoses
  - Detoxification, followed by relapse-prevention treatment using the opioid antagonist naltrexone, is useful for patients motivated to abstain from opioid use
  - Subgroups of individuals with OUD may require, specialized, tailored care such as
    - Women and pregnant women, children and adolescents, the elderly, indigenous populations, migrants, sex workers, people with different sexual orientation and gender identity, people with disabilities, people with limited education, people with comorbid health conditions, people in contact with the criminal justice system, and homeless or unemployed people who lack social support

Opiate Dependence Treatment – Guidelines

- Department of Health and Human Services, 2021
  - To further expand access to buprenorphine for the treatment of OUD, in April 2021, the DHHS released new guidelines, the Practice Guidelines for the Administration of Buprenorphine for Treating OUD, allowing eligible physicians, physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists, and certified nurse midwives to prescribe buprenorphine to up to 30 patients outside of completing all the previous waiver requirements (e.g., training, counseling, psychosocial services)
  - The guidance emphasizes, however, that those who forego the training will be limited to treating a maximum of 30 patients, and prescribers must still submit a Notice of Intent (NOI) before prescribing buprenorphine

Opiate Dependence Treatment

- naloxone HCl (Zimhi)
  - **October 2021: The FDA has approved a new formulation of naloxone HCl, Zimhi, an opioid antagonist, indicated in adult and pediatric pts for the emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or CNS depression; it is intended for immediate administration as emergency therapy in settings where opioids may be present and is not a substitute for emergency medical care**
  - **Indication**
    - **Indicated in adult and pediatric patients for the emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression**
    - **Intended for immediate administration as emergency therapy in settings where opioids may be present**
    - **Not a substitute for emergency medical care**
  - **Limitation**
    - **Risk of Recurrent Respiratory and CNS Depression: Due to the duration of action of naloxone relative to the opioid, keep patient under continued surveillance and administer repeat doses of naloxone using a new nasal spray with each dose, as necessary, while awaiting emergency medical assistance**
  - **Dosage**
    - **For intramuscular or subcutaneous use only**
    - **Seek emergency medical care immediately after use**
    - **Intended to be administered by individuals 12 years of age or older**
    - **Administer to adult or pediatric patients into the anterolateral aspect of the thigh, through clothing if necessary**
  - **Availability**
    - **Injection: 5 mg/0.5 mL naloxone hydrochloride solution in a single-dose, prefilled syringe**

Opiate Dependence Treatment

- **FDA Communication- 1/4/2022**
  - FDA issued Drug Safety Communication warning that dental problems, including tooth decay, cavities, oral infections, and loss of teeth, have been reported with medicines containing buprenorphine that are dissolved in the mouth
  - The dental problems, including serious cases, have been reported even in patients with no history of dental issues
  - Despite this, the FDA states the benefits of these medicines outweigh the risks for OUD
  - Healthcare Practitioners should inquire about dental concerns and advise pts of the importance of taking extra steps after the medicine has completely dissolved, including to gently rinse their teeth and gums with water and then swallow and wait at least 1 hour before brushing their teeth

- **New Formulation**
  - Naloxone Injection- 2/28/2022
    - FDA approved naloxone inj. 10 mg for use by military personnel and chemical incident responders for:
      - (1) Emergency treatment of patients ≥ 12 years old where use of high-potency opioids, such as fentanyl analogues, as a chemical weapon is suspected
      - (2) Temporary prophylaxis of respiratory and/or CNS depression in military personnel and chemical incident responders entering an area contaminated with high-potency opioids such as fentanyl analogues

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Stimulants & Related Agents:

ADHD / ANTI-NARCOLEPSY : DOPAMINE AND NOREPINEPHRINE REUPTAKE INHIBITORS (DNRIS)
ADHD / ANTI-NARCOLEPSY : HISTAMINE H3-RECEPTOR ANTAGONIST / INVERSE AGONIST
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 & Guidelines

- **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, which has been diagnosed in approximately 15% of children 4 to 17 years of age and about 4% of adults, is a chronic condition with core symptoms of inattention, hyperactivity, and difficulty controlling behavior
  - It may also be accompanied by internalized disorders, such as sadness and anxiety, as well as aggressive and oppositional disorders
  - The 3 main types of ADHD are primary hyperactive, primary inattentive, and mixed

- **The Medical Letter, 2020**
  - Suggests that school-age children, adolescents, and adults begin with an oral stimulant, noting that none of the agents have shown to be more effective than another; however, some patients may respond better to amphetamines than to methylphenidate and vice versa
  - They advised that use of long-acting formulations, which generally contain both immediate- and extended-release components, has become standard clinical practice and the addition of a short-acting stimulants may improve symptom control early in the morning or to prolong the duration of action in the afternoon
  - While the alpha$_2$-agonists clonidine and guanfacine and the selective norepinephrine reuptake inhibitor atomoxetine can reduce ADHD symptoms, these agents are considered less effective than stimulants
  - Use of pitolisant and solriamfetol were not addressed Drugs for ADHD

Stimulants & Related Agents

- **amphetamine sulfate (Evekeo ODT)**
  - April 2021: The FDA approved Evekeo ODT for the treatment of ADHD in pediatric patients 3 to 17 years of age; previously, it was only approved in children ≥ 6 years old
  - April 2021: The FDA approved a 2.5 mg ODT strength was approved; it was already approved as 5 mg, 10 mg, 15 mg, and 20 mg ODT
  - Indication
    - The treatment of Attention Deficit Hyperactivity Disorder (ADHD) in pediatric patients 3 to 17 years of age
  - Warnings
    - BBW: CNS stimulants have a high potential for abuse and dependence
    - Blood Pressure and Heart Rate Increases: Monitor blood pressure and pulse. Consider benefits and risks before use in patients for whom blood pressure increases may be problematic
    - Psychiatric Adverse Reactions: May cause psychotic or manic symptoms in patients with no prior history, or exacerbation of symptoms in patients with pre-existing psychosis. Evaluate for bipolar disorder prior to use
    - Pregnancy: May cause fetal harm
  - Dosage
    - Pediatric patients 3 to 5 years of age: Recommended starting dosage is 2.5 mg daily. If necessary, administer an additional dose after 4 to 6 hours. Titrate the dosage in increments of 2.5 mg at weekly intervals
    - Pediatric patients 6 to 17 years of age: Recommended starting dosage is 5 mg once or twice daily. If necessary, administer an additional dose after 4 to 6 hours. Titrate the dosage in increments of 2.5 mg or 5 mg at weekly intervals
  - Availability
    - Orally disintegrating tablets: 2.5, 5 mg, 10 mg, 15 mg, and 20 mg

Stimulants & Related Agents

- **viloxazine (Qelbree)**
  - **April 2022: The FDA approved expanded indication of viloxazine for use in adults with ADHD. Previously approved for pediatric patients ≥ 6 years of age**
  - **Indication**
    - **The treatment of Attention Deficit Hyperactivity Disorder (ADHD) in adults and pediatric patients 6 years and older**
  - **Warnings**
    - BBW: In clinical trials, higher rates of suicidal thoughts and behavior were reported in patients treated with Qelbree than in patients treated with placebo. Closely monitor for worsening and emergence of suicidal thoughts and behaviors
    - Blood Pressure and Heart Rate Increases: Assess heart rate and blood pressure prior to initiating treatment, following increases in dosage, and periodically while on therapy
    - Activation of Mania or Hypomania: Screen patients for bipolar disorder
    - Pregnancy: May cause fetal harm; discontinue when pregnancy is recognized
  - **Dosage**
    - Pediatric patients 6 to 11 years of age: Recommended starting dosage is 100 mg once daily. May titrate in increments of 100 mg weekly to the maximum recommended dosage of 400 mg once daily
    - Pediatric patients 12 to 17 years of age: Recommended starting dosage is 200 mg once daily. May titrate after 1 week, by an increment of 200mg, to the maximum recommended dosage of 400 mg once daily
    - **Adult patients: Recommended starting dosage is 200 mg once daily. May titrate in increments of 200 mg weekly, to maximum recommended dosage of 600 mg once daily**
  - **Availability**
    - Extended-release capsules: 100 mg, 150 mg and 200 mg

Stimulants & Related Agents

- **amphetamine (Dyanavel XR)**
  - **November 2021: The FDA approved a new extended-release (ER) tablet formulation of amphetamine (Dyanavel XR) for the treatment of ADHD in patients ≥ 6 years of age**
  - **Indication**
    - The treatment of Attention Deficit Hyperactivity Disorder (ADHD) in adults and pediatric patients 6 years and older
  - **Warnings**
    - BBW: CNS stimulants have a high potential for abuse and dependence
    - Blood Pressure and Heart Rate Increases: Monitor blood pressure and pulse. Consider benefits and risks before use in patients for whom blood pressure increases may be problematic
    - Psychiatric Adverse Reactions: May cause psychotic or manic symptoms in patients with no prior history, or exacerbation of symptoms in patients with pre-existing psychosis. Evaluate for bipolar disorder prior to use
    - Pregnancy: May cause fetal harm
  - **Dosage**
    - Recommended starting dosage is 2.5 mg or 5 mg once daily in the morning
    - Dosage may be increased in increments of 2.5 mg to 10 mg per day every 4 to 7 days up to a maximum daily dose of 20 mg
    - Dyanavel XR oral suspension can be substituted with Dyanavel XR tablets on a milligram per milligram basis
  - **Availability**
    - Extended-release oral suspension: containing 2.5 mg amphetamine base equivalents per mL
    - **Extended-release tablets: 5 mg (functionally scored), 10 mg, 15 mg, 20 mg**

Stimulants & Related Agents

- **dextroamphetamine (Xelstrym)**
  - **March 2022: The FDA has approved a new transdermal system formulation of dextroamphetamine (Xelstrym)**
  - **Indication**
    - **The treatment of Attention Deficit Hyperactivity Disorder (ADHD) in adults and pediatric patients 6 years and older**
  - **Warnings**
    - **BBW: CNS stimulants have a high potential for abuse and dependence**
    - **Blood Pressure and Heart Rate Increases: Monitor blood pressure and pulse. Consider benefits and risks before use in patients for whom blood pressure increases may be problematic**
    - **Psychiatric Adverse Reactions: May cause psychotic or manic symptoms in patients with no prior history, or exacerbation of symptoms in patients with pre-existing psychosis. Evaluate for bipolar disorder prior to Xelstrym use**
    - **Pregnancy: May cause fetal harm**
    - **Renal Impairment: Dose adjustment recommended for Severe Renal Impairment and ESRD**
  - **Dosage**
    - **Pediatric patients (6 to 17 years): Recommended starting dose is 4.5 mg/9 hours. Titrate dosage in weekly increments of 4.5 mg up to a maximum recommended dose of 18 mg/9 hours**
    - **Adults: Recommended starting dose is 9 mg/9 hours; maximum recommended dose is 18 mg/9 hours**
    - **Apply one transdermal system 2 hours before an effect is needed and remove within 9 hours**
  - **Availability**
    - **Transdermal system: 4.5 mg/9 hours, 9 mg/9 hours, 13.5 mg/9 hours, 18 mg/9 hours**

Stimulants & Related Agents

- **methylphenidate (Relexxii)**
  - **June 2022: The FDA approved methylphenidate ER tablets (Relexxii) via 505(b)(2) for the treatment of ADHD in pediatric patients ≥ 6 years of age and adults ≤ 65 years of age**
  - **Indication**
    - **Treatment of Attention Deficit Hyperactivity Disorder (ADHD) in adults (up to the age of 65 years) and pediatric patients 6 years of age and older**
  - **Warnings**
    - **BBW: CNS stimulants have a high potential for abuse and dependence**
    - **Blood Pressure and Heart Rate Increases: Assess heart rate and blood pressure prior to initiating treatment, following increases in dosage, and periodically while on therapy**
    - **Long-Term Suppression of Growth: monitor height and weight at appropriate intervals in pediatric patients**
    - **Gastrointestinal Obstruction: Avoid use with preexisting GI narrowing**
  - **Dosage**
    - **Pediatric patients 6 to 17 years: Starting dosage is 18 mg once daily. Dosage may be increased by 18 mg once per day at weekly intervals**
      - **Maximum dosage for pediatric patients 6 to 12 years: 54 mg once daily**
      - **Maximum dosage for pediatric patients 13 to 17 years: 72 mg once daily**
    - **Adults (up to 65 years): Starting dosage is 18 mg or 36 mg once daily. Dosage may be increased by 18 mg once daily at weekly intervals. Maximum dosage: 72 mg once daily.**
  - **Availability**
    - **Extended-release tablets:18 mg, 27 mg, 36 mg, 45 mg, 54 mg, 63 mg, and 72 mg**

Stimulants & Related Agents

- **methylphenidate- March 2022**
  - First FDA-approved generic for Noven's Daytrana from Mylan

- **Recall**
  - guanfacine extended-release – April 2021
    - Apotex issued voluntary recall of 3 lots of Guanfacine Extended-Release Tablets 2 mg to the consumer level due to trace amounts of Quetiapine Fumarate in 1 lot (RX1663)
    - Out of caution, 2 other lots are also being recalled (RX1662 and RX1664)
    - No adverse effects related to this recall have been reported, but exposure in trace amounts could result in a hypersensitivity reaction
    - In addition, exposure to quetiapine could result in additive effects in lowering blood pressure, sleepiness/sedation, and dizziness

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Anti-Allergens, Oral

Allergenic Extracts/Biologicals

Allergenic Extracts/Biologicals - Disease State Description & Guidelines

- **Allergic Rhinitis (hay fever)**
  - With or without allergic conjunctivitis, affects approximately 8% of adults and 9% of children in the United States
  - Allergen avoidance and medication therapy can provide significant symptom relief, but for many, symptoms remain
  - For some of these patients, allergen immunotherapy is a reasonable alternative
  - Subcutaneous immunotherapy (SCIT) has proven to be effective in the management of allergic rhinitis and asthma since the early twentieth century; however, it requires regular injections, typically over a period of 3 to 5 years, and carries the potential of serious systemic allergic reactions in response to the treatment itself

Allergenic Extracts/Biologicals

- **short ragweed pollen allergen extract (Ragwitek)**
  - **January 2020: The FDA approved an expanded indication for Ragwitek to include pediatric patients as young as 5 years old for the treatment of short ragweed pollen-induced allergic rhinitis, with or without conjunctivitis, confirmed by positive skin test or in vitro testing for pollen-specific IgE antibodies for short ragweed pollen; previously, it was approved in adults 18 to 65 years of age**

  - **Indication**
    - **Treatment of short ragweed pollen-induced allergic rhinitis, with or without conjunctivitis, confirmed by positive skin test or in vitro testing for pollen-specific IgE antibodies for short ragweed pollen. Approved for use in persons 5 through 65 years of age.**
  - **Warnings and Precautions**
    - BBW: Can cause life-threatening allergic reactions such as anaphylaxis and severe laryngopharyngeal restriction
    - BBW: Do not administer RAGWITEK to patients with severe, unstable or uncontrolled asthma
    - BBW: Prescribe auto-injectable epinephrine, instruct and train patients or parents/guardians on its appropriate use, and instruct patients or parents/guardians to seek immediate medical care upon its use
  - **Dosage**
    - One tablet daily
  - **Availability**
    - Sublingual Tablet: 12 Amb a 1-Unit (Amb a 1-U)

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Antipsychotics:

ANTIPSYCHOTICS / ANTIMANIC AGENTS : ANTIPSYCHOTICS - 2ND GENERATION
ANTIPSYCHOTICS / ANTIMANIC AGENTS : ANTIPSYCHOTICS - COMBINATIONS
ANTIPSYCHOTICS / ANTIMANIC AGENTS : PARKINSONS PSYCHOTIC DISORDER

Antipsychotics – Disease State Description/Guidelines

Schizophrenia

- The most common psychotic illness is schizophrenia, which affects 1% of the population
- Between 25% and 50% of schizophrenic patients attempt suicide, and 10% of patients succeed in their attempt
- Symptoms include delusions, hallucinations, disorganized speech, disorganized or catatonic behavior, and negative symptoms, and at least 1 of these should be delusions, hallucinations, or disorganized speech

Diagnostic and Statistical Manual of Mental Disorders, 5th Edition; 2013

- American Academy of Child and Adolescent Psychiatry (AACAP), 2013
  - Recommend antipsychotic medication as primary treatment for schizophrenia spectrum disorders in children and adolescents
  - Recommend against the use of clozapine as a first-line agent (should be reserved for treatment-resistant patients), state that ziprasidone has not demonstrated efficacy in this population and is not FDA indicated for this population, and caution on its use with olanzapine due to weight gain
  - Ultimately, they state that the choice of which agent is based on FDA approval, adverse effect profile, patient and family preferences, provider comfort and/or familiarity, and cost
  - **As this practice parameter is more than 5 years old, it is considered an AACAP historical practice parameter; however, newer guidance is not available**

Antipsychotics –Guidelines

- American Psychiatric Association (APA), 2020
  - Since schizophrenia is a chronic illness that afflicts all aspects of life, the goals of treatment are to stabilize the patient (reduce acute symptoms) to return to baseline functioning, prevent recurrent of symptoms, and maximize functioning and quality of life
    - Goals may also be based on individual patient preferences impacting school, employment, and other quality of life-impacting components
  - Guidelines recommend 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 that the same antipsychotic be used
    - They recommend clozapine specifically be used 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
    - A long-acting injectable is suggested for patients who prefer this therapy or for patients with a history of uncertain or poor adherence
  - Notably, the guidelines state that an evidence-based ranking or algorithm approach for antipsychotic selection is not practical due to clinical trial heterogeneity and limited comparative trials
  - 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
    - With the exception of clozapine, no antipsychotic has demonstrated superior efficacy when compared to other agents within the class
  - They 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/Guidelines

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
- Criterion used to diagnose bipolar I disorder is the presence of a manic episode (persistent elevated, expansive, or irritable mood for at least 1 week with increased energy/activity) or a mixed features specifier (rapidly alternating polarity of mood, sadness, irritability, and mania for at least 1 week), and 3 or more other characteristic symptoms
  - These symptoms include 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

Diagnostic and Statistical Manual of Mental Disorders, 5th Edition; 2013

- American Psychiatric Association (APA), 2002
  - There is no cure for bipolar disorder, but the appropriate pharmacological treatment can decrease morbidity and mortality
  - 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

- **paliperidone palmitate (Invega Hafyera)**
  - **September 2021: FDA approved an every-6-month injection for the treatment of schizophrenia in adults after they have been adequately treated with Invega Sustenna (once-monthly) or Invega Trinza (every-3-month) regimen. Approved as injectable suspension in 1,092 mg/3.5 mL and 1,560 mg/5 mL single-dose prefilled syringes.**
  - **Indication**
    - **Indicated for the treatment of schizophrenia in adults after they have been adequately treated with:**
      - **A once-a-month paliperidone palmitate extended-release injectable suspension (e.g Invega Sustena) for at least four months or**
      - **An every-three-month paliperidone palmitate extended-release injectable suspension (e.g , Invega Trinza) for at least one three-month cycle**
  - **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**
    - **Renal Impairment: Not recommended**
  - **Dosage**
    - **Stratified by indication and previous medication**
  - **Availability**
    - **Extended-release injectable suspension: 1,092 mg/3.5 mL or 1,560 mg/5 mL single-dose prefilled syringes**

Antipsychotics

- **lumateperone (Caplyta)**
  - **December 2021: The FDA has approved a new indication for lumateperone for the treatment of depressive episodes associated with bipolar I or II disorder (bipolar depression) in adults, as monotherapy and as adjunctive therapy with lithium or valproate. Lumateperone is already approved for schizophrenia in adults**
  - **May 2022: FDA approved 2 new strengths of Caplyta: 10.5 mg and 21 mg capsules. It was already approved as 42 mg capsules**
  - **Indication**
    - Schizophrenia in adults
    - **Depressive episodes associated with bipolar I or II disorder (bipolar depression) in adults, as monotherapy and as adjunctive therapy with lithium or valproate**
  - **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**
    - 42 mg once daily
  - **Availability**
    - **Capsules:** 42 mg, **21 mg, 10.5 mg**

Antipsychotics

- **brexpiprazole (Rexulti)**
  - **December 2021: The FDA has expanded the indication of brexpiprazole to include treatment of schizophrenia in pediatric patients 13 to 17 years old; previously, brexpiprazole was only indicated for use in adults**
  - **Indication**
    - Use as an adjunctive therapy to antidepressants for the treatment of major depressive disorder (MDD) in adults
    - **Treatment of schizophrenia in adults and pediatric patients ages 13 years and older**
  - **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
    - BBW: Antidepressants increase the risk of suicidal thoughts and behaviors in patients aged 24 years and younger
    - 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**
    - MDD (Adults): Starting Dose: 0.5-1mg/day; Recommended Dose: 2 mg/day; Max Dose: 3 mg/day
    - Schizophrenia (Adults): Starting Dose: 1mg/day; Recommended Dose: 2-4 mg/day; Max Dose: 4 mg/day
    - **Schizophrenia (Pediatric): Starting Dose: 0.5mg/day; Recommended Dose: 2-4 mg/day; Max Dose: 4 mg/day**
  - **Availability**
    - Tablets: 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, and 4 mg

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Movement Disorders

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Ophthalmic Agents, Glaucoma

GLAUCOMA AGENTS : ADRENERGIC AGENTS
GLAUCOMA AGENTS : ADRENERGIC AGENTS COMBINATIONS
GLAUCOMA AGENTS : BETA - BLOCKERS
GLAUCOMA AGENTS : BETA - BLOCKERS COMBINATIONS
GLAUCOMA AGENTS : CARBONIC ANHYDRASE INHIBITORS
GLAUCOMA AGENTS : KINASE INHIBITORS
GLAUCOMA AGENTS : MIOTICS
GLAUCOMA AGENTS : PROSTAGLANDINS

Ophthalmic, Glaucoma Agents – Disease State Description/Guidelines

- Approximately 2.7 million people in the United States (U.S.) suffer from glaucoma
  - It is the second most common cause of permanent blindness in the U.S. and the most common cause of blindness among African Americans and Hispanics
  - Risk factors for the development of glaucoma include elevated IOP, advancing age (> 40 years), family history of glaucoma, and African American or Hispanic descent
- Increased IOP is common in glaucoma and is believed to contribute to the damage to the optic nerve, which can lead to loss of visual sensitivity and field
  - However, some patients with glaucoma have normal IOP, and many patients with elevated IOP do not have glaucoma
  - IOP alone is no longer considered a diagnostic criterion for glaucoma
- Two major types of glaucoma have been identified: open-angle and closed-angle
  - In open-angle glaucoma, there is reduced flow through the trabecular meshwork
    - Open-angle glaucoma accounts for the majority of cases
  - In closed-angle glaucoma, the iris is pushed forward against the trabecular meshwork, blocking fluid from escaping
- Reduction of IOP may be achieved either by decreasing the rate of production of aqueous humor or increasing the rate of outflow of aqueous humor from the anterior chamber of the eye
- Topical ocular hypotensive agents can delay or prevent the development of primary open-angle glaucoma in some patients

American Academy of Ophthalmology, 2017

Ophthalmic, Glaucoma Agents – Guidelines

- **Discontinuation**
  - **dorzolamide (Trusopt)– April 2022**
    - **Merck reported to the FDA intent to discontinue Trusopt 2% ophthalmic solution on April 15, 2022**
    - **Generics remain available**

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Ophthalmic Agents: Immunomodulators

Ophthalmic Agents, Immunomodulators - Disease State Description

- **Keratoconjunctivitis sicca (KCS)**
  - Defined as dry eye disease (DED) related to either decreased tear volume (aqueous deficient dry eyes) or rapid evaporative loss (evaporative dry eyes) due to poor tear quality
    - Both of these conditions may be present in dry eye syndrome (DES)
  - The terms dry eye syndrome, dry eye disease, keratoconjunctivitis sicca, and keratitis sicca are often used interchangeably, with the term keratoconjunctivitis sicca being an older term
  - There is considerable overlap with other ophthalmic conditions, such as meibomian gland dysfunction
  - DES/KCS affects approximately 10% to 30% of the United States (US) population and occurs more commonly in patients over 50 years of age, with approximately twice as many women as men affected
    - However, due to increased use of soft contact lenses and frequent smartphone and computer usage, the prevalence of DES is increasing among young adults aged 18 to 34 years
  - Patients with KCS/DES may have the following complaints: sensations of ocular dryness, grittiness, a foreign body, or irritation; hyperemia; mucoid discharge; excessive tearing; photophobia; and blurry vision

Ophthalmic Agents, Immunomodulators

- **New Generic**
  - **cyclosporine ophthalmic emulsion– February 2022**
    - **FDA approved the first generic for Restasis (cyclosporine ophthalmic emulsion 0.05% to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca (commonly known as dry eye)**
    - **Launch occurred in February 2022**

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Idiopathic Pulmonary Fibrosis

Respiratory Agents: Pulmonary Fibrosing Agents

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Smoking Cessation Agents

Smoking Deterrents: Misc - Other

Magellan Rx MANAGEMENT

Magellan Medicaid Administration

Oncology, Oral – Prostate

ONCOLOGY AGENTS : ANDROGEN BIOSYNTHESIS INHIBITORS – ORAL

ONCOLOGY AGENTS : ANTIANDROGENS - ORAL

Oncology, Oral- Prostate – Overview of Disease State

- In the United States (US), prostate cancer is the most commonly diagnosed cancer in men (excluding non-melanoma skin cancers), with an estimated 248,530 cases projected to be diagnosed in 2021
- While prostate cancer accounts for the largest percentage of diagnosed cases in US males (26%), it only accounts for about 11% of all cancer deaths in this population, far behind lung cancer, the leading cause of cancer death, which accounts for 22% of US male cancer deaths
- Prostate cancer is rare in men under the age of 40 years, but the risk increases with each subsequent decade of life
- Overall, 1 in 8 US men will develop prostate cancer during their lifetime. Aside from age, the risk factors most strongly associated with development of prostate cancer include race/ethnicity and family history
  - Prostate cancer mortality in non-Hispanic African Americans is more than twice that seen in the US Caucasian population
  - Prostate cancer may represent an indolent disease in some patients and a highly aggressive disease in others

Oncology, Oral- Prostate – Overview of Disease State

- Androgens (specifically testosterone) are a known growth signal for prostate cancer, and the majority of prostate cancers are hormonally dependent
- Due to the hormone responsiveness of the tumor, androgen deprivation therapy (ADT) is a cornerstone of prostate cancer treatment
  - ADT is utilized as the backbone of therapy in advanced or metastatic disease as well as in combination with radiation therapy for clinically localized disease
  - ADT can be accomplished by utilizing either a surgical approach (bilateral orchiectomy) or a medical approach with the administration of a luteinizing hormone-releasing hormone (LHRH) agonist or a LHRH antagonist, to suppress serum testosterone concentrations to castrate levels (< 50 ng/dL)
- Intravenous chemotherapy options, such as docetaxel and cabazitaxel (Jevtana), as well as immunotherapy options for certain patients, including sipuleucel-T (Provenge) or pembrolizumab (Keytruda), and a radiopharmaceutical option, radium-223 (Xofigo), may also be utilized in the treatment of metastatic prostate cancer

Oncology, Oral- Prostate

- darolutamide (Nubeqa)
  - **July 2022: The FDA approved expanded indication for the treatment of adults with metastatic hormone-sensitive prostate cancer (mHSPC) in combination with docetaxel; previously approved for non-metastatic castration-resistant prostate cancer (nmCRPC)**
  - **Indications**
    - The treatment of adult patients with:
      - Non-metastatic castration-resistant prostate cancer (nmCRPC)
      - **Metastatic hormone-sensitive prostate cancer (mHSPC) in combination with docetaxel**
  - **Warning/Precautions**
    - Embryo-Fetal Toxicity: Can cause fetal harm and loss of pregnancy. Advise males with female partners of reproductive potential to use effective contraception
    - Severe Renal Impairment (not on hemodialysis): Recommended dose is 300 mg twice daily
    - Moderate Hepatic Impairment: Recommended dose is 300 mg twice daily
  - **Dosage**
    - Recommended Dosage: 600 mg, (two 300 mg tablets) administered orally twice daily. Swallow tablets whole
  - **Availability**
    - Tablets: 300 mg

- New Generic
  - **abiraterone acetate- July 2022**
    - **FDA approved first generic for Sun's Yonsa tablets, by Teva**

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Oncology, Oral – Hematologic

ONCOLOGY AGENTS : ANTINEOPLASTICS - MISC COMBINATIONS – ORAL
ONCOLOGY AGENTS : HEDGEHOG PATHWAY INHIBITORS – ORAL
ONCOLOGY AGENTS : MULTIKINASE INHIBITORS – ORAL
ONCOLOGY AGENTS : TYROSINE KINASE INHIBITORS – ORAL
ONCOLOGY AGENTS : HEDGEHOG PATHWAY INHIBITORS – ORAL
ONCOLOGY AGENTS : MULTIKINASE INHIBITORS – ORAL
ONCOLOGY AGENTS : TYROSINE KINASE INHIBITORS - ORAL

Oncology, Oral- Hematological - Overview of Disease State

- MULTIKINASE INHIBITORS- ORAL
  - Rydapt
  - **Ukoniq**
- PHOSPHATIDYLINOSITOL 3-KINASE (PI3K) INHIBITORS – ORAL
  - Copiktra
  - **Zydelig**
- PROTEASOME INHIBITORS – ORAL
  - **Ninlaro**
- RETINOIDS– ORAL
  - Tretinoin
- THALIDOMIDE ANALOGUES
  - **Lenalidomide**
  - Pomalidomide
  - Thalidomide
  - Pomalyst
  - Revlimid
- TYROSINE KINASE INHIBITORS – ORAL
  - Bosulif
  - **Brukinsa**
  - **Calquence**
  - Gleevec
  - Iclusig
  - Imatinib
  - **Imbruvica**
  - **Scemblix**
  - Sprycel
  - **Tasigna**
  - Xospata

Oncology, Oral- Hematological – Overview of Disease State

- **Graft versus Host Disease (GVHD)**
  - GVHD is an immune-mediated disease that can result following hematopoietic stem cell transplant (HSCT) when the transplanted cells (graft) recognize the recipient's body as foreign
    - Organ systems most commonly impacted by acute GVHD (aGVHD) include the skin, GI tract, and liver
  - Chronic GVHD (cGVHD) is generally an extension of acute GVHD that often develops more than 100 days after transplant, but it can also occur in those without acute GVHD. Symptoms include ocular manifestations (e.g., burning, irritation, photophobia, pain), oral or gastrointestinal (GI) manifestations (e.g., food sensitivity, oral dryness, pain, weight loss), respiratory manifestations (e.g., wheezing, dyspnea, cough), and neuromuscular manifestations (weakness, neuropathic pain, muscle cramps).

- **Treatment**
  - The American Society for Blood and Marrow Transplantation (re-named The American Society for Transplantation and Cellular Therapy [ASTCT] in 2019) published a clinical practice guideline in 2012 around the first- and second-line treatment of aGVHD
    - These guidelines state that corticosteroids are the standard of care for the initial treatment of aGVHD and note that the literature does not support the choice of any specific agent for secondary therapy of aGVHD
    - These guidelines were published prior to the May 2019 FDA approval of ruxolitinib (Jakafi) for the treatment of corticosteroid-refractory aGVHD in adult and pediatric patients ≥ 12 years of age
  - In 2019, the NCCN published their first set of clinical practice guidelines around hematopoietic cell transplantation (HCT)
    - The 3.2021 version of these guidelines recommend ruxolitinib as a category 1 option for patients with steroid-refractory aGVHD
  - The National Institutes of Health (NIH) recommend that corticosteroids are most commonly the initial systemic therapy choice for most patients with moderate to severe cGVHD
    - Adjunctive supportive care may also be used (e.g., artificial tears, artificial saliva). Ibrutinib was the first drug approved for cGVHD in patients who have failed ≥ 1 systemic treatment, but many other therapies have been used off-label and for primary or secondary therapy (e.g., low-dose methotrexate, mycophenolate mofetil [CellCept], sirolimus [Rapamune])
    - The NCCN 3.2021 guidelines list ibrutinib as a category 2A recommendation for steroid-refractory cGVHD along with multiple other agents also listed as category 2A recommendations

Oncology, Oral- Hematological – Overview of Disease State

- **Waldenström's macroglobulinemia**
  - Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma (WM/LPL) is a B-cell disorder presenting as bone marrow infiltration with lymphoplasmacytic cells that are CD19+, CD20+, and CD22+
  - The 1.2022 NCCN guideline recommends treating only those patients who are symptomatic
    - These symptoms may include hyperviscosity, neuropathy, symptomatic adenopathy or organomegaly, amyloidosis, cryoglobulinemia, and cytopenias
    - Both zanubrutinib and ibrutinib with or without rituximab are listed as options for primary treatment (both category 1, preferred), while ixazomib combined with rituximab and dexamethasone is a category 2A, other recommended regimen for primary therapy
    - For patients who have received previous therapies for Waldenström's macroglobulinemia, zanubrutinib and ibrutinib with or without rituximab are category 1, preferred regimens. Acalabrutinib is a category 2A, other recommended treatment option
    - Up to 40% of WM patients may have recurrent mutations in the CXCR4 gene and certain CXCR4 mutations may confer resistance to ibrutinib; therefore, the NCCN guidelines recommend consideration of CXCR4 gene mutation testing for patients being initiated on ibrutinib therapy as a category 2A, useful in certain circumstances recommendation
  - No current US guidelines exist for the treatment of erythema nodosum leprosum, hypereosinophilic syndrome, or chronic eosinophilic leukemia

Oncology, Oral- Hematological – Overview of Disease State

- **Philadelphia chromosome positive (Ph+) ALL**
  - Ph+ ALL is rare in pediatric cases of ALL, occurring in approximately 2% of cases. In contrast, approximately 25% of adult cases of ALL are Ph+

- **Treatment**
  - The 2.2021 National Comprehensive Cancer Network (NCCN) guidelines recommend incorporation of a tyrosine kinase inhibitor (TKI) in the frontline regimen for Ph+ ALL as an established standard of care for adolescents/young adults and adult patients
    - The TKI may be combined with either chemotherapy or corticosteroids depending on the patient's age and comorbidities
    - TKI options for induction therapy of Ph+ ALL in adolescents, young adults, and adult patents include imatinib (Gleevec), dasatinib (Sprycel), nilotinib (Tasigna), bosutinib (Bosulif), and ponatinib (Iclusig)
    - The NCCN states that dasatinib and imatinib are the preferred TKIs for induction therapy while ponatinib is preferred as part of the hyper-CVAD chemotherapy regimen
    - In addition, the NCCN ALL guidelines also note bosutinib (Bosulif) is an option but state there is limited data for that particular TKI in Ph+ ALL
    - Mutation testing for the ABL gene should be considered as this mutation can confer greater resistance or susceptibility to a particular TKI, and the choice of a specific TKI should also be based on disease-related features
    - Pediatric patients with Ph+ ALL are also candidates for TKI therapy
  - The 3.2021 NCCN guidelines for pediatric ALL specifically list combined treatment regimens containing imatinib or dasatinib
    - A study by the Children's Oncology Group (COG) utilizing imatinib for children with Ph+ ALL demonstrated a 5-year event-free survival of 70% (standard error, ± 12%) which is superior to historical controls prior to the introduction of imatinib

Oncology, Oral- Hematological – Overview of Disease State

- **Mantle Cell Lymphoma (MCL)**
  - MCL, while technically classified as an aggressive lymphoma, possesses characteristics of both indolent and aggressive NHLs
  - The median overall survival is approximately 4 to 5 years, but there is no evidence of a survival plateau, which is similar to indolent lymphomas. The chromosomal translocation t(11;14) is usually present in MCL
  - MCL is highly resistant to conventional chemotherapy and displays an aggressive disease course

- **Treatment**:
  - The 2022 B-cell lymphoma NCCN guidelines indicate that lenalidomide plus rituximab is one of several regimens that may be utilized for induction therapy when a less aggressive regimen is indicated
  - In the second-line setting, all BTK inhibitors, including acalabrutinib (Calquence), ibrutinib (Imbruvia), with or without rituximab, and zanubrutinib (Brukinsa), as well as lenalidomide plus rituximab (if BTK inhibitor is contraindicated), are listed as preferred options
  - The NCCN guidelines note that acalabrutinib and zanubrutinib have not been shown to be effective for ibrutinib-refractory MCL with BTK C481S mutations; however, patients with intolerance to ibrutinib have been successfully treated with acalabrutinib or zanubrutinib without recurrence of symptoms
  - Venetoclax with or without rituximab is a category 2A, useful in certain circumstances recommendation

Oncology, Oral- Hematological

- zanubrutinib (Brukinsa)
  - **September 2021: FDA approved a new indication for the treatment of adult pts with Waldenström's macroglobulinemia (WM)**
  - **Indications**
    - Mantle cell lymphoma (MCL) who have received at least one prior therapy
    - **Waldenström's macroglobulinemia (WM)**
    - Relapsed or refractory marginal zone lymphoma (MZL) who have received at least one anti-CD20-based regimen
    - **Note: This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial**
  - **Warnings and Precautions**
    - Infections: Monitor patients for signs and symptoms of infection, including opportunistic infections, and treat as needed
    - Cytopenias: Monitor complete blood counts during treatment
    - Cardiac Arrhythmias: Monitor for atrial fibrillation and atrial flutter and manage appropriately
    - Embryo-Fetal Toxicity: Can cause fetal harm. Advise women of the potential risk to a fetus and to avoid pregnancy
  - **Dosage**
    - 160 mg orally twice daily or 320 mg orally once daily; swallow whole with water and with or without food
    - Reduce dose in patients with severe hepatic impairment
  - **Availability**
    - Capsules: 80 mg

Oncology, Oral- Hematological

- nilotinib (Tasigna)
  - **October 2021: FDA approved label revision for Tasigna for the treatment of pediatric patients ≥ 1 year of age with chronic phase and accelerated phase Philadelphia chromosome positive CML with resistance or intolerance to prior TKI therapy; previously, it was approved in this population for chronic phase only**
  - **Indication**
    - Adult and pediatric patients greater than or equal to 1 year of age with newly diagnosed Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase
    - Adult patients with chronic phase (CP) and accelerated phase (AP) Ph+ CML resistant to or intolerant to prior therapy that included imatinib
    - **Pediatric patients greater than or equal to 1 year of age with Ph+ CML-CP and CML-AP resistant or intolerant to prior tyrosine-kinase inhibitor (TKI) therapy**
  - **Warnings and Precautions**
    - Embryo-Fetal Toxicity: Advise females of reproductive potential of potential risk to a fetus and to use effective contraception
    - Tumor Lysis Syndrome: Maintain adequate hydration and correct uric acid levels prior to initiating therapy with Tasigna
    - Hepatotoxicity: Monitor hepatic function tests monthly or as clinically indicated
  - **Dosage**
    - **Recommended Adult Dose: Newly diagnosed Ph+ CML-CP: 300 mg orally twice daily. Resistant or intolerant Ph+ CML-CP and CML-AP: 400 mg orally twice daily**
    - **Recommended Pediatric Dose: Newly Diagnosed Ph+ CML-CP or Ph+ CML-CP and CML-AP resistant or intolerant to prior TKI therapy: 230 mg/m2 orally twice daily, rounded to the nearest 50 mg dose (to a maximum single dose of 400 mg)**
  - **Availability**
    - Capsules: 50 mg, 150 mg, and 200 mg

Oncology, Oral- Hematological

- asciminib (Scemblix)
  - November 2021: FDA approved Scemblix, a kinase inhibitor indicated for the treatment of adult pts with Philadelphia chromosome-positive (Ph+) CML in chronic phase (CP), previously treated with 2 or more TKIs (approved under Accelerated Approval based on major molecular response [MMR]; continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial); and (2) Ph+ CML in CP with the T315I mutation
  - Indications
    - Adult patients with Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP), previously treated with two or more tyrosine kinase inhibitors (TKIs)
    - Ph+ CML in CP with the T315I mutation
  - Warnings and Precautions
    - Cardiovascular Toxicity: Cardiovascular toxicity may occur. Monitor patients with history of cardiovascular risk factors for cardiovascular signs and symptoms. Initiate appropriate treatment as clinically indicated
    - Embryo-Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception
  - Dosage
    - Recommended Adult Dose: Newly diagnosed Ph+ CML-CP: 300 mg orally twice daily. Resistant or intolerant Ph+ CML-CP and CML-AP: 400 mg orally twice daily
    - Recommended Pediatric Dose: Newly Diagnosed Ph+ CML-CP or Ph+ CML-CP and CML-AP resistant or intolerant to prior TKI therapy: 230 mg/m2 orally twice daily, rounded to the nearest 50 mg dose (to a maximum single dose of 400 mg)
  - Availability
    - Film-coated tablets: 20 mg and 40 mg

Oncology, Oral- Hematological

- ixazomib (Ninlaro)
  - **May 2022: The indication revised with limitation of use stating it is not recommended in the maintenance setting or in newly diagnosed multiple myeloma in combination with lenalidomide and dexamethasone outside of controlled clinical trials**
  - **Indication**
    - In combination with lenalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received at least one prior therapy
    - **Limitations of Use: Not recommended for use in the maintenance setting or in newly diagnosed multiple myeloma in combination with lenalidomide and dexamethasone outside of controlled clinical trials**
  - **Warnings and Precautions**
    - Thrombocytopenia: Monitor platelet counts at least monthly during treatment and adjust dosing, as needed
    - Gastrointestinal Toxicities: Adjust dosing for severe diarrhea, constipation, nausea, and vomiting, as needed
    - Peripheral Neuropathy: Monitor patients for symptoms of peripheral neuropathy and adjust dosing, as needed
    - Hepatic Impairment: Reduce starting dose to 3 mg in patients with moderate or severe hepatic impairment
    - Renal Impairment: Reduce starting dose to 3 mg in patients with severe renal impairment or end-stage renal disease requiring dialysis
  - **Dosage**
    - Recommended starting dose of 4 mg taken orally on Days 1, 8, and 15 of a 28-day cycle
  - **Availability**
    - Capsules: 4 mg, 3 mg, and 2.3 mg

Oncology, Oral- Hematological

- acalabrutinib (Calquence)
  - **August 2022: The FDA approved a new formulation (tablets) for the treatment of adults with chronic lymphocytic leukemia (CLL), and small lymphocytic lymphoma (SLL). The treatment of adult patients with mantle cell lymphoma (MCL) who have received ≥ 1 prior therapy was also granted under Accelerated Approval contingent on confirmatory trials**
  - **Indication**
    - Mantle cell lymphoma (MCL) who have received at least one prior therapy
      - This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials
    - Chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)
  - **Warnings and Precautions**
    - Pregnancy: May cause fetal harm and dystocia
    - Serious and Opportunistic Infections: Monitor for signs and symptoms of infection and treat promptly
    - Hemorrhage: Monitor for bleeding and manage appropriately
    - Cytopenias: Monitor complete blood counts regularly
  - **Dosage**
    - Recommended dose is 100 mg orally approximately every 12 hours; swallow whole with water and with or without food
  - **Availability**
    - Capsules: 100 mg
    - **Tablets: 100 mg**

Oncology, Oral- Hematological

- ibrutinib (Imbruvica)
  - **May 2022: The FDA has expanded the indication for chronic graft versus host disease (cGVHD) after failure of ≥ 1 lines of systemic therapy to include pediatric patients ≥ 1 years of age; previously, it was only indicated for use in adults.** Ibrutinib is also indicated for use in certain adults with mantle cell lymphoma, chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL), Waldenström's macroglobulinemia, and marginal zone lymphoma
  - **Warnings and Precautions**
    - Hepatic Impairment: Avoid use in patients with severe hepatic impairment. In patients with mild or moderate impairment, reduce dose
    - Hemorrhage: Monitor for bleeding and manage appropriately
    - Cytopenias: Monitor complete blood counts monthly
    - Second Primary Malignancies: Other malignancies have occurred in patients, including skin cancers, and other carcinomas
  - **Dosage**
    - **cGVHD:**
      - **Patients 12 years and older: 420 mg taken orally once daily**
      - **Patients 1 to less than 12 years of age: 240 mg/m2 taken orally once daily (up to a dose of 420 mg)**
  - **Availability**
    - Capsules: 100 mg
    - **Tablets: 100 mg**

Oncology, Oral- Hematological

- **FDA Communications**
  - **Umbralisib (Ukoniq)**
    - **February 2022:**
      - **FDA is investigating possible increased risk of death with lymphoma medicine umbralisib based on interim data from the UNITY trial in patients with chronic lymphocytic leukemia, an unapproved clinical use**
      - **Interim study data revealed a possible increased risk of death in patients treated with a combination of umbralisib and an anti-CD20 monoclonal antibody drug compared to those treated with standard treatment**
      - **Umbralisib is FDA-approved to treat relapsed or refractory marginal zone lymphoma and follicular lymphoma**
      - **FDA is advising Healthcare Practitioners to review patient progress and discuss risks/benefits of Ukoniq with patients**
    - **April 2022:**
      - **The manufacturer has voluntarily withdrawn Ukoniq from sale for the indications of adults with marginal zone lymphoma (MZL) who have received ≥ 1 prior anti-CD20-based regimen and for the treatment of adults with follicular lymphoma (FL) who have received ≥ 3 prior systemic therapies**
      - **These Accelerated Approvals were granted in February 2021**
    - **June 2022:**
      - **The FDA published a Drug Safety Communication stating that Ukoniq (umbralisib) approval has been withdrawn for marginal zone lymphoma & follicular lymphoma due to safety concerns**
      - **FDA advises HCPs to switch patients to alternative treatments**
      - **For limited cases, Ukoniq will be available via expanded access from TG Therapeutics**

- **New Generic**
  - **Lenalidomide- October 2021**
    - **FDA approved first generic to Celgene's Revlimid in the strengths of 2.5 mg and 20 mg by Dr. Reddy's.**

Oncology, Oral- Hematological

- **FDA Communications**
  - **Idelalisib (Zydelig)- February 2022**
    - **Gilead announced the voluntary withdrawal of indications for the treatment of relapsed follicular B-cell non-Hodgkin lymphoma (FL) and relapsed small lymphocytic lymphoma (SLL) which were approved under an Accelerated Approval based on objective response rates of 54% and 58%, respectively**
    - **The decision to withdraw these indications is based on an ongoing challenge of enrolling patients in the confirmatory trial**

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Oncology, Oral – Breast

ONCOLOGY AGENTS : ANTINEOPLASTICS - MISC COMBINATIONS – ORAL
ONCOLOGY AGENTS : CYCLIN DEPENDENT KINASES (CDK) INHIBITORS – ORAL
ONCOLOGY AGENTS : POLY (ADP-RIBOSE) POLYMERASE (PARP) INHIBITORS - ORAL
ONCOLOGY AGENTS : TYROSINE KINASE INHIBITORS - ORAL

Oncology, Oral- Breast – Overview of Disease State

- Breast cancer is the most common site of cancer for women in the United States (US), accounting for 30% of all cancer diagnoses, and is second only to lung cancer as a cause of cancer death in American women

- It is estimated that there will be 287,850 new cases of breast cancer diagnosed in the US in 2022 and there will be an estimated 43,500 deaths
  - The incidence of breast cancer in US women continues to increase by about 0.5% per year
  - Known risk factors that may be contributing to this increased incidence of breast cancer include a decline in fertility rates and an increase in body weight
  - Despite this increasing incidence, death rates from breast cancer have declined by 42% since 1989, largely due to improvements in both early detection and treatment
  - The overall 5-year survival for women diagnosed with breast cancer is 99%
  - Patients who present with localized disease have a 98.9% 5-year survival rate; however, prognosis for patients presenting with distant metastatic disease is much poorer, with a 5-year survival rate of only 29%
  - Breast cancer is most frequently diagnosed in women between the ages of 55 to 64 with the median age at diagnosis being 62 years

- Rarely, breast cancer may be diagnosed in men

- Other risk factors include various endocrine, genetic, environmental, and lifestyle factors

- Some of these risk factors are modifiable, some are not, and the impact of these factors are variable

Oncology, Oral- Breast – Guidelines

Neoadjuvant treatment of breast cancer

- Historically, the role for neoadjuvant chemotherapy was limited to breast cancer patients with inoperable, locally advanced disease, but contemporary breast cancer treatment protocols now often include neoadjuvant therapy
- There are several reasons for this expanded role of neoadjuvant therapy
  - First, neoadjuvant therapy can increase the likelihood of patients being able to undergo breast-conserving surgery
  - Second, studies have shown that patients with triple-negative breast cancer (TNBC) and those with HER2-positive disease who achieve a pathologic complete response (pCR), defined as the absence of invasive disease in the breast and lymph nodes, following neoadjuvant therapy have an improved prognosis
- Recently, published research has focused on response to neoadjuvant treatment as a predictive marker and a guide for selecting subsequent adjuvant therapy

- **ASCO Guidelines, 2021**
  - Regarding neoadjuvant chemotherapy, endocrine therapy, and targeted therapy recommends neoadjuvant therapy with any of these modalities if the patient has inflammatory breast cancer or if the patient has unresectable or locally advanced disease at presentation such that the disease may be rendered resectable with neoadjuvant treatment
  - Furthermore, the ASCO guideline states neoadjuvant systemic therapy should be offered to patients with high-risk TNBC in whom the finding of residual disease at time of surgery would guide recommendations related to adjuvant therapy
  - Regarding neoadjuvant endocrine therapy, the ASCO guideline states that postmenopausal patients with HR-positive/HER2-negative disease may receive a neoadjuvant aromatase inhibitor (AI) therapy to increase locoregional treatment options, or if there is no intent for surgery, endocrine therapy may be used for disease control
  - However, for premenopausal patients with HR-positive/HER2-negative early-stage diseases, neoadjuvant endocrine therapy should not be routinely offered outside of a clinical trial

Oncology, Oral- Breast

- ONCOLOGY AGENTS : ANTINEOPLASTICS - MISC COMBINATIONS – ORAL
  - **Kisqali**
  - Femara

- ONCOLOGY AGENTS : CYCLIN DEPENDENT KINASES (CDK) INHIBITORS – ORAL
  - Ibrance
  - Kisqali
  - **Verzenio**

- ONCOLOGY AGENTS : POLY (ADP-RIBOSE) POLYMERASE (PARP) INHIBITORS – ORAL
  - **Lynparza**
  - **Rubraca**
  - **Talzenna**

- ONCOLOGY AGENTS : TYROSINE KINASE INHIBITORS – ORAL
  - Lapatinib
  - Nerlynx
  - Tukysa
  - Tykerb

Oncology, Oral- Breast

- talazoparib (Talzenna)
  - **October 2021: FDA approved 2 new strengths: 0.5 mg and 0.75 mg capsules (0.25 mg and 1 mg already approved)**
  - **Indication**
    - Treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) HER2-negative locally advanced or metastatic breast cancer
    - Select patients for therapy based on an FDA-approved companion diagnostic for Talzenna
  - **Warnings and Precautions**
    - Myelosuppression: May affect hematopoiesis and can cause anemia, neutropenia, and/or thrombocytopenia
    - Embryo-Fetal Toxicity: Can cause fetal harm. Advise of the potential risk to the fetus and to use effective contraception
  - **Dosage**
    - The recommended dose is 1 mg taken as a single oral daily dose, with or without food
    - Patients should be treated until disease progression or unacceptable toxicity occurs
    - For patients with moderate renal impairment (CLcr 30 – 59 mL/min), the recommended dose is 0.75 mg once daily
    - For patients with severe renal impairment (Clcr 15 – 29 mL/min), the recommended dose is 0.5 mg once daily
  - **Availability**
    - Capsules: 0.25 mg, **0.5 mg, 0.75 mg**, and 1 mg

Oncology, Oral- Breast

- abemaciclib (Verzenio)
  - **October 2021: FDA approved a new indication for Verzenio in combination with endocrine therapy (tamoxifen or an aromatase inhibitor) for adjuvant treatment of adult pts with HR-positive, HER2-negative, node-positive, early breast cancer at high risk of recurrence and a Ki-67 score ≥ 20%, as determined by an FDA approved test. The FDA also approved the Agilent's Ki-67 IHC MIB-1 pharmDx (Dako Omnis) assay as a companion diagnostic for this indication.**
  - **October 2021: In addition, the indication in combination with an aromatase inhibitor was expanded to include both postmenopausal women and men, and the indication in combination with fulvestrant was expanded to include adult pts (previously for women only)**
  - **Indication**
    - **In combination with endocrine therapy (tamoxifen or an aromatase inhibitor) for the adjuvant treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive, early breast cancer at high risk of recurrence and a Ki-67 score ≥20% as determined by an FDA approved test**
    - **In combination with an aromatase inhibitor as initial endocrine based therapy for the treatment of postmenopausal women, and men, with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer**
    - In combination with fulvestrant for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer with disease progression following endocrine therapy
    - As monotherapy for the treatment of adult patients with HRpositive, HER2-negative advanced or metastatic breast cancer with disease progression following endocrine therapy and prior chemotherapy in the metastatic setting
  - **Warnings and Precautions**
    - Embryo-Fetal Toxicity: Can cause fetal harm. Advise of the potential risk to the fetus and to use effective contraception
  - **Dosage**
    - Recommended starting dose in combination with fulvestrant, tamoxifen, or an aromatase inhibitor: 150 mg twice daily
    - Recommended starting dose as monotherapy: 200 mg twice daily
  - **Availability**
    - Tablets: 50 mg, 100 mg, 150 mg, and 200 mg

Oncology, Oral- Breast

- ribociclib; ribociclib/letrozole (Kisqali; Kisqali/Femara)
  - **December 2021: FDA approved expanded indication to include men for the treatment of with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic cancer in combination with fulvestrant as initial endocrine-based therapy or following disease progression on endocrine therapy; previously only for postmenopausal women for this indication**
  - **Indication**
    - Treatment of adult patients with hormone receptor (HR)- positive, human epidermal growth factor receptor 2 (HER2)- negative advanced or metastatic cancer in combination with:
      - An aromatase inhibitor as initial endocrine-based therapy
      - **Fulvestrant as initial endocrine-based therapy or following disease progression on endocrine therapy in postmenopausal women or in men**
  - **Warnings and Precautions**
    - Neutropenia: Perform complete blood count (CBC) before initiating therapy with Kisqali. Monitor CBC every 2 weeks for the first 2 cycles, at the beginning of each subsequent 4 cycles, and as clinically indicated
    - Embryo-Fetal Toxicity: Can cause fetal harm. Advise of the potential risk to the fetus and to use effective contraception
  - **Dosage**
    - Recommended starting dose: 600 mg orally (three 200 mg tablets) taken once daily with or without food for 21 consecutive days followed by 7 days off treatment
  - **Availability**
    - Tablets: 200 mg

Oncology, Oral- Breast

- olaparib (Lynparza)
  - **March 2022: FDA approved new indication for the adjuvant treatment of adult patients with deleterious or suspected deleterious germline BRCA mutated HER2-negative high-risk early breast cancer who have previously been treated with neoadjuvant or adjuvant chemotherapy**
  - **September 2022: AstraZeneca has voluntarily withdrawn the indication for the treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) advanced ovarian cancer who have been treated with ≥ 3 prior lines of chemotherapy. Olaparib maintains indications for select patients with ovarian, breast, pancreatic, and prostate cancer**
  - **Warnings and Precautions**
    - Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML): Occurred in approximately 1.5% of patients exposed to Lynparza monotherapy and the majority of events had a fatal outcome. Monitor patients for hematological toxicity at baseline and monthly thereafter. Discontinue if MDS/AML is confirmed
    - Embryo-Fetal Toxicity: Can cause fetal harm. Advise of the potential risk to the fetus and to use effective contraception
  - **Dosage**
    - Recommended dosage is 300 mg taken orally twice daily with or without food. See Full Prescribing Information for the recommended duration
    - Patients receiving Lynparza for mCRPC should also receive a gonadotropin-releasing hormone (GnRH) analog concurrently or should have had bilateral orchiectomy
  - **Availability**
    - Tablets: 150 mg, 100 mg

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Oncology, Oral – Other

ONCOLOGY AGENTS : ANTINEOPLASTICS - MISC COMBINATIONS – ORAL
ONCOLOGY AGENTS : FGFR KINASE INHIBITORS – ORAL
ONCOLOGY AGENTS : MEK INHIBITORS – ORAL
ONCOLOGY AGENTS : MULTIKINASE INHIBITORS – ORAL
ONCOLOGY AGENTS : POLY (ADP-RIBOSE) POLYMERASE (PARP) INHIBITORS – ORAL
ONCOLOGY AGENTS : TROPOMYOSIN RECEPTOR KINASE INHIBITORS – ORAL
ONCOLOGY AGENTS : TYROSINE KINASE INHIBITORS - ORAL

Oncology, Oral- Other

- ONCOLOGY AGENTS : ANTINEOPLASTICS - MISC COMBINATIONS – ORAL
  - Lonsurf
- ONCOLOGY AGENTS : FGFR KINASE INHIBITORS – ORAL
  - Balversa
  - Pemazyre
  - **Truseltiq**
- ONCOLOGY AGENTS : MEK INHIBITORS – ORAL
  - Koselugo
- ONCOLOGY AGENTS : MULTIKINASE INHIBITORS – ORAL
  - Stivarga
- ONCOLOGY AGENTS : POLY (ADP-RIBOSE) POLYMERASE (PARP) INHIBITORS – ORAL
  - Lynparza
  - **Rubraca**
  - Zejula
- ONCOLOGY AGENTS : TROPOMYOSIN RECEPTOR KINASE INHIBITORS – ORAL
  - Vitrakvi
- ONCOLOGY AGENTS : TYROSINE KINASE INHIBITORS – ORAL
  - Ayvakit
  - Caprelsa
  - Cometriq
  - Qinlock
  - Turalio

Oncology, Oral- Other

- infigratinib (Truseltiq)
  - **June 2021: The FDA granted Accelerated Approval to infigratinib (Truseltiq), a kinase inhibitor, for adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement, as detected by an FDA-approved test**
  - **Indication**
    - **The treatment of adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement as detected by an FDA-approved test**
  - **Warnings and Precautions**
    - Ocular Toxicity: Can cause retinal pigment epithelial detachment (RPED). Perform comprehensive ophthalmic examination including optical coherence tomography (OCT) prior to initiation of TRUSELTIQ and at 1 month, at 3 months, and then every 3 months thereafter during treatment. Withhold as recommended
    - Embryo-Fetal Toxicity: Can cause fetal harm. Advise of the potential risk to the fetus and to use effective contraception
    - Renal Impairment: Dose adjustment recommended for mild-moderate renal impairment
    - Hepatic Impairment: Dose adjustment recommended for mild-moderate hepatic impairment
  - **Dosage**
    - Recommended dosage: 125 mg orally once daily for 21 consecutive days followed by 7 days off therapy, in 28-day cycles
  - **Availability**
    - Capsules: 25 mg and 100 mg

Oncology, Oral- Breast

- **FDA Communications**
  - **rucaparib camsylate (Rubraca)- June 2022**
    - **Clovis Oncology has voluntarily withdrawn the indication of rucaparib for monotherapy in patients with deleterious BRCA mutation (germline and/or somatic) associated epithelial ovarian, fallopian tube, or primary peritoneal cancer after ≥ 2 chemotherapies**
    - **This indication was approved under an Accelerated Approval in December 2016**

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Oncology, Oral – Lung

ONCOLOGY AGENTS : TOPOISOMERASE INHIBITORS – ORAL
ONCOLOGY AGENTS : TROPOMYOSIN RECEPTOR KINASE INHIBITORS – ORAL
ONCOLOGY AGENTS : TYROSINE KINASE INHIBITORS - ORAL

Oncology, Oral- Lung – Overview of Disease State

- Lung cancer is the leading cause of cancer death in both men and women in the United States (US)
  - In 2022, an estimated 236,740 new cases of lung cancer will be diagnosed, and 130,180deaths are estimated to occur
  - Currently, 5-year survival is estimated to be 22.9%, an increase from 18.6% reported in 2019
  - Declines in lung cancer mortality in the US have been accelerating in recent years
  - From 2005 through 2014, lung cancer mortality declined 4.9%, but from 2014 through 2019, this decline more than doubled, resulting in a 4.9% decline in lung cancer mortality over that period
  - Additionally, there has been a steady decline in the incidence of lung cancer diagnoses in the US; the number of diagnoses declined 2.3% in the most recent measurement
  - Despite these encouraging trends, there are still more US lung cancer deaths annually than deaths from breast cancer, prostate cancer, and colorectal cancer combined

- The primary risk factor for the development of lung cancer is smoking tobacco, accounting for approximately 85% to 90% of all cases of lung cancer
  - The carcinogenic chemicals in cigarette smoke are responsible for most lung cancer-related deaths, while exposure to second-hand smoke also results in an increased relative risk of developing lung cancer

- While chemoprevention agents are not yet established, lung cancer screening using low-dose computerized tomography (LDCT) is recommended by the US Preventive Services Task Force (USPSTF), who expanded their lung cancer screening guidelines in 2021
  - The USPSTF guidelines now recommend annual screening with LDCT for patients 50 to 80 years of age who are current smokers with at least a 20 pack-year smoking history and former smokers who have quit within the past 15 years

Oncology, Lung – Guidelines

- **EGFR sensitizing mutations**
  - NCCN guidelines
    - Have been updated to incorporate the use of osimertinib (Tagrisso) in the adjuvant setting of earlier stage NSCLC
    - The guidelines recommend the use of osimertinib for patients with stage 2B to 3A disease who have undergone complete resection or for patients with high risk stage 1B to 2A, EGFR mutation-positive disease who received previous adjuvant chemotherapy or are ineligible to receive platinum-based chemotherapy
  - ASCO/Ontario Health (Cancer Care Ontario) guidelines, 2021
    - Regarding stage 4 NSCLC with driver mutations
    - Indicate that osimertinib should be offered in the first-line setting for patients with T790M, L858R, or exon 19 deletion EGFR mutations
    - If osimertinib is not available in the first-line setting, gefitinib with chemotherapy or dacomitinib may be offered
    - Other options listed by the ASCO guidelines include afatinib or erlotinib/bevacizumab; erlotinib/ramucirumab; or gefitinib, erlotinib, or icotinib (not available in the US) as single agents
- ***BRAF V600E point mutations***
  - For patients with advanced or metastatic lung cancer who are found to have a BRAF V600E mutation, a combination of dabrafenib (Tafinlar) plus trametinib (Mekinist) is recommended as preferred first-line therapy by NCCN, while single agent vemurafenib (Zelboraf) may be an option if the combination of dabrafenib plus trametinib is not tolerated
  - According to ASCO guidelines
    - Patients with stage 4 NSCLC and BRAF V600E mutations should be offered dabrafenib/trametinib in the first-line setting
    - For patients who receive targeted therapy in the first-line setting, second-line therapy should consist of standard nondriver mutation guideline recommendations

Oncology, Lung – Guidelines

- ***MET exon 14 skipping mutations***
  - Both capmatinib (Tabrecta) and tepotinib (Tepmetko) are listed as NCCN category 2A, preferred options, while crizotinib (Xalkori) is classified as a category 2A, useful in certain circumstances recommendation
  - ASCO guidelines recommend offering capmatinib or tepotinib in the first-line setting
  - If the patient does not receive one of these therapies in the first-line setting, it may be offered in the second-line setting

- ***ALK rearrangements***
  - ASCO 2021 updated guidelines regarding patients with stage 4 NSCLC who harbor an ALK rearrangement recommend that alectinib or brigatinib be offered in the first-line setting
    - The guidelines recommend that if alectinib and brigatinib are not available, patients should be offered ceritinib or crizotinib
    - The ASCO guidelines also outline drug choices for the second-line setting
    - Lorlatinib in the second-line setting is recommended if the patient received alectinib or brigatinib in the first-line setting
    - If the patient received crizotinib in the first-line setting, then alectinib, brigatinib, or ceritinib should be offered
    - In the third-line setting, lorlatinib may be offered

- ***ROS1 rearrangements***
  - ASCO guidelines recommend crizotinib or entrectinib in the first-line setting
  - Other options include ceritinib or lorlatinib
  - If targeted therapy was given in the first-line setting, then ASCO guidelines recommend that the standard treatment based on nondriver mutation guidelines should be followed

Oncology, Lung – Guidelines

- ***RET rearrangements***
  - Both pralsetinib (Gavreto) and selpercatinib (Retevmo) are listed as NCCN category 2A, preferred first-line options
  - ASCO guidelines state that selpercatinib or standard therapy based on nondriver mutation guidelines may be offered in the first-line setting
  - At the time of the ASCO publication, the pralsetinib recommendation in the first-line setting was provisional, pending confirmatory data
  - Recommendations for second-line setting for RET rearrangements are dependent on the therapy received in the first-line; if targeted therapy with pralsetinib or selpercatinib were not given in the first-line setting, they may be offered as second-line therapy

- ***NTRK fusions***
  - Both entrectinib (Rozlytrek) and larotrectinib (Vitrakvi) are NCCN category 2A preferred options in the first-line setting
  - ASCO guidelines also recommend entrectinib or larotrectinib in this setting, and these drugs may also be offered in the second-line setting for patients with NTRK gene fusions who did not receive them in the first-line setting

Oncology, Oral- Lung

- ONCOLOGY AGENTS : MULTIKINASE INHIBITORS - ORAL
  - Tepmetko
- ONCOLOGY AGENTS : TOPOISOMERASE INHIBITORS – ORAL
  - Hycamtin
- ONCOLOGY AGENTS : TROPOMYOSIN RECEPTOR KINASE INHIBITORS – ORAL
  - Rozlytrek
- ONCOLOGY AGENTS : TYROSINE KINASE INHIBITORS – ORAL
  - Alecensa
  - Alunbrig
  - Erlotinib
  - **Exkivity**
  - Gavreto
  - Gilotrif
  - Iressa
  - Lorbrena
  - Retevmo
  - Tabrecta
  - Tagrisso
  - Tarceva
  - Vizimpro
  - **Xalkori**
  - Zykadia

Oncology, Oral- Lung

- mobocertinib (Exkivity)
  - **September 2021: The FDA has granted Accelerated Approval to mobocertinib (Exkivity), a kinase inhibitor, for the treatment of adult pts with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 20 insertion mutations, as detected by an FDA-approved test, whose disease has progressed on or after platinum-based chemotherapy**
  - **Indication**
    - **The treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 20 insertion mutations, as detected by an FDA-approved test, whose disease has progressed on or after platinum-based chemotherapy**
  - **Warnings and Precautions**
    - **BBW: Can cause life-threatening heart rate-corrected QT (QTc) prolongation, including Torsades de Pointes, which can be fatal, and requires monitoring of QTc and electrolytes at baseline and periodically during treatment. Increase monitoring frequency in patients with risk factors for QTc prolongation**
    - **Cardiac Toxicity: Monitor cardiac function, including left ventricular ejection fraction, at baseline and during treatment. Withhold, resume at reduced dose or permanently discontinue based on severity**
    - **Embryo-Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective non-hormonal contraception**
  - **Dosage**
    - **Recommended Dosage: 160 mg orally once daily, with or without food**
  - **Availability**
    - **Capsules: 40 mg**

Oncology, Oral- Lung

- **crizotinib (Xalkori)**
  - **July 2022: FDA approved for the treatment of adults and peds ≥ 1 yo with unresectable, recurrent, or refractory inflammatory myofibroblastic tumor (IMT) that is anaplastic lymphoma kinase (ALK)-positive**
  - **Indications**
    - Patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK) or ROS1-positive as detected by an FDA-approved test
    - Pediatric patients 1 year of age and older and young adults with relapsed or refractory, systemic anaplastic large cell lymphoma (ALCL) that ALK-positive
    - **Adult and pediatric patients 1 year of age and older with unresectable, recurrent, or refractory inflammatory myofibroblastic tumor (IMT) that is ALK-positive**
  - **Warnings and Precautions**
    - Interstitial Lung Disease (ILD)/Pneumonitis: Permanently discontinue in patients with ILD/pneumonitis
    - QTc Interval Prolongation: Monitor electrocardiograms and electrolytes in patients who have a history or predisposition for QTc prolongation, or those who are taking medications that are known to prolong the QTc interval. Withhold then restart at a reduced dose or permanently discontinue Xalkori
    - Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients of the potential risk to a fetus and use of effective contraception
  - **Dosage**
    - **Unresectable IMT:**
      - **Adult: The recommended dosage is 250 mg orally twice daily**
      - **Pediatric: The recommended dosage is 280 mg/m2 orally twice daily based on body surface area**
  - **Availability**
    - Capsules: 250 mg, 200 mg

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Oncology, Oral – Renal Cell Carcinoma

ONCOLOGY AGENTS : MTOR KINASE INHIBITORS – ORAL
ONCOLOGY AGENTS : MULTIKINASE INHIBITORS – ORAL
ONCOLOGY AGENTS : TYROSINE KINASE INHIBITORS - ORAL

Oncology, Oral- Renal Cell Carcinoma – Overview of Disease State

- Cancers of the kidney and renal pelvis account for approximately 4% of all newly-diagnosed cancers in the United States (US), with a 5% incidence in males and a 3% incidence in females
  - The median age at diagnosis is 65 years, and > 75% of cases are diagnosed in patients ages 55 or older
  - The overall 5-year survival for patients diagnosed with RCC was 76.5% from the period of 2012 to 2018
  - If the disease is localized at time of diagnosis, outcomes are excellent with a 5-year survival of approximately 93%; however, patients diagnosed with advanced, metastatic disease, accounting for approximately 16% of diagnoses, have much poorer outcomes with approximately a 15.3% survival rate at 5 years

- Approximately 85% of kidney tumors are RCC, and approximately 70% of all RCC have a clear cell histology
  - Other less common histologies are usually grouped together as “non-clear cell” tumors

- The incidence of RCC in men is more than twice that of women in the US

- The most common presenting triad of symptoms includes hematuria, flank mass, and flank pain; however, as the use of routine imaging has become more widespread, the frequency of incidental detection of RCC has increased, and only about 30% of patients are now diagnosed on the basis of symptoms

Oncology, Oral- Renal Cell Carcinoma – Guidelines

- NCCN Guidelines, 2022
  - For first-line systemic therapy of favorable risk, clear cell histology, relapsed or stage 4 RCC recommend a TKI plus an immune checkpoint inhibitor (CPI) as the category 1, preferred options
  - Specifically, axitinib (Inlyta) plus pembrolizumab (Keytruda) or cabozantinib (Cabometyx) plus nivolumab (Opdivo) or lenvatinib (Lenvima) plus pembrolizumab are the 3 TKI/CPI regimens included
  - Other recommended regimens for this same group of patients include monotherapy with sunitinib (Sutent) or pazopanib (Votrient), or the combination of axitinib (Inlyta) plus avelumab
  - Axitinib monotherapy is a NCCN category 2B recommendation listed as useful in certain circumstances
  - For this same group of patients with poor or intermediate risk, rather than favorable risk, the same 3 TKI/CPI regimens are listed as category 1, preferred along with single agent cabozantinib being a category 2A, preferred option
  - Other options for these patients with poor or intermediate risk largely mirror the favorable risk options defined above. For subsequent therapy of RCC with clear cell histology, category 1, preferred options include cabozantinib and lenvatinib plus everolimus (Afinitor)
  - Additional options include axitinib as either a single agent (category 1) or in combination with pembrolizumab (category 2A), cabozantinib plus nivolumab, lenvatinib plus pembrolizumab, or single agent pazopanib, sunitinib, or tivozanib (all category 2A)
  - Everolimus as a single agent is included as a category 2A, useful in certain circumstances. For patients with non-clear cell histology, single agent cabozantinib, sunitinib, axitinib, pazopanib, and everolimus are all category 2A recommendations though cabozantinib and sunitinib are the preferred regimens
  - Importantly, sorafenib is now only included in the NCCN guidelines as a category 3 recommendation for subsequent therapy that may be useful in certain circumstances

Oncology, Oral- Renal Cell Carcinoma

- ONCOLOGY AGENTS : MTOR KINASE INHIBITORS - ORAL
  - Afinitor
  - Everolimus

- ONCOLOGY AGENTS : MULTIKINASE INHIBITORS - ORAL
  - Fotvida
  - Nexavar
  - Sutent

- ONCOLOGY AGENTS : TYROSINE KINASE INHIBITORS - ORAL
  - Cabometyx
  - Inlyta
  - **Lenvima**
  - Votrient

Oncology, Oral- Renal Cell Carcinoma

- **lenvatinib (Lenvima)**
  - **July 2021: New indication in combination with avelumab or pembrolizumab for the first-line treatment of patients with advanced renal cell carcinoma (RCC). Previously approved as a single agent, for the treatment of advanced RCC after failure of 1 prior systemic therapy**
  - **Indications**
    - **Renal Cell Carcinoma (RCC)**
      - **In combination with pembrolizumab, for the first line treatment of adult patients with advanced renal cell carcinoma (RCC)**
      - In combination with everolimus, for the treatment of adult patients with advanced renal cell carcinoma (RCC) following one prior antiangiogenic therapy
  - **Warnings and Precautions**
    - Hypertension: Control blood pressure prior to treatment and monitor during treatment. Withhold for Grade 3 hypertension despite optimal antihypertensive therapy. Discontinue for Grade 4 hypertension
    - Cardiac Dysfunction: Monitor for clinical symptoms or signs of cardiac dysfunction. Withhold or discontinue for Grade 3 cardiac dysfunction. Discontinue for Grade 4 cardiac dysfunction
    - Arterial Thromboembolic Events: Discontinue following an arterial thromboembolic event
    - Embryo-Fetal Toxicity: Can cause fetal harm. Advise of potential risk to a fetus and use of effective contraception
  - **Dosage**
    - **RCC: The recommended dosage is 20 mg orally once daily with pembrolizumab 200 mg administered as an intravenous infusion over 30 minutes every 3 weeks. Dosages for other indications can be found in PI/TCR**
  - **Availability**
    - **4 mg and 10 mg capsules**

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Oncology, Oral – Skin

ONCOLOGY AGENTS : BRAF KINASE INHIBITORS – ORAL
ONCOLOGY AGENTS : HEDGEHOG PATHWAY INHIBITORS – ORAL
ONCOLOGY AGENTS : MEK INHIBITORS - ORAL

Oncology, Oral- Skin– Overview of Disease State

- **Melanoma Skin Cancer**
  - The incidence of melanoma skin cancer in the US is increasing, but the death rate due to melanoma is declining
    - From 2002 to 2006, the incidence of melanoma increased at a rate of 33% for men and 23% for women
    - Melanoma is increasing more rapidly than any other malignancy except lung cancer in women
    - Conversely, there have been recent declines in mortality for melanoma
    - From 2009 to 2013, the death rate for melanoma was stable, but from 2014 to 2018, the mortality due to melanoma declined 5.7% annually
  - In the US, it is estimated that there will be 106,110 new cases of melanoma diagnosed in 2021, and there will be an estimated 7,180 deaths due to melanoma
    - The median age at diagnosis is 65 years
    - Risk factors for the development of melanoma include both genetic factors (skin type, inherited germline mutations) and environmental factors (excess sun exposure, UV-based artificial tanning)
    - Despite the relationship to UV exposure, melanoma can also occur in areas of the body without substantial sun exposure and can occur in any ethnic group
  - There are also noncutaneous forms of melanoma, arising from melanocytes present in mucosal membranes or the uveal tract of the eye
    - The treatment of noncutaneous melanoma may differ from that of cutaneous melanoma, and treatment should be individualized for these patients

Oncology, Oral- Skin

- ONCOLOGY AGENTS : BRAF KINASE INHIBITORS – ORAL
  - Braftovi
  - **Tafinlar**
  - Zelboraf

- ONCOLOGY AGENTS : HEDGEHOG PATHWAY INHIBITORS – ORAL
  - Erivedge
  - Odomzo

- ONCOLOGY AGENTS : MEK INHIBITORS – ORAL
  - Cotellic
  - **Mekinist**
  - Mektovi

Oncology, Oral- Renal Cell Carcinoma

- **dabrafenib (Tafinlar)**
  - **June 2022: FDA approved dabrafenib (Tafinlar), in combination with trametinib (Mekinist), for the treatment of adult and pediatric patients ≥ 6 years of age with unresectable or metastatic solid tumors with BRAF V600E mutation who have progressed following prior treatment and have no satisfactory alternative treatment options; this Accelerated Approval requires verification of benefit in confirmatory trials**
  - **Indications**
    - The treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test
    - The adjuvant treatment of patients with melanoma with BRAF V600E or V600K mutations, as detected by an FDA-approved test, and involvement of lymph node(s), following complete resection
    - The treatment of patients with metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation as detected by an FDA-approved test
    - The treatment of patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) with BRAF V600E mutation and with no satisfactory locoregional treatment options
    - **The treatment of adult and pediatric patients 6 years of age and older with unresectable or metastatic solid tumors with BRAF V600E mutation who have progressed following prior treatment and have no satisfactory alternative treatment options. This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s)**
  - **Dosage**
    - **The recommended dosage in adult patients is 2 mg orally once daily**
    - **The recommended dosage in pediatric patients is based on body weight**
  - **Availability**
    - **50 mg and 75 mg capsules**

Oncology, Oral- Renal Cell Carcinoma

- **trametinib (Mekinist)**
  - **June 2022: FDA approved trametinib (Mekinist), in combination with dabrafenib (Tafinlar), for the treatment of adult and pediatric patients ≥ 6 yo with unresectable or metastatic solid tumors with BRAF V600E mutation who have progressed following prior treatment and have no satisfactory alternative treatment options; this Accelerated Approval requires verification of benefit in confirmatory trials**
  - **Indications**
    - The treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test
    - The adjuvant treatment of patients with melanoma with BRAF V600E or V600K mutations, as detected by an FDA-approved test, and involvement of lymph node(s), following complete resection
    - The treatment of patients with metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation as detected by an FDA-approved test
    - The treatment of patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) with BRAF V600E mutation and with no satisfactory locoregional treatment options
    - **The treatment of adult and pediatric patients 6 years of age and older with unresectable or metastatic solid tumors with BRAF V600E mutation who have progressed following prior treatment and have no satisfactory alternative treatment options. This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s)**
  - **Dosage**
    - **The recommended dosage in adult patients is 150 mg (two 75 mg capsules) orally twice daily**
    - **The recommended dosage in pediatric patients is based on body weight**
  - **Availability**
    - **0.5 and 2 mg Tablets**

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Oncology, Oral – Retinoids

ONCOLOGY AGENTS : RETINOIDS - ORAL

Appendices

Multiple Sclerosis Agents – Guidelines

- American Academy of Neurology (AAN), 2019
  - Issued guidelines regarding vaccinations in patients with MS
  - Recommend clinicians discuss immunization options with patients to develop an optimal strategy for each patient, taking into account all vaccine standards and local recommendations, patient risks and benefits, contraindications, and patient preferences
  - Notably, they recommend that prescribers should assess and address vaccination status at least 4 to 6 weeks prior to initiating immune-suppressing MS therapy, as advised by each agent's prescribing information (Level B), and further state that clinicians should address vaccination status as soon as possible following diagnosis, regardless of the initial therapeutic plan, to prevent future treatment delays (Level C)
  - They also recommend that all patients receive an annual influenza vaccine, unless contraindicated (Level B)
  - Recommend against the use of live attenuated vaccines in patients receiving immune-suppressing MS therapy or in those who have recently discontinued one of these agents; however, the use of these vaccines may be recommended if the risk of infection is high and alternatives are unavailable (Level C)
  - Prescribers should also screen for select infections, including hepatitis, tuberculosis, and varicella zoster, as described in product labeling of individual products or regardless of this recommendation in endemic or high-risk areas (Level A), treating discovered latent infections (Level B), prior to initiating therapy. Vaccination should be delayed in patients experiencing a relapse until clinical resolution or no longer active (Level B)

Ophthalmic, Glaucoma Agents – Guidelines

- American Academy of Ophthalmology, 2018
  - The goal of treatment is to maintain the IOP in a range at which loss of visual field is unlikely to significantly affect a patient's health related quality of life over their lifetime
  - An initial target pressure is at least 25% lower than pretreatment IOP
    - However, target pressure is an estimate and should be individualized based on disease course; lower IOP targets are reasonable in patients with more severe optic nerve damage
  - Medical therapy is the most common initial intervention to lower IOP
    - Medication classes used in the management of glaucoma include beta-blockers, miotics, sympathomimetics, topical and oral carbonic anhydrase inhibitors, and prostaglandin F2α analogs
    - Monotherapy or combination therapy may be used to treat glaucoma and delay the need for surgery and prevent functional vision loss

- American Academy of Ophthalmology, 2020
  - Preferred practice patterns, prostaglandin analogs are the most frequently prescribed eye drops to lower IOP due to their efficacy, safety profile, and once-daily regimen
  - Sufficient management of glaucoma is dependent on a high level of adherence to therapy
  - Data has suggested the addition of a second medication can lead to reduced adherence; therefore, fixed dose combinations may potentially increase adherence and decrease exposure to preservatives
  - Although fixed dose combinations are not usually recommended as initial therapy, a fixed dose combination agent may be warranted in patients requiring a greater IOP reduction than available with a single agent